

BRITISH MEDICAL JOURNAL

CYA-1406585-106-P 25567
SATURDAY 7 OCTOBER 1967

Leading Articles

Sainsbury Report (p. 1). Broken Hearts (p. 2). Prevention of Rhesus Haemolytic Disease (p. 3). Metronidazole and Syphilis (p. 4). More Retroperitoneal Fibrosis (p. 5). Mental Handicap and the Family (p. 5). Visible Alternatives (p. 6).

Papers and Originals

Prevention of Rh-Haemolytic Disease	C. A. CLARKE	7
Mortality of Bereavement	W. DEWI REES AND SYLVIA G. LUTKINS	13
Severe Outbreak of Septic Sepsis Due to <i>Staphylococcus aureus</i> of Unusual Type and Origin	RICHARD W. PAYNE	17
Glucose Tolerance and Serum Insulin in Unaffected Identical Twins of Diabetics	D. A. PYKE AND K. W. TAYLOR	21
Glucose Tolerance and Serum Insulin in the Unaffected First-degree Relatives of Diabetics	K. W. TAYLOR, JOANNA SHELTON, D. A. PYKE, AND W. G. OAKLEY	22
Platelet Stickiness in Patients with Intracranial Tumours	P. MILLAC	25
Impedance Spirometry in Clinical Monitoring	J. V. FARMAN AND D. A. JUETT	27
Haemoglobin E and α -Thalassaemia	P. WASI, M. SOOKANEK, S. POOTRAKUL, S. NA-NAKORN, AND A. SUINGDUMRONG	29

Medical Memoranda

Cantharides Intoxication	R. D. ROSIN	33
Dangerous Consequences from Use of Phenytoin in Atrial Flutter	JAMES H. GRISSOM, BENITO G. SY, JOHN P. DUFFY, AND GEORGE DUNEA	34
Cardiac Involvement in Psittacosis	RAYMOND COLL AND ISRAEL HORNER	35
Urticaria after Insertion of Smith-Petersen Vitallium Nail	A. W. MCKENZIE, C. V. E. AITKEN, AND R. RIDSDILL-SMITH	36
Human Abortion Associated with Infection by Ovine Abortion Agent	W. ROBERTS, N. R. CRIST, AND P. GIROUD	37
Treatment and Survival after Massive Overdose of Adrenaline	MICHAEL A. LEWIS	38

Current Practice

Road Safety Act, 1967	39
Fallacies in Four Fevers	41
Any Questions?	43

Book Reviews

Obituary Notices

Sir James Learmonth, F.R.C.S., C.B.E., CH.M., F.R.C.S.	58
Leonard Colebrook, F.R.C.S., F.R.C.O.G., F.R.S.	59
A. B. Porteous, M.D., D.P.M.	59
W. Weiner, M.D., F.C.P.A.	59
G. Lissant Cox, C.B.E., M.D.	60
S. Bolton, M.D., F.R.C.S.D.	60
J. H. Palmer, M.B., D.M.S.	61
R. A. J. Stanford, M.B.	61
F. J. Bentley, M.D., F.R.C.P.	61

Middle Articles

Medical History	
"Guérir quelquefois, Soulagé souvent, Consoler toujours"	47
New Appliances	
Cardiff Laryngoscope for Infants	48

SUPPLEMENT

- Committee on Medical Science, Education, and Research, p. 1
- Medical Staffing in the N.H.S., p. 3
- Private Practice Committee, p. 9

Correspondence

Advantages of Health Centres	E. J. LACE, M.R.C.S., and H. I. HOWARD, M.R.C.S.	49
Melanoma, Halothane, and Liver Necrosis	G. S. W. ORGANE, F.R.C.S., and G. L. B. THURSTON, M.R.C.P.	49
Prescribing and Withholding Psychotropic Drugs	C. H. FOGGIU, M.B.	49
Treatment of Poisoning by Antidepressants	J. L. CRAMMER, D.P.M.; A. B. BAKER, M.B.; B. J. PROUT, PH.D., M.R.C.P.	50
Kwashiorkor in Children	B. A. WHARTON, M.R.C.P.	50
Carcinogenic Properties of Ortho-dianisidine	E. D. ACHESON, F.R.C.P.	51
Nephrotic Syndrome in Patient Taking the "Pill"	A. J. RILEY, M.B.	51
Aversion Therapy in Management of Homosexuals	M. J. MACCULLOCH, D.P.M., and M. P. FELDMAN, PH.D.	51
Screening by Cervical Cytology	G. R. OSBORN, F.R.C.P.	52
Drugs and Driving	J. C. BARKER, M.D., D.P.M.	52
Taking Blood Samples	W. JOAN FERRABY, M.B.	52
Doctors for Industry	G. A. LARVENSEN, L.R.C.P.E.D.; M. E. M. HERFORD, M.D.	53
Restrictions on Doctor in South Africa	Sir Geoffrey Keynes, F.R.C.S., and others	53
Emergency Admissions for the Elderly	D. F. C. DEACON, M.R.C.S.	53
Resuscitation of the Elderly	B. R. W. LODGE, M.R.C.S.	53
Neasden Memorandum	O. H. E. BAYLES, F.F.A. R.C.S.	54
Remission in Acute Leukaemia	L. MASSIMO, M.D., and others	54
Menace of Smoking	J. HAMILTON GIFFORD, M.B.	54
Sodium Uptake in Peritoneal Dialysis	J. D. SWALES, M.R.C.P.	55
Place of the Mentally Retarded	T. McKEOWN, F.R.C.P., and I. LECK, PH.D., M.B.	55
Streptomycin, I.N.H., and Thiacetazone	S. N. DUTTA, M.S.(MED.), and others	55
Dangers of Humidification	B. J. FREEDMAN, M.R.C.P.	55
Diabetes Mellitus Complicating Alkaptonuria	B. NAGANNA, D.S.C., and G. ETHIRAJULU	55
Psychological Factors and Ulcerative Colitis	R. G. R. WEST, D.PHIL., M.D.; G. L. ENGEL, M.D.	56
Paraproteins and Bence Jones Protein	E. N. WARDLE, M.R.C.P.	56
Diabetic Lipaemia	Judith A. Trowell, M.B.	56
Sales Promotion	B. Y. MARSHALL, M.B.	56
Drug Names	M. KEATING, F.I.P.A.	57
Reprints: Who Should Pay?	S. E. BROWNE, M.B.	57
Doctors in the Armed Forces	Surgeon-Lieutenant-Commander R. P. DOHERTY, M.R.C.O.G.	57
B.M.A. as a Negotiating Body	C. J. BOLT, M.B.	57
Christmas Gifts Appeal	Sir Zachary Cope, F.R.C.S.	57

News and Notes

Epidemiology	62
Medical News	63

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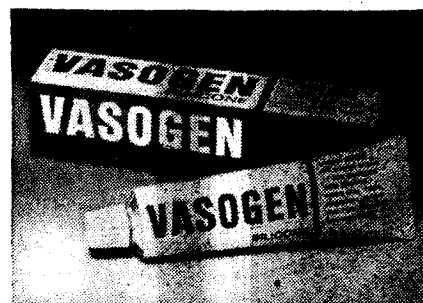
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Leading Articles

Postgraduate Education in Scotland (p. 65). Origin of Penicillinase (p. 66). Spread of Influenza (p. 67). Postoperative Gas Gangrene (p. 68). Standardization in Human Cytogenetics (p. 69). Health Priorities (p. 69). Wandering Oesophagus (p. 70). International Relations (p. 70).

Papers and Originals

- Origin and Function of Penicillinase: a Problem in Biochemical Evolution
M. R. POLLOCK ... 71
- Direct Exchange Blood Transfusion in Treatment of Hepatic Coma
J. A. MCLEAN AND H. A. LUKE ... 78
- Survey of Influenza Antibody in England by the Strain-specific Complement-fixation Test
MARGUERITE S. PEREIRA, PRATIMA CHAKRAVERTY, T. M. POLLOCK, AND J. G. POPE ... 80
- Antibodies in Children's Sera for Serologically Different Recently Isolated Strains of Influenza Viruses A₂ and B
G. C. SCHILD AND C. H. STUART-HARRIS ... 82
- Measurement of Blood Loss by Means of a Whole-body Counter
J. M. HOLT, F. G. H. MAYET, G. T. WARNER, AND S. T. CALLENDER ... 86
- Effect of Transfusion Materials on Rouleaux Formation and Sedimentation Rate of Erythrocytes
A. J. SALSURY ... 88
- Paget's Disease: a Family with Six Cases
J. VERRIER JONES AND MERVYN F. REED ... 90

Preliminary Communications

- Evidence for Autonomic Denervation in Familial Dysautonomia, the Riley-Day Syndrome
ELLIOT SHINEBOURNE, J. M. SNEDDON, AND PAUL TURNER ... 91

Medical Memoranda

- Corrosive Damage to Stomach Simulating Carcinoma
S. C. KENNEDY AND A. E. BAVAKI ... 93
- Haemolysis and Agranulocytosis Complicating Treatment with Methyl dopa
K. G. A. CLARK ... 94
- Goodpasture's Syndrome: Survival after Acute Renal Failure
J. F. MUNRO, A. M. GEDDES, AND W. L. LAMB ... 95
- Acquired Ichthyosis from Breast Cancer
A. R. HASTE ... 96

Current Practice

- Disease of the Digestive System
Dyspepsia N. F. COGHILL ... 97
- Medicine Today
Management of Rheumatoid Arthritis ... 99
- Any Questions? ... 101

Middle Articles

- Medical Ethics
Experiments on Man ... 105
- Conferences and Meetings
British Association of Physical Medicine ... 106

Book Reviews

Obituary Notices

- J. B. McDougall, C.B.E., M.D., F.R.C.P. (ED.), F.R.C.P. (GLASG.) ... 115
- S. B. Radley, F.R.C.S. ... 115
- B. Thomas, F.R.C.S. (ED.) ... 115
- C. M. Barker, M.B. ... 116
- F. O. Walker, M.R.C.S., D.P.M., D.O. ... 116
- W. L. Winslow Smith, M.C., M.B. ... 116
- M. G. Garry, L.R.C.P. & S.I., L.M. ... 117
- Leonard Colebrook, F.R.C.S., F.R.C.O.G., F.R.S. ... 117
- Sir James Learmonth, K.C.V.O., C.B.E., CH.M., F.R.C.S. ... 117
- Terence East, D.M., F.R.C.P. ... 117

Correspondence

- Laboratory Screening Procedures. M. G. Rinsler, M.D. ... 107
- Aspirin and Gastric Bleeding. T. C. Dann, M.D.; G. H. Jennings, F.R.C.P.; H. J. S. Mathew, F.R.C.P. (ED.), and A. T. Proudfoot, M.R.C.P. (ED.); J. C. Bowie, M.B. ... 107
- Treatment of Poisoning by Antidepressant Drugs. C. A. Fuge, F.F.A. R.C.S. ... 108
- Psychotropic Drugs. P. Leyburn, M.R.C.P. (ED.), D.P.M., and others ... 108
- Advantages of Health Centres. E. V. Kuenssberg, M.B. ... 108
- Intestinal Obstruction. F. O. Stephens, F.R.A.C.S. ... 109
- Subcutaneous Atrophy after Local Corticosteroid Injection. E. Grunwaldt, M.D.; E. N. Glick, M.R.C.P. ... 109
- Cyst of Popliteal Artery. H. Taylor, F.R.C.S., and others ... 109
- Elusive Popliteal Pulse. T. G. Davis, M.D. ... 110
- Retinal Changes after Cardiac Arrest. P. J. Tomlin, F.F.A. R.C.S. ... 110
- Pernicious Anaemia and Intestinal Malabsorption. I. M. Murray-Lyon, M.R.C.P., and N. D. C. Finlayson, M.R.C.P. (ED.) ... 110
- Alcohol and the Law. J. B. Enticknap, M.D.; A. L. Wingfield, F.R.C.P. ... 110
- Doctors for Industry. F. E. S. Hatfield, D.P.M.; J. W. Todd, M.D. ... 111
- Antinuclear Factor. R. L. F. Nienhuis, M.D., and E. Mandema, M.D. ... 111
- Warming Blood. B. Philpott, F.F.A. R.C.S., and I. P. Slee, M.B. ... 111
- National Kidney Centre. M. H. F. Coigley, M.B., and I. R. McWhinney, M.D. ... 112
- Use of Thorotrast. G. A. Granger, M.D. ... 112
- Insulin Allergy. J. G. Devlin, M.D., and D. K. O'Donovan, F.R.C.P. ... 112
- Obstetric Complications and School Performance. M. H. Dale, M.R.C.S. ... 112
- Folate Deficiency in the Elderly. J. D. B. Andrews, M.D. ... 113
- Admirable Drug. R. W. Cockshut, M.B. ... 113
- Menace of Smoking. Lennox Johnston, M.B. ... 113
- Headlight Glare. A. E. Mourant, F.R.C.P., F.R.S. ... 113
- Court Lees School. J. B. Wrathall Rowe, M.B. ... 114
- Portable Pharmacy. R. J. Rabett, M.R.C.S. ... 114
- Visible Alternatives. L. McAskie, M.R.C.S. ... 114
- Enticing the Emigrants Home Again. C. C. M. Watson, M.B. ... 114
- Miserable Conditions. G. R. Addlestone, M.B. ... 114
- How Many 'Old People'? K. Hazell, F.R.C.P. (ED.) ... 114

News and Notes

- Epidemiology ... 118
- Motoring ... 119
- Medical News ... 120

SUPPLEMENT

- Scottish Committee for Hospital Medical Services, p. 11
- Occupational Health Committee, p. 13

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SATURDAY 21 OCTOBER 1967

Leading Articles

Teaching the Behavioural Sciences (p. 123). L.S.D. and Chromosomes (p. 124). Getting on Their Nerves (p. 125). Dysmenorrhoea (p. 125). Westward Ho! (p. 126). Surgery in Pulmonary Tuberculosis (p. 127). No Change (p. 128). Stanley Morison and the B.M.J. (p. 128).

Papers and Originals

Cancer Hazards of the Pharmacy	GEORGIANA M. BONSER ...	129
Six Cases of Acrylamide Poisoning	T. O. GARLAND AND M. W. H. PATTERSON ...	134
Fructose Intolerance	J. A. BLACK AND K. SIMPSON ...	138
Abnormal Splitting of the Second Heart Sound in Renal Failure	D. G. GIBSON ...	141
Effect of Glucagon on Intravenous Glucose Tolerance	D. A. TURNER, T. K. AUDHYA, D. G. CRAMP, C. D. HOLDSWORTH, AND NEIL MCINTYRE ...	145
The Thyroid and Fibrinolysis	N. B. BENNETT, C. M. OGSTON, AND G. M. McANDREW ...	147
Injury, Serum Lipids, Fat Embolism, and Clofibrate	M. O'DRISCOLL AND F. J. POWELL ...	149
Behçet's Syndrome with Aortic Aneurysms	ELIZABETH A. HILLS ...	152

Medical Memoranda

Murmur over Liver in Cases of Severe Anaemia	N. R. KONAR, S. K. DATTA, A. NAG, AND A. KONAR ...	154
Carbamazepine-induced Jaundice	IAN D. RAMSAY ...	155
IgG Myeloma in Cerebrospinal Fluid with a Total Protein of 32 mg./100 ml.	KETTY GAVRILESCU AND A. PAPAKRIVOPOULOS ...	156

Middle Articles

Growing Points	
Spare-part Surgery	
NORMAN BROWSE ...	157
Conferences and Meetings	
Paediatric Neurology ...	162

Current Practice

Disease of the Digestive System	
Gastritis D. N. CROFT ...	164
Any Questions? ...	167

Obituary Notices

Sir Archibald Gray, K.C.V.O., C.B.E., T.D., F.R.C.P., F.R.C.S. ...	178
A. G. Timbrell Fisher, M.C., F.R.C.S., F.A.C.S. ...	178
L. Surzynski, M.D. ...	179
K. J. L. Scott, M.D., M.R.C.P. ...	179

Correspondence

"Geriatric Emergencies." G. D. Walker, D.M. ...	171
Anaemia in Elderly Housebound Patients. R. H. Morgan, M.D. ...	171
Massive Overdose of Adrenaline. M. C. Crocker, F.F.A.R.C.S.; B. J. Freedman, M.R.C.P. ...	171
Bottle Cuts. M. J. McArthur, M.R.C.S. ...	171
Humidification of Oxygen. C. A. Sara, F.F.A.R.C.S. ...	172
Respiratory Distress Syndrome. T. H. Hughes-Davies, B.M. ...	172
Anxiety State after "Sex Education." B. H. Burne, D.P.H. ...	172
Hospital Admissions among Students. T. C. Dann, M.D. ...	172
Carcinogenic Properties of Ortho-dianisidine. D. G. Illingworth, F.R.C.P.E.D.; E. Boyland, D.Sc., and R. A. M. Case, M.D. ...	172
Melanoma, Halothane, and Liver Necrosis. M. W. Johnstone, M.D., F.F.A.R.C.S. ...	173
Adenomyoma of Stomach. I. D. O. Frew, M.D., and others ...	173
Operations on the Gall Bladder. D. A. Jennings, B.M. ...	173
Phenobarbitone and the Shoulder-Hand Syndrome. A. D. Desai, M.R.C.P., and H. M. Dastur, F.R.C.S.ED. ...	173
Aspirin and Gastric Bleeding. A. J. Quick, M.D. ...	173
Children with Myelomeningocele. P. Robson, D.C.H., and D. R. Scrutton; Maud F. Forrester-Brown, M.D. ...	174
Psychotropic Drugs. R. W. Simpson, M.D. ...	174
Stress Incontinence. K. P. S. Caldwell, F.R.C.S.; J. K. Willson-Pepper, F.R.C.S. ...	175
Early Discharge of Maternity Patients. M. W. Artherton, M.D., and others ...	175
Carpal Tunnel Syndrome Associated with a Scribner Shunt. D. B. Evans, M.R.C.P. ...	175
Sodium Chlorate Poisoning. R. K. Knight, M.R.C.P., and others ...	175
Headlight Glare. N. R. Grist, F.R.C.P.ED. ...	175
Fluoridation of Water Supplies. R. L. Kerr, M.R.C.S. ...	175
Mortality of Bereavement. S. W. A. Gunn, M.D. ...	175
Intestinal Spirochaetosis. S. C. Dyke, F.R.C.P. ...	175
Approval of Emergency Treatment Service. W. P. Lambie, M.R.C.S. ...	175
Dependent Relatives. G. C. Price, M.R.C.S. ...	177
Vocational Training for General Practice. F. Gray, M.B. ...	177
Mileage Allowances. E. D. L. Bennett, F.F.A.R.C.S.; R. J. Purnell, F.F.A.R.C.S. ...	177
Post-registration Nurses. Margaret F. Young, R.N.T., S.R.N. ...	177

Book Reviews

News and Notes

Epidemiology ...	180
Medical News ...	181

SUPPLEMENT

• Scottish Council, p. 17
• Edinburgh Conference on Better Medical Care, p. 18
• Committee on Overseas Affairs, p. 20
• Opinions on Distinction Awards, p. 22
• Proceedings of Council, p. 23



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BRITISH MEDICAL JOURNAL

SATURDAY 28 OCTOBER 1967

Leading Articles

Prophylaxis in Rubella (p. 183). Men of Vision (p. 185). Fall-out from Space Travel (p. 186). Plan for Hospitals (p. 187). Health Education of Asian Immigrants (p. 187). Students Abroad (p. 188). Meeting in Australia (p. 188).

Papers and Originals

- Intrauterine Transfusion in Rh-isoimmunization** D. V. I. FAIRWEATHER, D. TACCHI, A. COXON, M. I. HUGHES, S. MURRAY, AND W. WALKER ... 189
- Skin Water Loss and Accidental Hypothermia in Psoriasis, Ichthyosis, and Erythroderma** KATHERINE A. GRICE AND F. R. BETTLEY ... 195
- Intracardiac Pacing as Emergency Treatment in Adams-Stokes Syndrome** GUNNAR BAY AND EGIL SIVERTSEN ... 199
- Oxygen Concentrations in Tents and Incubators in Paediatric Practice** HAMISH SIMPSON AND DOREEN J. RUSSELL ... 201
- Ulcerative Colitis in the Tropics** H. K. CHUTTANI, S. P. NIGAM, S. K. SAMA, P. C. DHANDA, AND P. S. GUPTA ... 204
- Electroencephalogram and Retinal Vessels in Congenital Cyanotic Heart Disease Before and After Surgery** EVA M. KOHNER, E. M. ALLEN, K. B. SAUNDERS, V. M. EMERY, AND C. PALLIS ... 207
- Catabolism of Serum γ G-globulins in a Cancer Patient and a Normal Volunteer** D. E. H. TEE AND J. WATKINS ... 210

Preliminary Communications

- Demonstration of an Enzyme Variant in a Case of Congenital Methaemoglobinemia** C. A. WEST, B. D. GOMPERS, E. R. HUEHNS, I. KESSEL, AND J. R. ASHBY ... 212

Medical Memoranda

- Severe Anaphylactic Reaction after a Soap Enema** DONALD SMITH ... 215
- Fatal Lactic Acidosis after an Overdose of Phenformin** D. W. PROCTOR AND J. M. STOWERS ... 216
- New X Wave in Electrocardiographic Complex** B. L. AGARWAL AND C. B. GUPTA ... 217

Current Practice

- Disease of the Digestive System**
Hiatus Hernia ... 218
MICHAEL ATKINSON ... 218
- Any Questions?** ... 221
- New Appliances**
Repeated Haemodialysis with a Straight Silicone Rubber Cannula ... 226

Clinicopathological Conference

- A Case of Crohn's Disease in a Patient with Treated Adult Coeliac Disease** ... 222

Book Reviews

... 227

Middle Articles

- Conferences and Meetings**
Chemotherapy of Tuberculosis in Developing Countries ... 230
- European Views on Liver Disease** ... 232

Obituary Notices

- F. E. Stabler, M.D., F.R.C.S., F.R.C.O.G. 240
- W. Patrick, T.D., F.R.C.S.ED., F.R.C.S. GLASG. ... 240
- Major-General F. J. O'Meara, A.M.S. (RTD.), C.B., M.D., F.R.C.P.I. ... 240
- I. W. Gallant, M.D., M.R.C.P. ... 241
- I. F. Rose, M.B.E., F.R.C.S. ... 241
- R. T. Payne, M.S., F.R.C.S. ... 241
- A. S. Jarrett, M.D. ... 242
- K. S. Maurice-Smith, M.R.C.S. ... 242
- E. A. Andrade, M.B., D.OBST.R.C.O.G. ... 242
- G. J. Murray, M.D., M.R.C.P. ... 242

Correspondence

- Psychotropic Drugs. P. J. Dally, F.R.C.P., D.P.M.; Gwendoline M. Langham-Hobart, M.B. ... 233
- Future of the Regional Hospitals. P. J. W. Mills, F.R.C.P. ... 233
- Pyloric Stenosis in Turner's Syndrome. H. van den Berghe, M.D. ... 234
- Medical and Surgical Vagotomy and Intrinsic Factor Secretion. P. M. Christiansen, M.D., and Paul Rødbro, M.D. ... 234
- Human Infection with Porcine Ascaris. F. J. F. O'Rourke, PH.D., M.B. ... 234
- Insulinotropic Action of Secretin. R. J. Mahler, M.D., and H. Weisberg, M.D. ... 234
- Oculogyric Crises after Phenothiazines. J. B. Rogers, M.B. ... 235
- Vital Decision. Christine Brown, R.S.C.N., R.N.T.; G. W. Fleming, D.P.H. ... 235
- Paget's Disease in a Family. G. B. Stein, M.B. ... 235
- Gritti-Stokes Amputation. F. E. Weale, F.R.C.S.; D. M. Essenhigh, F.R.C.S., and D. J. Tibbs, F.R.C.S. ... 236
- Radiation in Retinal Vessels. A. C. Gillies, F.R.C.S.ED. ... 236
- Demonstration Aerosol Inhalers. A. Herxheimer, M.B. ... 236
- Thymic Structure. G. Middleton, M.B. ... 236
- Facial Palsy. R. G. Williams, F.R.C.S. ... 236
- "Geriatric Emergencies." W. Fine, M.D. ... 237
- Lithotomy Position for Forceps. P. Dransfield, M.B. ... 237
- Fallacies in Four Fevers. J. P. Telling, M.B.; J. M. Morfitt, D.P.H., D.C.H. ... 237
- Fatal Constipation in the Aged. D. B. Rao, M.B., and M. S. Kataria, D.P.H. ... 238
- Haemoglobin Levels and Dietary Iron. R. H. Morgan, M.D. ... 238
- M.A.O. Inhibitor Headache. C. A. H. Watts, M.D. ... 238
- Mercury Perchloride in Surgery. D. H. Patey, F.R.C.S. ... 238
- Cantharides Intoxication. S. G. Browne, F.R.C.P. ... 238
- Advantages of Health Centres. H. I. Howard, M.R.C.S., and E. J. Lacey, M.R.C.S. ... 239
- Interview Board for North America. D. V. Cashman, M.B. ... 239
- "Total Family Care" and Fees. A. F. Madge, M.B. ... 239
- More Forms. R. S. V. Marshall, M.B. ... 239
- Overseas Registration and Seniority. G. Murtaza, M.B. ... 239

News and Notes

- Epidemiology ... 243
- Medico-Legal ... 244
- Parliament ... 245
- Medical News ... 246

SUPPLEMENT

- Joint Annual Meeting with Australian Medical Association, Sydney, 12-16 August 1968: Provisional Programme, p. 25
- Retirement Pensions, p. 26

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BRITISH MEDICAL JOURNAL



SATURDAY 4 NOVEMBER 1967

Leading Articles

- Treatment of Myocardial Ischaemia (p. 249). Computers in Medicine (p. 250). Testing Drugs for Rheumatoid Arthritis (p. 251). No Need for Change? (p. 252). Modernizing Hospital Medicine (p. 252). Operation for Parkinsonism (p. 253). Complications of Vaccination (p. 253). Reform Needed (p. 254).

Papers and Originals

- Four Years of Respiratory Intensive Care DONALD CAMPBELL, J. M. REID, A. B. M. TELFER, AND W. FITCH ... 255
- Visuo-motor Disability in Schoolchildren MAY WOLFF BRENNER, SELMA GILLMAN, O. L. ZANGWILL, AND MARGARET FARRELL ... 259
- Effect of Salicylates in Urticaria MIRIAM MOORE-ROBINSON AND ROBERT P. WARIN ... 262
- Clinical Measurement of the Anti-inflammatory Effects of Salicylates in Rheumatoid Arthritis P. L. BOARDMAN AND F. DUDLEY HART ... 264
- Glyceryl Trinitrate in Angina Pectoris: Tablet or Aerosol? G. SANDLER AND G. A. CLAYTON ... 268
- Intravascular Coagulation in a Case of Clostridium perfringens Septicaemia: Treatment by Exchange Transfusion and Heparin M. L. RUBENBERG, L. R. I. BAKER, J. A. MCBRIDE, L. H. SEVITT, AND M. C. BRAIN ... 271
- Comparison of Betamethasone 17-Valerate Ointment with Fluocortolone and Fluocortolone Caprate Ointment DOWLING D. MUNRO, H. T. H. WILSON, AND ELLEN L. RHODES ... 275

Medical Memoranda

- Unusual Cause of Charcot Joints in Early Adolescence (Riley-Day Syndrome) PETER W. BRUNT ... 277
- Spinal Subarachnoid Haemorrhage in Patient with Coarctation of Aorta A. B. WATSON ... 278
- True Heartburn A. D. ROY ... 279

Current Practice

- Disease of the Digestive System
Duodenal Ulcer—I IAIN E. GILLESPIE ... 281
- Any Questions? ... 284

Middle Articles

- General Practice Observed
Survey of General-practitioner Maternity Units in England and Wales M. S. T. HOBBS ... 287
- Medical Management in Hospitals ... 291

Book Reviews ... 285

Obituary Notices

- H. G. Garland, T.D., M.D., F.R.C.P. ... 300
- P. T. Herring, M.D., F.R.C.P.ED. ... 300
- J. C. Dick, M.D., F.R.C.P.GLASG. ... 301
- W. Napier, M.D. ... 301

News and Notes

- Epidemiology ... 302
- Parliament ... 303
- Medico-Legal ... 303
- Medical News ... 304

Correspondence

- Obstetric Forceps or Vacuum Extractor? J. A. Chalmers, F.R.C.O.G.; T. G. E. White, M.D.; W. H. Laird, F.R.C.O.G.; R. J. Benzie, M.B. ... 292
- Psychotropic Drugs. G. H. Gundy, D.P.M.; C. M. B. Pare, M.D., D.P.M. ... 293
- Massive Overdose of Adrenaline. W. E. Glover, M.D., and R. G. Shanks, M.D. ... 293
- National Kidney Centre. B. H. B. Robinson, M.R.C.P. ... 294
- Cancer Chemotherapy. Mario Fiorentino, M.D., and Enzo Finotto, M.D. ... 294
- Safer Dental Anaesthesia. A. Lyall, F.R.C.S.ED. ... 294
- Mental Handicap and the Family. Lilly C. Hall, D.P.H.; B. A. Smith, D.P.H., and others; Mary E. Cochrane-Dyett, M.B. ... 295
- Chronic Thyrotoxic Myopathy. W. M. Priest, F.R.C.P. ... 295
- Corrosive Poisons. D. R. Munasinghe, M.D. ... 296
- Taking Blood Samples. I. Martin-Scott, M.D. ... 296
- Prevention of Rh-haemolytic Disease. Sheila Murray, M.D., F.C.PATH. ... 296
- Salmonella in Tortoises. L. T. Newman, M.B. ... 296
- Abortion and Conscience. M. Sim, M.D., D.P.M. ... 297
- Fluoridation of Water Supplies. A. J. Dalzell-Ward, D.P.H.; H. T. Edmunds, M.B.; W. H. Spoor, M.R.C.S.; R. F. Fagan, D.P.H.; W. H. Emslie, M.B.; H. V. Dicks, F.R.C.P.; G. R. Mitchell, L.R.C.P.ED.; R. D. Emslie, F.D.S. R.C.S. ... 297
- Adams-Stokes Syndrome. J. G. M. Hamilton, F.R.C.P.ED. ... 298
- Use of Thorotrast. A. O. Langlands, M.B., F.F.R. ... 298
- Oculogyric Crises after Phenothiazines. W. J. O'Connell, M.B. ... 298
- Consultant Distinction Awards. T. Manners, M.D. ... 298
- Approval of Emergency Treatment Service. M. Mundy, M.R.C.S.; B. J. Maxwell, M.B. ... 299
- Foreign Residents. O. S. Thompson, M.R.C.S. ... 299
- Was it a Drug? I. M. Segal, M.R.C.S. ... 299

SUPPLEMENT

- Proceedings of Council, p. 29
- Central Committee for Hospital Medical Services, p. 36

“IS THERE AN ALTERNATIVE?”

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BRITISH MEDICAL JOURNAL



SATURDAY 11 NOVEMBER 1967

Leading Articles

Respiratory Infection in Early Childhood (p. 307). Cowpox and Paravaccinia (p. 308). Pseudomonas Infection in Hospital (p. 309). Body Building by Drugs (p. 310). Mismanagement of Non-disease (p. 311). Oesophageal Function in Diabetes (p. 311). Ventricular Aneurysm (p. 312).

Papers and Originals

Cross-infection by *Pseudomonas aeruginosa* as a Hazard of Intensive Surgery
J. E. TINNE, A. M. GORDON, W. H. BAIN, AND W. A. MACKEY ... 313

Deaths Associated with Respiratory Tract Infection in Childhood
P. S. GARDNER, D. C. TURK, W. A. AHERNE, T. BIRD, M. D. HOLDAWAY,
AND S. D. M. COURT ... 316

Further Experience of Reactions, Especially of a Cerebral Nature, in
Conjunction with Triple Vaccination: A Study Based on Vaccinations in
Sweden 1959-65 JUSTUS STRÖM ... 320

Survival of Burkitt's Lymphoma Patients in Mulago Hospital, Uganda
R. H. MORROW, M. C. PIKE, AND A. KISULE ... 323

Hypokalaemic Alkalosis and Hyperplasia of the Juxtaglomerular Apparatus
without Hypertension or Oedema L. J. BEILIN, N. SCHIFFMAN,
M. CRANE, AND D. H. NELSON ... 327

Total Parathyroidectomy in Treatment of Secondary (Renal) Hyperpara-
thyroidism C. S. OGG ... 331

Syndrome of Sclerodactyly, Calcinosis, Raynaud's Phenomenon, and
Telangiectasia A. W. DELLIPIANI AND M. GEORGE ... 334

Medical Memoranda

Incest, Inbreeding, and Mental Abilities D. F. ROBERTS ... 336

Tongue Pain with Giant Cell Arteritis A. H. HENDERSON ... 337

Bacterial Endocarditis Presenting as Pseudobulbar Palsy J. SHAFAR ... 338

Current Practice

Disease of the Digestive System
Duodenal Ulcer—II
IAIN E. GILLESPIE ... 339

Medicine Today
Low Back Pain ... 341

Any Questions? ... 342

Middle Articles

Contemporary Themes
Clients of Alcoholism Informa-
tion Centres GRIFFITH
EDWARDS, MARION KELLOG
FISHER, ANN HAWKER, AND
CELIA HENSMAN ... 346

Conferences and Meetings
Uses of Niridazole ... 349

Hospital Topics
Organization of Hospital Work 350

New Appliances
Prototype Cryosurgical Probe 351

Book Reviews

Obituary Notices

L. E. C. Norbury, O.B.E., F.R.C.S. ... 362

R. Hale-White, M.C., M.D., M.R.C.P. ... 362

W. Hoffer, M.D., L.R.C.P.&S.ED., L.R.F.P.S.
GLASG. ... 363

F. A. Pickworth, B.Sc., M.B. ... 363

W. C. Fothergill, M.D., D.M.R.E. ... 363

J. Kruszynski, M.D. ... 364

Rev. M. Hatfield Wright, M.B., D.O.M.S. ... 364

N. J. L. Rollason, M.D. ... 364

H. C. Miller, M.D. ... 364

J. A. Adams, M.B. ... 365

A. W. Rattrie, M.C., M.B. ... 365

Sir Archibald Gray, K.C.V.O., C.B.E., T.D.,
F.R.C.P., F.R.C.S. ... 365

News and Notes

Epidemiology ... 366

Parliament ... 367

Medical News ... 368

Correspondence

Postoperative Gas Gangrene. R. H.
Maudsley, F.R.C.S. ... 352

Abortion Act. J. S. Bailey, M.R.C.S. ... 352

Hiatus Hernia and Coronary Disease. D.
Evan Beaford, F.R.C.P. ... 352

Surgery in Pulmonary Tuberculosis. J. W.
Crofton, F.R.C.P.; J. B. Morrison, M.D. ... 353

Body Building on Drugs. D. E. Pearsons,
M.B. ... 353

Epidemic Keratoconjunctivitis. N. R. Grist,
F.R.C.P.ED. ... 353

Obstetric Forceps or Vacuum Extractor?
A. J. M. Cavenagh, B.M. ... 354

Prevention of Rh-haemolytic Disease. N. P.
Walsh, M.C.PATH., and S. R. Hewitt,
F.R.C.O.G. ... 354

Acute Industrial Poisoning T. D. Aylvor,
F.F.A. R.C.S. ... 354

Vasectomy for Contraception. D. H. Young,
F.R.C.S.ED. ... 354

Institutional Care of the Mentally Sub-
normal. Alison C. Campbell, PH.D.;
U. P. Seidel, D.P.M. ... 355

Hypercalcaemia and Malignant Tumours.
W. E. Medd, M.D., and others ... 355

Swallowed Dental Reamer. R. A. D.
Booth, F.R.C.S., and others ... 356

Dyspepsia. H. J. Goldsmith, M.D. ... 356

Paraproteins and Bence Jones Protein. J. R.
Hobbs, M.D., M.C.PATH. ... 356

Glucagon and Intravenous Glucose Toler-
ance. R. J. Jarrett, M.D. ... 357

Intestinal Spirochaetosis. W. A. Harland,
F.R.C.P.C., and F. D. Lee, M.C.PATH.;
Lieutenant-Colonel C. O. Burdick, M.D.
Dysmenorrhoea. A. Davis, F.R.C.O.G. ... 357

Railroading in Retinal Vessels. P. D. L.
John, D.P.M. ... 357

M.A.O. Inhibitor Headache. R. K. Rondel,
M.B. ... 357

Early Discharge of Maternity Patients. D. J.
Bryson, M.R.C.O.G. ... 357

Fallacies in Four Fevers. J. E. Hodgkin,
B.M.; J. F. Warin, M.D. ... 358

Treatment of Poisoning by Antidepressant
Drugs. W. R. Edwards, M.B. ... 358

Acute Necrotizing Encephalitis. J. Hume
Adams, M.B., and others ... 358

Diet and Diverticulitis. E. H. Goulston,
M.B. ... 359

Courtesy between Colleagues. P. B.
Schofield, F.C.PATH. ... 359

Prospects for Hospital Doctors. E. A.
Harvey-Smith, M.R.C.P. ... 359

Casualty Staffing. G. Rigby-Jones,
F.R.C.S.ED. ... 360

Approval of Emergency Treatment Service.
I. M. Jones, M.B. ... 360

Consultants' Views of General Practitioners.
W. Belton, D.P.H. ... 360

Menace of Smoking. R. Bell, M.B. ... 360

Vocational Training for General Practice.
D. C. Bowie, F.R.C.S.ED. ... 361

Mileage Allowances. N. L. Rowe, M.R.C.S.,
F.D.S. ... 361

SUPPLEMENT

• G.M.S. Committee, p. 43

• G.M.S. Committee (Scotland), p. 47

• S.H.M.O.s Group Council, p. 49

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BRITISH MEDICAL JOURNAL



SATURDAY 18 NOVEMBER 1967

Leading Articles

Congenital Dislocation of the Hip (p. 371). Mumps and Cardiac Embryopathy (p. 372). Hazards of Ambulance Journeys (p. 373). *Escherichia coli* Pneumonia (p. 374). Health of the Child (p. 374). Diagnostic Value of Fluorescent Antibodies (p. 375). Living in Flats (p. 376).

Papers and Originals

Dislocatable Hip and Dislocated Hip in the Newborn Infant
H. V. L. FINLAY, R. H. MAUDSLEY, AND P. I. BUSFIELD ... 377

Families in Flats D. M. FANNING ... 382

Effect of Gastrin II on Gastric Emptying and Secretion During a Test Meal
J. N. HUNT AND N. RAMSBOTTOM ... 386

Which Stethoscope? C. S. HAMPTON AND A. CHALONER ... 388

Location of Placenta by Means of a Colour Autoscan Technique
W. THOMPSON, T. K. BELL, AND J. H. M. PINKERTON ... 390

Adrenocorticotrophic Action of Long-acting Tetracosactrin Compared with Corticotrophin-gel G. M. BESSER, P. W. P. BUTLER, AND F. S. PLUMPTON ... 391

Simple Screening Test for Cushing's Syndrome D. MATTINGLY AND CHRISTINE TYLER ... 394

Case of Tuberos Sclerosis and Haemorrhagic Retinopathy (with Fundus Photographs) A. M. DYER, R. HILL, R. M. ROWAN, AND W. O. G. TAYLOR 398

Medical Memoranda

Stellate Ganglion Block in Treatment of Total Blindness Due to Quinine
P. P. BRICKNELL, H. G. MIDDLETON, A. HOLLINGSWORTH, AND E. M. L. EVANS ... 400

Scorbutic Megaloblastic Anaemia Responding to Ascorbic Acid Alone
P. ASQUITH, M. H. OELBAUM, AND D. W. DAWSON ... 402

Current Practice

Disease of the Digestive System
Postgastrectomy Problems—I
J. ALEXANDER WILLIAMS ... 403

Any Questions? ... 406

Middle Articles

Medical History
Tercentenary of Blood Transfusion Sir GEOFFREY KEYNES ... 410

Contemporary Themes
Some Weaknesses in Hospital Service Organization
GEORGE DISCOMBE ... 411

Conferences and Meetings
Clinical Electroencephalography in Childhood ... 413

Disabilities in Middle-age ... 414

New Appliances
New Bone Needle ... 415

Book Reviews

... 407

Obituary Notices

M. Davidson, D.M., F.R.C.P. ... 424

F. Boyes Korkis, M.B., F.R.C.S. ... 424

D. K. Adams, M.D., F.R.C.P. ... 425

C. D. Grange, O.B.E., F.R.C.S. ... 425

E. Burstal, D.M. ... 425

V. G. Best, M.D. ... 426

E. Fraser Brown, M.B. ... 426

S. S. Datta, M.D. ... 426

W. F. D. Benton, M.R.C.S. ... 426

T. H. McLeod, M.R.C.S. ... 426

G. Lang, M.B. ... 427

D. P. Thomas, M.R.C.S. ... 427

K. B. Jones, M.R.C.S. ... 427

G. C. C. Wharton, M.R.C.S. ... 427

A. Bowie, M.M., M.B. ... 427

Sir James Learmonth, K.C.V.O., C.B.E., CH.M., F.R.C.S. ... 427

News and Notes

Epidemiology ... 428

Parliament ... 429

Medical News ... 430

Correspondence

Deaths from Tuberculosis. A. Pines, M.D. 416

"Big Spleen" Disease. E. J. Watson-Williams, M.R.C.P., and others ... 416

North America Interview Board. J. Stanners, M.D.; C. D. H. Elton, M.R.C.S., and I. W. M. Wright, F.R.C.S.ED. ... 416

Acrylamide Poisoning A. P. Hopkins, M.R.C.P., and R. W. Gilliatt, F.R.C.P. ... 417

Oral Contraceptives and Dental Care. D. N. Barber, M.B. ... 417

Psychotropic Drugs. P. Leyburn, M.R.C.P.ED., D.P.M., and others ... 417

Q Fever Endocarditis. D. C. Lamb, M.C.PATH., and N. R. Grist, F.C.PATH. ... 418

Restrictions on Doctor in South Africa. J. F. Brock, F.R.C.P. ... 418

Case or Person? H. Gainsborough, F.R.C.P. 418

Thyroid Hormone and Catecholamines. R. C. Hill, B.S.C., and P. Turner, M.D. ... 419

Complication of Thyroid Cancer. A. C. B. Wicks, M.B., and G. K. T. Holmes, M.B. 419

Warming Blood. C. H. Chapman; P. J. Bennett, F.F.A.R.C.S., and F. Alladine, M.I.S.T. ... 419

Fallacies in Four Fevers. Jocelyn C. Kelsey, M.D. ... 420

Teaching the Behavioural Sciences. K. S. Holt, M.D. ... 420

M.A.O. Inhibitors and Headache. A. J. Cooper, D.P.M. ... 420

Railroading in Retinal Vessels. C. Cockburn, F.R.C.S.ED. ... 420

Multiple Sclerosis in South Africa. G. Dean, F.R.C.P. ... 420

Mushroom-worker's Lung. C. T. B. Adams, D.P.H. ... 421

Stress Incontinence. K. V. Bailey, F.R.C.O.G. 421

Glycosuria in Pregnancy. J. Fine, M.D. ... 421

Aspirin and Gastric Bleeding. J. M. Bone, M.B. ... 422

Conservative Treatment of Fractured Femur. D. S. Colbert, F.R.C.S.I. ... 422

Vasectomy for Contraception. P. H. Addison, M.R.C.S. ... 422

Fluoridation of Water Supplies. C. G. Learoyd, M.R.C.S. ... 422

"No Change." J. K. McCollum, F.R.C.S.ED.; C. Remington-Hobbs, F.R.C.S.ED. ... 423

Night Visits. G. I. Lumsden, M.B. ... 423

Service Overseas. H. V. Corbett, F.R.C.O.G. 423

Signs for Doctors' Cars. A. D. Manning, M.B. ... 423

SUPPLEMENT

- Assistants and Young Practitioners Subcommittee, p. 53
- Fellowship for Freedom in Medicine, p. 55

INDEPENDENT MEDICAL SERVICES

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¹ Ann. Inst. Pasteur, 1958, 95, 194.

² J. Bact., 1959, 78, 477.

³ Klin. Wschr., 1957, 35, 198.

⁴ Medizinische, 1959, 7, 296.

⁵ Lancet, 1957, 1, 899.



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BRITISH MEDICAL JOURNAL

SATURDAY 25 NOVEMBER 1967

Leading Articles

Cul Bono? (p. 433). Clomiphene for Ovulation (p. 434). Blue Blood (p. 435). Obstructive Airways Disease (p. 436). Realism and Addicts (p. 436). Surfer's Nodules (p. 437). Platelets in Uraemia (p. 437). Chicken-pox Pneumonia (p. 438). The Royal Society (p. 438).

Papers and Originals

Medical Science: Master or Servant? LORD PLATT ... 439
Factors Affecting the Response to Clomiphene Therapy
DAVID FERRIMAN, ANTHONY W. PURDIE, AND MICHAEL CORNS ... 444
Current Concepts in the Treatment of Anovulation E. RABAU,
D. M. SERR, S. MASHIACH, V. INSLEY, M. SALOMY, AND B. LUNENFELD ... 446
Three Swedish Families with Porphyria Variegata B. HAMNSTRÖM,
B. HAEGER-ARONSEN, J. WALDENSTRÖM, B. HYSING, AND J. MOLANDER ... 449
Double-blind Experiments on the Effect of a Peanut Extract on the Bleeding
Incidence in 92 Haemophiliacs M. VERSTRAETE AND C. A. J. RUYS ... 453
Effect of Vagotomy on Gastric Acid Secretion Stimulated by Pentagastrin and
Histamine R. A. PAYNE, ALAN G. COX, JOHN SPENCER, AND
F. C. Y. CHENG ... 456
Blood Groups and Enzymes of Human Red Cells after Five Years' Storage
in Liquid Nitrogen R. G. HUNTSMAN, B. A. L. HURN,
ELIZABETH W. IKIN, H. LEHMANN, AND J. LIDDELL ... 458
Haemorrhagic Necrosis of the Intestine J. S. MCKINNELL AND
M. S. KEARNEY ... 460

Preliminary Communications

Prevention of Delayed Traumatic Facial Palsy M. BRIGGS AND
JOHN M. POTTER ... 464

Medical Memoranda

Sarcoid Myopathy P. S. TALBOT ... 465
Transfusion Malaria in a Man with Christmas Disease
ANGELA E. VARTAN ... 466

Current Practice

Disease of the Digestive System
Postgastrectomy Problems—II
J. ALEXANDER WILLIAMS ... 467
Any Questions? ... 469

Book Reviews

Clinicopathological Conference

A Case of Cushing's Syndrome
with Misleading Urinary
Steroids ... 472

Middle Articles

Computers in Medicine
Computer Method for Deriving
Hospital Inpatient Morbidity
Statistics Based on the Person
as the Unit S. P. WATTS AND
E. D. ACHESON ... 476
Conferences and Meetings
Allergology ... 478
Television in Medical Educa-
tion ... 479
New Appliances
High Femoral Osteotomy with
New Compression Plate ... 480

Obituary Notices

Correspondence

Hospital Boards. R. G. Macbeth, F.R.C.S. 482
Varicose Ulcers and Use of Topical Cortico-
steroids. C. D. Evans, M.D., and others 482
Computers in Medicine. P. A. Parish, M.B. 483
Cerebral Localization of Psychological
Function. J. P. Crawford, M.D. 483
Visuo-motor Disability in Schoolchildren.
S. E. White, D.O.M.S. 483
Respiratory Monitoring. D. W. Bethune,
F.F.A.R.C.S., and J. M. Collis, F.F.A.R.C.S. 483
Gastritis, Aspirin, and Alcohol. C. E.
Astley, F.R.C.P. 484
Body Building on Drugs. J. R. Owen, D.C.H. 484
Coagulation of Rubber Latex in the
Stomach. K. Thirunavukkarasu, M.R.C.P.,
and K. Yoheswaran, F.R.C.S. 484
Prevention of Rh-haemolytic Disease. C. A.
Clarke, F.R.C.P. 484
Allergic Alveolitis. R. M. E. Seal, M.R.C.P.,
and J. C. Wagner, M.D. 485
Demonstration Aerosol Inhalers. H. E.
Lewis, M.R.C.S. 485
Purpura in a Patient Taking Chlordiazepox-
ide. I. J. Copperman, L.R.C.P.I. & L.M. 485
Salmonella in Tortoises. W. H. Parry, M.D. 486
Paraquat Poisoning. K. A. A. Mowin, M.B. 486
Low Back Pain. T. Hambly, M.R.C.S. 486
Intestinal Spirochaetosis. W. A. Harland,
F.R.C.P.C., and F. D. Lee, M.C.PATH. 486
A. G. Shera, M.D., F.C.PATH. 486
Obstetric Forceps or Vacuum Extractor?
D. B. Brown, M.R.C.O.G. 487
Alcoholism. J. J. MacSorley, D.P.H. 487
Hypersensitivity Reactions to Phenylbuta-
zone. J. G. Selwyn, M.D. 487
Elastic Band Injuries. G. Glew, M.B. 488
Nalidixic Acid and Intracranial Hyperten-
sion. L. M. Kremer, D.P.M., and others 488
Goodpasture's Syndrome and Dialysis. D.
Bainbridge, M.R.C.P. 488
Cowpox and Paravaccinia. W. A. Bryce,
M.B. 488
Percentages. R. Elsdon-Dew, M.D. 489
Measurement of Blood Loss. I. McL. Baird,
M.D., and S. Nasser, PH.D. 489
Thiothixene in Schizophrenia. K. Davison,
M.R.C.P., D.P.M., and others 489
Therapeutic Effects of a Thunderstorm.
W. F. Mainland, M.A. 489
Approval of Emergency Treatment Service.
A. Dowling, M.B. 490
Independent Medical Services. F. L. P.
Fouin, M.B. 490
Casualty Staffing. B. A. Juby, M.R.C.S. 490
Christmas Cards for Medical Charities.
R. Cove-Smith, M.R.C.P. 490

News and Notes

Epidemiology ... 494
Parliament ... 495
Medico-Legal ... 495
Medical News ... 496

SUPPLEMENT

• Ophthalmic Group Committee, p. 57



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BRITISH MEDICAL JOURNAL

SATURDAY 2 DECEMBER 1967

Leading Articles

Jaundice of Pregnancy (p. 499). Appointment Systems in General Practice (p. 500). Reappraisal of the Austin Flint Murmur (p. 501). Coal Mining, Pneumoconiosis, and Lung Cancer (p. 502). Foot-and-mouth Disease in Man (p. 503). Intestinal Absorption (p. 503). Premature Rupture of Membranes and Maternal Death (p. 504).

Papers and Originals

- Renal Glucose Threshold Variations with Age W. J. H. BUTTERFIELD, H. KEEN, AND M. J. WHICHELOW ... 505
- Beta-adrenergic Blockade and Cardiac Arrhythmias GRAEME SLOMAN AND MARY STANNARD ... 508
- Serum Folate Values in 423 Psychiatric Patients M. W. P. CARNEY ... 512
- Ascorbic Acid Nutrition in Gastrointestinal Disorders MAX M. COHEN AND ANNE M. DUNCAN ... 516
- Clinical Experience with Bethanidine in Treatment of Hypertension JULIAN BATH, DOUGLAS PICKERING, AND RICHARD TURNER ... 519
- Detection of Carriers of Benign X-Linked Muscular Dystrophy ALAN E. H. EMERY, ENID R. CLACK, SYBIL SIMON, AND JOHN L. TAYLOR ... 522
- Congenital Phocomelia in Monozygotic Twins S. G. I. HAMILTON ... 524
- ABO Blood Groups and Polyps of the Colon THOMAS C. FLEMING, HARVEY W. CAPLAN, GEORGE A. HYMAN, AND F. DAVID KITCHIN ... 526

Preliminary Communications

- Influence of Glucose and Insulin Administration on the Achilles Tendon Reflex Time M. ZACHMANN ... 528

Medical Memoranda

- Foot-and-mouth Disease in Man R. ARMSTRONG, J. DAVIE, AND R. S. HEDGER ... 529
- Recurrent Tetanus S. Y. D. C. WICKRAMASINGHE AND MALINIE FERNANDO ... 530
- Hip Arthroplasty in a Haemophiliac and Subsequent Prophylactic Therapy with Cryoprecipitate A. BELLINGHAM, D. FLETCHER, B. O'G. KIRWAN, T. A. J. PRANKERD, AND T. CLEGHORN ... 531
- Delayed Perforation of Large Bowel Due to Unusual Ingested Foreign Body D. D. GAUR ... 532

Current Practice

- Disease of the Digestive System
Carcinoma of the Stomach
J. L. DAWSON ... 533
- Today's Drugs: Allantoin ... 535
- Any Questions? ... 536

Book Reviews

Obituary Notices

News and Notes

- Epidemiology ... 560
- Motoring ... 561
- Parliament ... 562
- Medical News ... 563

Middle Articles

- Medical History
The Worshipful Society of
Apothecaries of London
W. S. C. COPEMAN ... 540
- General Practice Observed
An Appointment System Service for General Practitioners
BRUCE CARDEW ... 542
- An Appointment System in a Practice with Immigrant Patients STUART CARNE ... 544
- Conferences and Meetings ... 546

SUPPLEMENT

- G.M.S. Committee, p. 59

Correspondence

- Pseudomonas Infection in Hospital. J. Kohn, F.C.PATH.; Kristina Gullers, M.D., and others; R. E. Rewell, M.D., and W. E. Tulloch, A.I.M.L.T. ... 548
- Respiratory Infection in Early Childhood. H. G. Pledger, M.D. ... 549
- Brand Names of Drugs. E. B. Teesdale ... 549
- Abortion and Conscience. P. Darby, M.R.C.S. ... 549
- Institutional Care of the Mentally Subnormal. G. B. Simon, D.P.M. ... 549
- Ventricular Aneurysm. E. Montuschi, M.D., and H. E. S. Pearson, F.R.C.P. ... 550
- Errors in Blood Transfusion. D. A. Osborn, M.B., F.C.PATH. ... 550
- Alcoholism. E. L. Williams, M.R.C.S.; R. P. Swinson, M.B. ... 551
- Bottle Cuts. E. F. Adams, M.R.C.S. ... 551
- Paraquat Poisoning. A. A. B. Swan, M.R.C.P. ... 551
- Salmonella in Tortoises and Terrapins. P. G. Mann, M.D., and B. R. Eaton, M.C.PATH. ... 551
- Cancer Hazards. F. Beck, M.D., and others. M.A.O. Inhibitor Headache. E. H. J. Cotter, M.R.C.S. ... 552
- Treatment of Myocardial Ischaemia. G. R. Royston, M.D. ... 552
- Oxygen Concentrations in Tents. G. W. Burton, F.F.A.R.C.S., and G. Wray, F.F.A.R.C.S. ... 552
- Obstetric Forceps or Vacuum Extractor? N. K. Crooke, M.R.C.O.G.; D. E. Brooke, D.T.M.&H.; A. F. Clift, F.R.C.O.G. ... 553
- Deaths from Tuberculosis. F. B. Meade, M.R.C.P. ... 553
- Smallpox Revaccination. D. L. Ferguson, D.P.H. ... 553
- Screening for Phenylketonuria. D. A. Baxter, B.Sc., and M. E. York-Moore, M.B. ... 553
- Mercury Perchloride in Surgery. G. R. Gibson, M.B., and F. O. Stephens, M.B. ... 554
- Oculogyric Crisis after Phenothiazines. J. J. Kimerling, M.R.C.S., and S. R. Patel, M.B. ... 554
- Safety of Dimethoate Insecticide. E. F. Edson, M.B., and others ... 554
- Injury from High-speed Drills. N. E. A. Renner, M.B., L.D.S.R.C.S. ... 555
- Psychotropic Drugs. J. T. Hutchinson, M.D. ... 555
- Surgery in Pulmonary Tuberculosis. T. A. W. Edwards, M.R.C.P. ... 555
- In Advance. Mary N. M. Paulin, D.P.H. ... 555
- North America Interview Board. R. H. Barrett, D.P.H. ... 555
- Government-owned Health Centres. J. D. H. Mahony, M.D. ... 556
- Practice "Twinning" Arrangements. C. C. Lutton, M.B. ... 556
- "Mediflash." R. Snook, M.B. ... 556
- Prospects for Hospital Doctors. D. A. Walmsley, M.B. ... 556
- Seniority Payments. S. Stowe, M.B.; A. B. David, M.B. ... 557
- Improving General Practice. P. G. Brent, M.B. ... 557
- First Fellows of the Royal College of General Practitioners. B. I. Kohnsky, M.B. ... 557
- Christmas Gifts Fund Appeal. G. H. Bateman, F.R.C.S. ... 557



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MEDICAL JOURNAL

SATURDAY 9 DECEMBER 1967

Leading Articles

Young Disabled and Sick in Hospital (p. 565). Pulmonary Embolectomy (p. 566). Doctors' Diseases (p. 567). Arthritis and Sarcoidosis (p. 568). Investigation of the Young Hypertensive (p. 569). Intensive Care (p. 569). Outbreaks of Coxsackie B Infection (p. 570).

Papers and Originals

- Natural History of Cerebral Angiomas W. R. HENDERSON AND R. DE R. L. GOMEZ ... 571
- Coxsackie B5 Virus Infections during 1965 A REPORT TO THE DIRECTOR OF THE PUBLIC HEALTH LABORATORY SERVICE FROM VARIOUS LABORATORIES IN THE UNITED KINGDOM ... 575
- Normal Absorption in Thai Subjects with Non-specific Jejunal Abnormalities FRANK J. TRONCALE, GERALD T. KEUSCH, LOUIS H. MILLER, RAY A. OLSSON, AND RICHARD D. BUCHANAN ... 578
- Prognosis and Treatment of Idiopathic Facial (Bell's) Palsy D. TAVERNER, F. KEMBLE, AND S. B. COHEN ... 581
- Gamma-M Deficiency Predisposing to Meningococcal Septicaemia J. R. HOBBS, R. D. G. MILNER, AND P. J. WATT ... 583
- Access to Circulation by Permanent Arteriovenous Fistula in Regular Dialysis Treatment J. S. HANSON, M. CARMODY, B. KEOGH, AND W. F. O'DWYER ... 586
- Thyroidectomy after Treatment of Thyroid Disorders by Surgery or Radioiodine R. N. SMITH AND H. C. K. LALJEE ... 589
- Long-term Trial of Local Guanethidine in Treatment of Eye Signs of Thyroid Dysfunction and Idiopathic Lid Retraction A. L. CROMBIE AND A. A. H. LAWSON ... 592

Preliminary Communications

- Management of the Source of Pulmonary Emboli: the Value of Phlebography N. L. BROWSE, M. LEA THOMAS, AND M. J. SOLAN ... 596

Medical Memoranda

- Case of Late Pulmonary Embolectomy LORD BROCK, H. NABIL, AND R. V. GIBSON ... 598
- Hypoglycaemic Coma Occurring during Treatment with Chlorpromazine and Orphenadrine RICHARD M. BUCKLE AND JOHN GUILLEBAUD ... 599
- Case of Cronkhite-Canada Syndrome with Associated Jejunal Diverticulosis W. J. CUNLIFFE AND J. ANDERSON ... 601
- Haemoperitoneum Associated with a Ruptured Gall Bladder PAUL ATKINS ... 602

Current Practice

- Medicine in the Tropics
Malnutrition in Childhood in the Tropics C. GOPALAN 603
- Medicine Today: Management of Parkinsonism ... 607
- Today's Drugs: Griseofulvin ... 608
- Any Questions? ... 609

Book Reviews

Obituary Notices

Middle Articles

- Medical Education
Postgraduate Medical Education ... 613
- Conferences and Meetings
Tropical Splenomegaly Syndrome ... 614
- Aspects of Anxiety ... 614
- New Appliances
Grooved Probe Dilator ... 615

News and Notes

Correspondence

- Medical Science: Master or Servant? W. S. Peart, F.R.C.P.; B. Sandler, M.D. ... 616
- Hospital Boards. F. G. Collins, F.R.C.S.ED. 616
- Managing the Hospitals. J. Blundell, F.R.C.S.ED., and J. Lowry, F.R.C.P.I. ... 617
- Clomiphene for Ovulation. P. M. F. Bishop, F.R.C.P. ... 617
- Neutropenia Caused by Methyldopa. R. Greene, F.R.C.P., and A. W. Spence, F.R.C.P. ... 618
- Low Back Pain. A. W. F. Lettin, F.R.C.S.; W. I. D. Scott, M.D. ... 618
- Congenital Dislocation of the Hip. C. O. Cartier, D.M., F.R.C.P.; A. W. Fowler, F.R.C.S. ... 618
- Mushroom-worker's Lung. A. Sakula, M.R.C.P. ... 619
- Institutional Care of the Mentally Subnormal. T. W. H. Weir, M.D. ... 619
- Deaths from Tuberculosis. P. D. B. Davies, M.D. ... 619
- Tongue Pain and Giant Cell Arteritis. P. D. C. Kimmont, F.R.C.P., and D. I. McCallum, F.R.C.P.ED. ... 620
- Cross-infection in a Surgical Unit. P. A. P. Poma, M.B., and A. D. S. Caldwell, A.L.N.F.S.C. ... 620
- Which Stethoscope? B. J. Peck, M.R.C.S.; R. P. Ryan, D.P.H. ... 620
- Cardiac Involvement in Psittacosis. W. J. MacLennan, M.B., and others ... 620
- Deaths from Exposure. Frances M. Ulyatt, F.F.A.R.C.S. ... 621
- Varicose Ulcers and Use of Topical Corticosteroids. G. M. Jesner, M.B. ... 621
- Abortion and Conscience. A. L. Sanderson, M.R.C.P., D.P.M. ... 621
- Housing and Health. S. L. H. Smith, D.T.M.&H. ... 621
- "Big Spleen" Disease. W. C. Watson, M.D., and others ... 621
- Carcinogenicity of Tobacco and Tobacco Smoke. M. Glass, M.B. ... 621
- Dose of Phenoperidine. C. Langton Hewer, F.F.A.R.C.S. ... 622
- Crime and Sex Chromosome Anomalies. A. W. Griffiths, D.P.M., and J. Zaremba, B.M. ... 622
- Major Accident Procedure. C. J. Bolt, M.B. ... 622
- Computers in Medicine. R. H. Hardy, D.M. ... 622
- Doctors for Industry. Lieutenant-Colonel R. Y. Taylor, D.P.H. ... 622
- Consultant Distinction Awards. K. D. Crow, M.R.C.P. ... 623
- Countersigning of Forms. C. R. Nunan, D.P.H. ... 623
- Approval of Emergency Treatment Service. W. P. Fitt, M.B. ... 623
- Educating the Public. J. G. D. Simpson, M.B. ... 623
- Simplifying Filing. W. A. L. Collier, D.P.H. ... 623

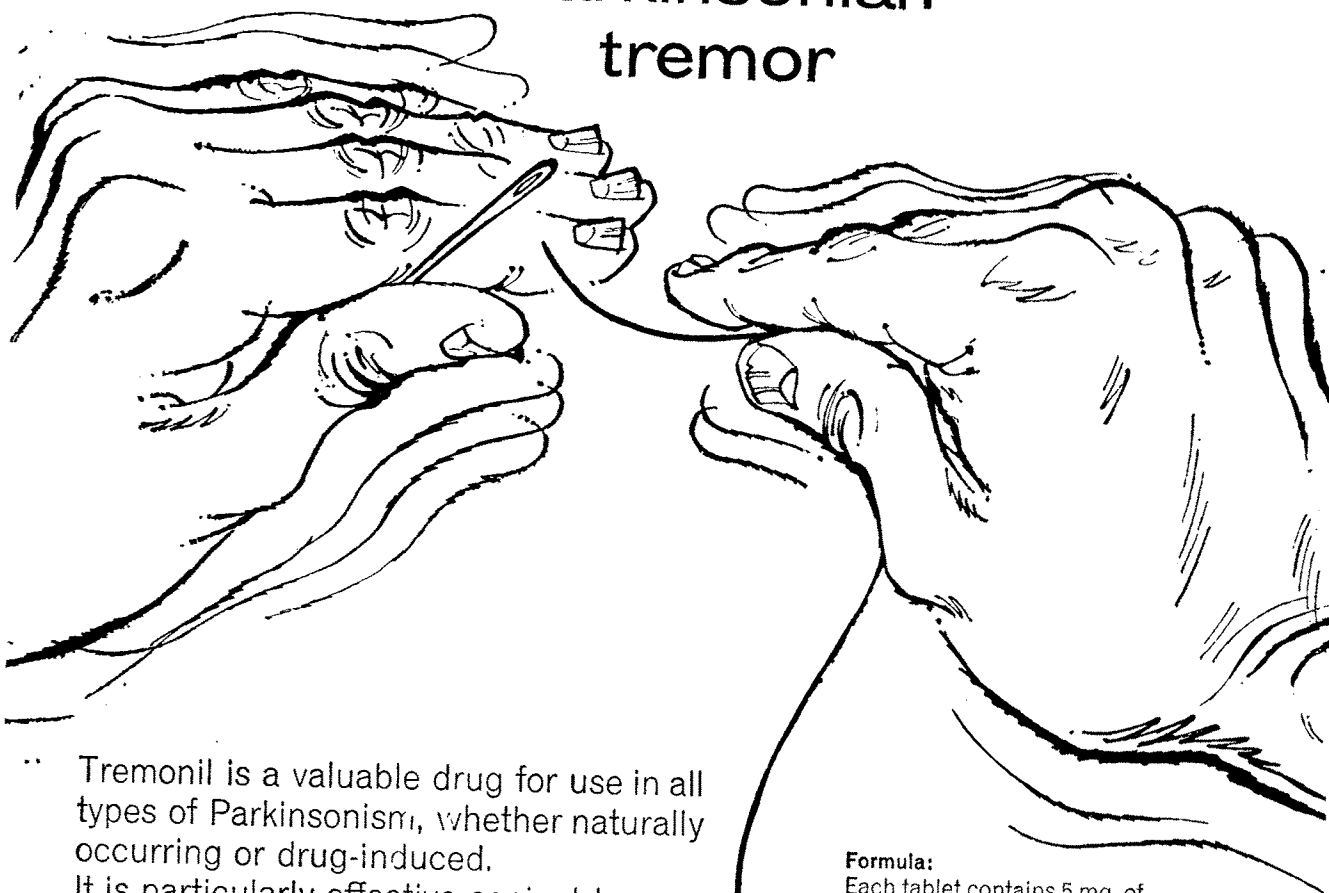
SUPPLEMENT

- Proceedings of Council, p. 65
- Private Practice Committee, p. 71.
- General Medical Council, p. 73

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BRITISH MEDICAL JOURNAL



SATURDAY 16 DECEMBER 1967

Leading Articles

Localization of Intracranial Tumours (p. 631). Acalculous Cholecystitis (p. 633). Novelty at Nottingham (p. 633). Monarticular Arthritis in Children (p. 634). Partnership in Medical Care (p. 634). Tetanus Prophylaxis (p. 635). Commonwealth Links (p. 636).

Papers and Originals

- Production of Lung Carcinomas in C57BL Mice Exposed to a Cigarette Smoke and Air Mixture R. J. C. HARRIS AND G. NEGRONI ... 637
- Spread of Hospital Staphylococci in Healthy Families—a Study from General Practice REPORT TO THE M.R.C. COMMITTEE FOR RESEARCH IN GENERAL PRACTICE ... 642
- Prolonged Survival of Liver Transplants in the Pig R. Y. CALNE, H. J. O. WHITE, D. E. YOFFA, R. M. BINNS, R. R. MAGINN, R. M. HERBERTSON, P. R. MILLARD, V. P. MOLINA, AND D. R. DAVIS ... 645
- Method for Detection of Bacteriuria Suitable for Use in General Practice J. M. BRADLEY, N. CROWLEY, AND J. H. DARRELL ... 649
- Blood Loss Using the Modified Two-layer Kiil Dialyser D. B. EVANS, E. M. CLARKSON, AND J. R. CURTIS ... 651
- Traveller's Diarrhoea: a Survey of Symptoms, Occurrence, and Possible Prophylaxis ANTHONY C. TURNER ... 653
- Urinary Leucocyte Excretion in Hypertension in Pregnancy M. A. CHADD, D. MICHAEL HUMPHREYS, H. M. LEATHER, AND S. A. WILLS ... 655
- Scleroderma Heart Disease E. FLETCHER AND P. MORTON ... 657

Medical Memoranda

- Fatal Hypercalcaemia Complicating Carcinoma of Breast, Resistant to Cortisone and Phosphate Administration V. PARSONS, G. STIRLING, AND E. KNIGHT ... 658
- Budd-Chiari Syndrome after Taking Oral Contraceptives KIRSTEN STERUP AND JOHANNES MOSBECH ... 660
- Epilepsy and Liver Dysfunction in Association with Hypernephroma A. G. STEWART AND J. G. SPRUNT ... 660
- Relapsing Polychondritis RICHARD L. HEWER ... 661

Current Practice

- Disease of the Digestive System
Dysphagia CLIFFORD F. HAWKINS ... 663
- Any Questions? ... 667

Book Reviews

Obituary Notices

- J. W. Linnell, M.C., M.D., F.R.C.P. ... 686
- B. A. Meyer, M.B. ... 686
- N. J. Nicholson, M.B., F.R.C.S.ED. ... 686

News and Notes

- Epidemiology ... 687
- Parliament ... 688
- Medical News ... 689

Middle Articles

- General Practice Observed
Extended Use of Nursing Services in General Practice J. WESTON SMITH AND E. M. MOTTRAM ... 672
- Contemporary Themes
Medical Partnership: Minister's Lecture at Glasgow ... 675
- Tomorrow's Buildings
Thamesmead: First Phase of Community Health Service 676
- Conferences and Meetings
Operating-rooms a Century after Lister—B.M.A. Symposium ... 678

Correspondence

- Psychotropic Drugs. I. Atkin, M.D.; A. U. MacKinnon, M.D.; Louis Rose, M.R.C.S. 680
- Clomiphene for Ovulation. A. Klopfer, M.D. ... 680
- Using Computers. B. Benjamin, PH.D. ... 681
- Animal Reservoirs of Salmonellae. R. L. Huckstep, F.R.C.S. ... 681
- Improving the Psychiatric Services. H. Jacobs, D.P.M. ... 681
- Intussusception Due to Hamartoma. D. P. Goodwin, F.R.C.S. ... 681
- Prevention of Rh-haemolytic Disease. Sheilagh M. C. Murray, M.D. ... 682
- Intrauterine Transfusion in Rh-isoimmunization. G. Masera, M.D., and A. Marini, M.D. ... 682
- Gastritis, Aspirin, and Alcohol. G. K. H. Hodgkin, M.R.C.P., and J. Whewell, M.B. 683
- Alcoholic Content. G. Bousfield, M.D. ... 683
- Endocarditis and the Mitral Valve. Mary M. Stannard, M.B., and A. J. Goble, F.R.A.C.P. ... 683
- Jaundice in Pregnancy. J. E. A. Oni-Orisan, M.B. ... 683
- Massive Overdose of Adrenaline. C. S. Jones, M.B. ... 683
- Homonymous Hemianopia after Oral Contraceptives. S. Behrman, F.R.C.P. ... 683
- Abortion and Conscience. M. Sim, M.D., D.P.M. ... 684
- Body Building on Drugs. M. T. Lucking, M.R.C.S. ... 684
- Restrictions on Doctor in South Africa. S. Shapiro, M.R.C.P. ... 684
- Overseas Registration and Seniority Payments. G. J. Drabu, M.B. ... 685
- Seniority Payments. K. G. Dickinson, M.B. 685
- Thirteen-week Certificate. G. Lloyd, M.R.C.O.G. ... 685
- "Mediflash." M. F. Hyatt, M.B. ... 685
- First Fellows of the Royal College of General Practitioners. B. D. Morgan Williams, B.M. ... 685

SUPPLEMENT

- Annual Representative Meeting, Eastbourne, 24-28 June 1968: Provisional Programme, p. 75
- General Medical Council, p. 77

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¹ *Ann. Inst. Pasteur*, 1958, 95, 194.

² *J. Bact.*, 1959, 78, 477.

³ *Klin. Wschr.*, 1957, 35, 198.

⁴ *Medizinische*, 1959, 7, 296.

⁵ *Lancet*, 1957, 1, 899.

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BRITISH MEDICAL JOURNAL



SATURDAY 23 DECEMBER 1967

Leading Articles

Diagnosis of Pyelonephritis in Children (p. 691). Substitutes for the Mitral Valve (p. 692). Amines and Migraine (p. 693). Life after Death (p. 693). Doctors in Court (p. 694). Foot-and-mouth Disease (p. 694). Symposium on Thyrotoxicosis (p. 695). Polycythaemia and Chorea (p. 696). M.I.A. Jubilee (p. 696). Return to Britain (p. 696).

Papers and Originals

- Cell and Bacterial Counts in the Urine of Normal Infants and Children
H. BRAUDE, J. O. FORFAR, J. C. GOULD, AND J. W. MCLEOD ... 697
- Diagnosis of Urinary Tract Infection in Childhood Based on Examination of Paired Non-catheter and Catheter Specimens of Urine H. BRAUDE, J. O. FORFAR, J. C. GOULD, AND J. W. MCLEOD ... 702
- "Clean Catch" Urines in the Newborn—Bacteriology and Cell Excretion Patterns in First Week of Life GILLIAN CRUICKSHANK AND ELIZABETH EDMOND ... 705
- Haemoglobin Concentration and Other Values in Women Using an Intra-uterine Device or Taking Corticosteroid Contraceptive Pills J. ALAGHBAND ZADEH, C. D. KARABUS, AND J. FIELDING ... 708
- Psychiatric Study of a Consecutive Series of 19 Patients with Regional Ileitis FRED FELDMAN, DAVID CANTOR, SIDNEY SOLL, AND WILLIAM BACHRACH 711
- Evaluation of a Screening Survey for Anaemia in Adult Non-pregnant Women P. C. ELWOOD, W. E. WATERS, W. J. GREENE, AND M. M. WOOD with the assistance of E. H. EVANS, J. DE SWIET, AND J. V. WILLIAMS ... 714
- Fibrin Degradation Products in Sera of Normal Subjects P. C. DAS, A. G. E. ALLAN, D. G. WOODFIELD, AND J. D. CASH ... 718

Medical Memoranda

- Malignant Tumour of Brown Fat in Patient with Turner's Syndrome W. S. B. LOWRY AND P. B. HALMOS ... 720
- Case of Mumps Nephritis G. E. MONTEIRO AND C. A. LILLICRAP ... 721

Current Practice

- Disease of the Digestive System
Bleeding from the Upper Gastrointestinal Tract G. N. CHANDLER ... 723
- Today's Drugs
Epsilon Aminocaproic Acid ... 725
- Any Questions? ... 727
- New Appliances
Peritoneal Dialysis with In-line Sterilization of Dialysate by Filtration ... 728
- Metabolic Balance Cot for the Newborn Infant ... 729

Book Reviews ... 730

Obituary Notices ... 748

News and Notes ... 752

Middle Articles

- Medical History
Queen Elizabeth Hospital for Children, London: Centenary of "The Queen's," 1867-1967 VALENTINE A. J. SWAIN ... 733
- Medical Education
Training of Nephrologists ... 735
- Conferences and Meetings
Exploration of Teaching in General Practice: Conference at R.C.G.P. ... 736
- Mathematics in Medicine:
B.M.A. Symposium ... 737
- Current Trends in Epilepsy ... 738
- Pharmacists and the Sainsbury Report ... 739
- Christmas Quiz ... 740

Correspondence

- Renal Glucose Threshold. L. Rosenthal, M.D.; R. D. Lawrence, F.R.C.P. ... 741
- Transfusion Malaria. L. J. Bruce-Chwatt, M.D. ... 741
- Viruses in Diarrhoeal Disease. Eleanor J. Bell and N. R. Grist, F.R.C.P.ED. ... 741
- Withdrawal of Heroin. F. Dudley Hart, F.R.C.P., and others ... 742
- Carcinogenic Properties of Ortho-dianisidine. E. D. Acheson, F.R.C.P. ... 742
- Streptomycin, I.N.H., and Thiactazone. Frank I. Tovey, F.R.C.S., and others ... 742
- Sarcoid Myopathy. D. G. James, F.R.C.P. ... 743
- Pseudomonas Infection in Hospital. J. S. Robinson, M.D., and others ... 743
- Achilles Tendon Reflex Time. C. D. Marsden, M.R.C.P., and J. C. Meadows, M.R.C.P. ... 743
- Resuscitation Appliance. M. L. Chiswick, M.B., and G. Foy, S.R.N. ... 743
- Body Building on Drugs. I. J. MacQueen, F.R.C.S. ... 743
- Why Sternal Marrow? Mary J. McG. Shaw, M.B. ... 744
- Investigating Hypertension. R. W. D. Turner, F.R.C.P. ... 744
- Primigravida or Primipara? R. S. Saxton, D.T.M.&H. ... 744
- Obstetric Forceps or Vacuum Extractor? J. A. Chalmers, F.R.C.O.G. ... 744
- β -Adrenergic Blockade and Cardiac Arrhythmias. D. A. L. Watt, M.R.C.P. ... 744
- Postgastrectomy Problems. A. G. Johnson, F.R.C.S. ... 745
- Coxsackie B5 Virus. J. H. Connolly, M.D. ... 745
- Congenital Dislocation of the Hip. T. G. Barlow, F.R.C.S. ... 745
- Which Stethoscope? J. Shackleton Bailey, M.R.C.S. ... 745
- "Mediflash." K. C. Easton, M.B. ... 745
- Megaloblastic Anaemia and Ascorbic Acid. R. E. Davis and A. F. Fleming, M.B. ... 745
- Hypercalcaemia and Malignant Tumours. W. M. Keynes, F.R.C.S. ... 745
- Medical Science: Master or Servant? R. V. Facey, B.M. ... 745
- Institutional Care of the Mentally Sub-normal. T. McKeown, F.R.C.P., and I. Leck, M.B. ... 74
- Patient or Ailment? J. B. Glass, M.B. ... 74
- Hospital Management. J. E. Duffield, D.M. ... 74
- Forging Prescriptions. B. D. Lascelles, M.B., and G. B. Sturrock, M.B. ... 74
- Mileage Allowances. J. G. McWhirter, M.B. ... 74
- Sickness Benefits. D. C. Williams, M.B. ... 74
- Terms of Service—1805. G. R. Usmar, M.R.C.S. ... 74

SUPPLEMENT

- G.M.S. Committee, p. 81
- Organization Committee, p. 84
- G.M.S. Committee (Scotland), p. 8
- Scottish Committee for Hospital Medical Services, p. 87

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BRITISH MEDICAL JOURNAL



SATURDAY 30 DECEMBER 1967

Leading Articles

Cardiac Transplantation (p. 757). Disease from Monkeys (p. 758). Health Centre Explosion (p. 759). Intra-arterial Chemotherapy for Recurrent Neoplasms (p. 760). Clinical Lessons from Developmental Neurology (p. 761). Miliary Crohn's Disease (p. 761). Cerebral Angiomas (p. 762). B.M.A. Awards (p. 762).

Papers and Originals

Neurological Sequelae of Prenatal and Perinatal Complications	
H. F. R. PRECHTL	763
Concentration of Methoxyflurane for Obstetric Analgesia by Self-administered Intermittent Inhalation	
VALERIE MAJOR, MICHAEL ROSEN, AND WILLIAM W. MUSHIN	767
Improving the Acceptability of Oral Continuous Progestogens in Microdosage for Fertility Control	
JUAN ZAÑARTU	771
Transfer Factor (Diffusing Capacity) for the Lung in Simple Pneumoconiosis of Coal Workers	
J. P. LYONS, W. G. CLARKE, A. M. HALL, AND J. E. COTES	772
Outbreak of E.C.H.O. Virus Type 30 in a General Practice	
D. H. IRVINE, A. B. H. IRVINE, AND P. S. GARDNER	774
Calf Muscle Denervation for Intermittent Claudication	
N. V. ADDISON	776
Gynaecomastia in Chronic Renal Failure	
R. M. LINDSAY, J. D. BRIGGS, R. G. LUKE, I. T. BOYLE, AND A. C. KENNEDY	779
ABO Blood Groups and Infantile Hypertrophic Pyloric Stenosis	
J. A. DODGE	781

Medical Memoranda

Neoplasia Complicating Uretero-sigmoidostomy	JOHN N. KILLE AND SELWYN GLICK	783
Nail-gun Fatality	JOHN CRAGG	784

Clinicopathological Conference

A Case of Congenital Heart Disease in Mother and Child ... 785

Current Practice

Disease of the Digestive System	
Surgical Treatment of Upper Alimentary Bleeding	
H. L. DUTHIE	790
Any Questions?	793

Book Reviews

Middle Articles

General Practice Observed	
Use of General Practitioners in the School Health Service	
ALAN R. BUCHAN AND A. PARRY JONES	797
Medical History	
A Letter from Sir Morell Mackenzie	MAXWELL ELLIS 799
Conferences and Meetings	
Family Doctors Practising from Health Centres	800

News and Notes

Epidemiology	810
Medical News	811

Correspondence

Requests for Abortion	W. G. Mills, F.R.C.O.G.	802
Clomiphene for Ovulation	P. M. F. Bishop, F.R.C.P.; H. J. E. Cox, D.C.H.	802
Nursing Services in General Practice	G. W. Roberts, D.P.H.; D. L. Williams, M.B.	803
Early Work with Blood Transfusion	J. F. Fleetwood, D.P.H.	803
"Acrosclerosis"	Stephanie A. Davies, M.B., and F. J. Woodroffe, M.R.C.P.	804
Disinfectants and Plastic Mop Heads	J. W. Gibson, A.I.S.T., and others	804
Carcinogenicity of Tobacco and Tobacco Smoke	P. R. Peacock, F.R.C.P.GLASG.	804
Antibiotic Combination in Staphylococcal Infections	R. J. Bulger, M.D.	805
Dysmenorrhoea	G. W. Theobald, F.R.C.O.G.	805
Improving the Psychiatric Services	J. H. Raphael, M.B.	806
Tetanus Prophylaxis	M. Ellis, F.R.C.S.	806
Low Back Pain	A. M. Blain, M.B.	806
Bromism	A. F. Boyles, M.B., and D. J. Martin, M.B.	806
Cause of Death	S. Bradshaw, M.B.	806
Hospital Management	J. Wedgwood, M.D.; J. Anderson, F.R.C.P.	806
Approval of Emergency Treatment Service	A. Dowling, M.B.; K. A. Harden, M.B.	807

Obituary Notices

G. L. Roberts, M.B., F.D.S. R.C.S.	808
V. H. J. Davies, M.D., F.R.C.S.ED.	808
C. R. Whittaker, F.R.C.S.ED.	809
G. Hamilton, M.B., D.A.	809
H. C. Jennings, M.B., D.P.H.	809
W. R. Sadler, L.R.C.P.ED., L.R.F.P.S.GLASG.	809

SUPPLEMENT

- Central Committee for Hospital Medical Services, p. 89
- Committee on Medical Science, Education, and Research, p. 92
- Public Health Medical Officers' Salary Claim, p. 94

ALCOHOL & ROAD TRAFFIC

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Pointers

Rh-haemolytic Disease: Genetic studies in Swallowtail butterflies led to the Liverpool team's interest in the Rh blood groups, culminating in clinical trials in which rhesus-negative mothers were successfully protected by anti-D gammaglobulin against immunization (p. 7). Leader at p. 3.

Death from a Broken Heart: Results of a survey in a semi-rural area confirmed statistically that there is a relation between bereavement, especially at home, and death of close relatives within the succeeding year (p. 13). Leader at p. 2.

Infection in the Theatre: Outbreak of *Staph. aureus* wound infection traced to anaesthetist suffering from psoriasis and carrying and disseminating the same strains of organism (p. 17).

Relatives of Diabetic Patients: Seemingly normal twins and close relatives of diabetic patients showed impaired glucose tolerance and low serum insulin levels after glucose which may be due to inherited abnormality of the beta cell associated with insulin release (pp. 21 and 22).

Platelets and Brain Tumours: Increased stickiness observed in patients with invasive tumours may be consequent on acute degradation of neural tissue (p. 25).

Respiratory Monitoring: Description of technique which displays changes in transthoracic electrical impedance, thereby providing information on cardio-respiratory function (p. 27).

Anaemia in Thailand: New thalassaemia-like condition benefiting only from blood transfusion described. Probably due to combination of three abnormal genes (p. 29).

Brief Case Reports: Cantharides—not an aphrodisiac but dangerous poison (p. 33). Danger of phenytoin in atrial flutter (p. 34). Cardiac involvement in psittacosis (p. 35). Urticaria from Smith-Petersen nail (p. 36). Human abortion attributable to ovine agent (p. 37). Massive overdose of adrenaline (p. 38).

Road Safety Act, 1967: Review of changes in procedure when doctors are called to examine drinking drivers (p. 39).

Lingering Fallacies: Correct modern management of four common infectious diseases of childhood (p. 41).

Physician's Role: Possible origin of a familiar quotation (p. 47).

Health Centres: Time to share experience (p. 49).

Medical Benevolence: Christmas appeal (p. 57).

Amphetamine: B.M.A. working party (*Supplement*, p. 2).

Medical Staffing in N.H.S.: Tables showing distribution by specialty (*Supplement*, p. 3).

Private Practice Committee: *Supplement*, p. 9.

Sainsbury Report

Last week the report of the Sainsbury Committee¹ was published as a Command Paper. Appointed in May 1965 by the Minister of Health and the Secretary of State for Scotland, the Committee was asked to look into the relationship of the pharmaceutical industry in Great Britain with the National Health Service. In its inquiries it was to have regard to the structure of the industry, to the commercial policies of the firms comprising it, to pricing and sales promotion practices, to the effects of patents, and to the relevance and value of research. And it was asked to make recommendations. As well as taking evidence from interested associations and professional bodies (including the Royal Colleges and the B.M.A.), Lord Sainsbury and his colleagues initiated several inquiries of their own. They obtained from the pharmaceutical industry replies to a financial questionnaire; they visited factories; at their request the Government Social Survey carried out a study of the sources of information on drugs of 500 general practitioners and how these related to their prescribing habits; and they tested the degree of concordance between two expert panels, one in London and the other in Edinburgh, who were asked independently to categorize on the basis of therapeutic effectiveness some 2,657 proprietary preparations listed in the Monthly Index of Medical Specialties (M.I.M.S.) for December 1965. The result of this searching investigation has been in the hands of the appointing Ministers for some little time.

By far the largest buyer of drugs in this country is the State. That a customer in such a dominant position should find it necessary to inquire into the business methods of those it shops with gives an impression of seeking a tool to impose greater control over the producer than the normal workings of the market—weighted in this case in the customer's favour—have made possible or warranted. The medical profession, which has reason to be grateful for the drug manufacturers' contribution to advances in medicine, will therefore welcome the Committee's acknowledgement, though somewhat grudgingly made, that the industry "cannot be said to have failed to provide the people of this country with many medicines of great value." On the questions of prices and profits, medical men are not as competent to comment as a body with such an eminent business man at its head as Lord Sainsbury. But the majority of doctors, as indeed of the public, will be glad that nationalization as a panacea for the problems of the industry is rejected.

If—as the Committee states—the industry in many ways has "admirably served the public interest," it must also be agreed that the importance of drugs and medicines for human welfare imposes a special responsibility on both the industry and the Health Departments. The Committee gives short shrift to those who argue that most research which leads to new medical products is done in the universities and that the pharmaceutical industry lives by exploiting other people's inventions. In fact the industry is far from being wholly or even largely dependent on the

universities for basic research, and the major part it has played in the great advances in therapeutics during the past few decades is recognized by the Committee.

Some 55 to 60 firms in Britain account for over nine-tenths of the total value of sales of "prescription medicines." Many of these firms are foreign owned. In 1966 nearly half (by value) of the medical specialty products (ethical proprietary preparations) prescribed under the N.H.S. came from U.S.-owned companies in Britain, 27% from British companies, 14% from Swiss companies, and 10% from other European-owned companies. This picture omits the export performance of these firms, which is impressive—an increase of over 50% between 1961 and 1965, with "by far the largest contribution" by British-owned firms. In 1965-6 the cost of medicines, dressings, and appliances in the Hospital Services had risen threefold over 16 years to £24.6m., while in the General Medical and Pharmaceutical Services there had been a fourfold rise to £148.9m. Of N.H.S. expenditure on medicines, dressings, and appliances 90% is for medical specialties, so their importance for this inquiry is clear.

After a thorough consideration of the many factors relevant to a fair level of profit—the size of the risk, need for incentive, patent monopoly, product competition, and so on—the Committee concluded that the actual level of profits was in some cases much higher than could be considered reasonable, and that the Ministry's voluntary price regulations schemes had serious weaknesses. The Committee proposes new pricing arrangements, which include the statutory provision of an audited financial return by companies supplying N.H.S. medicines and a standard cost return for new drugs and existing ones with N.H.S. sales exceeding £250,000 annually. Its recommendation for the appointment of a separate Economic Development Committee to watch over the development of the industry comes rather oddly in relation to an industry which has been so successful. The Committee also wants new pharmaceutical products to be marketed only under an approved name, and not by brand name. This last proposal should help to make clinical therapeutics easier and perhaps more rational. Certainly it goes in a direction favoured by much of the medical evidence given to the Committee, including that of the B.M.A.

In many ways the most far reaching of the Committee's recommendations is that for the Medicines Commission. It is not without significance that the Government issued its White Paper² on its own proposals for legislation on drugs and medicines just a fortnight in advance of the Sainsbury report. As we noted at the time,³ the Medicines Commission the Government wants would have as its first task the giving of advice to the Ministers of Health and Agriculture, and its members would be appointed (after consultation with "appropriate organizations") by the Ministers themselves. It would in fact be an extension of the Government machine. The Sainsbury Committee, on the other hand, recommends an independent Medicines Commission. "We consider," the report states, "that a new body is required. It should have an independent constitution and be plainly seen to be independent. It is our aim that except for its necessary dependence upon the Government for the allocation of funds, it should be free from direct control by the Ministry of the day." The Commission, which would have statutory powers,

would advise the Health Departments on the licensing ultimately of all prescription medicines sold in Britain. It would perform the duties now carried out by the Committee on Safety of Drugs (Dunlop Committee) and the Standing Joint Committee on the Classification of Proprietary Preparations (Macgregor Committee), and take over from the G.M.C. its pharmacopoeial responsibilities. It would also be the statutory body to which the Government could turn for advice on all questions involving medicines.

The Committee believes that the Commission should become in due course the accepted source of information on all matters concerning the use of medicines. It thinks it unsatisfactory that so large a part of the information on medicines available to doctors should come from the industry selling them, and equally unsatisfactory that the profession should be under the impression that much of the other information represents only the views of the Health Departments and is activated wholly or mainly by a desire to save money. "The profession would in our view have much greater confidence in such information were it given by the independent, professionally staffed Commission." It is envisaged that the Commission would ensure that all information tendered to doctors by pharmaceutical companies is "impartially presented, complete, and as accurate as possible."

It is to be doubted whether the Medicines Commission would "from its very constitution" gain the confidence of the profession, as the Committee thinks that it would. The virtues of the Commission's independent status are likely to be dimmed in doctors' eyes when they contemplate its all-embracing powers and the bureaucratic machine that will be needed to operate them. Its responsibilities would be so onerous that they might prove unmanageable. And in contrast to its remit "to examine the relationship of the pharmaceutical industry in Great Britain with the National Health Service" the Committee's proposals for the Medicines Commission cover the whole of medical practice, not only the N.H.S. In this context it is difficult to agree with the Committee's thesis that the Commission should in due course become the accepted source of information on all matters concerning the use of medicines. There is at present in the medical journals a widely accepted source of factual information on current therapeutics which has played no small part in bringing together the reputable products of the pharmaceutical industry and the patients that benefit from them. It would have been easier to see the wisdom of some of the Sainsbury Committee's proposals had it been readier to recognize some of the virtues of the existing system.

Broken Hearts

William Heberden's mortality tables¹ for the City of London listed "griefs" as a cause of death, but it is doubtful if such a diagnosis would be accepted today. Deaths following bereavement used to be attributed to a "broken heart," and in 1835 Benjamin Rush² described rupture of the auricles and ventricles as the cause of death in such cases. The possibility that this may be something more than a medical myth is suggested by the recent work of C. M. Parkes and B. Benjamin.³ These workers showed that the increase in mortality rate among London widowers during the first six months of bereavement is largely attributable to deaths from coronary thrombosis and arteriosclerotic heart disease.

¹ *Report of the Committee of Enquiry into the Relationship of the Pharmaceutical Industry with the National Health Service, 1965-67, 1967, Cmd. 3410. H.M.S.O.*

² *Forthcoming Legislation on the Safety, Quality, and Description of Drugs and Medicines, 1967. Cmd. 3395. H.M.S.O.*

³ *Brit. med. J.*, 1967, 3, 689.

A paper by W. D. Rees and S. G. Lutkins printed at page 13 of this week's *B.M.J.* describes the effect of a death in the family on the death-rate of the surviving members. Their most striking finding in the semi-rural Welsh community which they studied is a mortality rate among newly bereaved family members six times greater than the mortality rate among non-bereaved control families. They confirm the findings of several other studies that there is an increase in mortality rates among widows and widowers and that this increase is most marked during the first year of bereavement.

Granted that there is an association between bereavement and mortality, how can this be explained? The evidence so far reported does not allow us to do more than guess. Does bereavement influence the incidence of disease or simply increase the mortality rate among those already affected? Is it the psychological state of grief which alters physiological processes in a pathological manner? Or does grief have secondary effects on diet, smoking habits, and alcohol intake, which are themselves pathological in their effects? Further research must answer these questions, but in the meantime doctors should ask themselves whether there is anything which they should be doing to mitigate the effects of bereavement.

In public health terms the relatives of dying patients are a high-risk group akin to the relatives of patients with tuberculosis. Rees and Lutkins's figures suggest that young and middle-aged men who lose wives from an illness which causes them to die away from home are particularly at risk. Recent work in Britain and the United States seems to indicate that major bereavements influence physical and mental health in many ways and that bereaved people commonly seek help from their medical practitioners. The clergyman, whose traditional role includes the succouring of the bereaved, has now in Britain been largely replaced by the general practitioner, the professional man to whom the bereaved will turn most readily. It is unfortunate that medical education does little to prepare doctors for this role.

Much is known about the form and nature of grief. Grief is the psychological process which cushions the impact of disaster and enables a bereaved person gradually to work towards an acceptance of what has happened. It is a mixture of pining and resignation, searching and apathy, denial and acceptance; small wonder that some are unable to cope effectively with this conflict. Pathological forms of grief have been recognized since E. Lindemann's classic account⁴ of grief among the relatives of those who died in the Coconut Grove fire. More recently papers by C. Anderson⁵ and Parkes⁶ have enabled the classification of bereavement reactions to be carried out. A common form is the "chronic grief" syndrome epitomized by Queen Victoria. Here, intense grief, instead of resolving, becomes habitual, and mourning persists. Another form may occur among persons who defend themselves so vigorously against the pain of grief that they "feel nothing" for months after bereavement. Thereafter they tend to break down with a particularly severe reaction. Identification symptoms (hypochondriacal symptoms resembling those suffered by the dead person during his terminal illness), panic attacks, insomnia, and headaches are

all likely to bring the bereaved person* into the care of a physician.

At present too little is known about the factors which decide who will break down and who will emerge from the stress of grief stronger and wiser. Personality factors, social isolation, age (old people withstand bereavement better than young), and the nature and magnitude of the loss itself all seem to be important factors. When the bereaved person is supported by a united and affectionate family, when there is something left to live for, when the person has been adequately prepared for the loss, and when it can be fitted into a secure religious or philosophical attitude to life and death there will seldom be much need for professional help. When, however, the bereaved person is left alone in a world which is seen as hostile and insecure, when the future is black and the loss has not been prepared for, help may be needed.

What can doctors offer? A willing ear, tolerant of confusion and anger, and a knowledge of community resources are probably more important than tonics and sedatives. In addition, the Cruse Clubs Counselling Service for Widows,⁷ the citizens' advice bureaux, the local church, mental welfare officers, social workers, and voluntary organizations of all kinds are available in many areas. There is little doubt that time spent in helping patients to prepare for and cope with the disasters in their lives will improve community mental health and may even reduce the post-bereavement mortality rate.

Prevention of Rhesus Haemolytic Disease

Rhesus haemolytic disease of infants takes several forms. In the mildest cases the infant is merely jaundiced and this soon disappears; in severer cases there is actual haemolytic anaemia, and this, if untreated, can be fatal; the disease can so affect the foetus that it will die in utero and be stillborn; and the hyperbilirubinaemia can affect the brain, producing the condition of kernicterus, which causes mental abnormality. The anaemia has been successfully treated by the method of exchange transfusion, and recently this procedure has been carried out before birth by the technique of intrauterine transfusion.¹ Early induction of labour has reduced the number of stillbirths, especially since the introduction of a method of using samples of amniotic fluid to give warning of dangerous concentrations of bilirubin.^{2,3} Nevertheless, it would be far more satisfactory to prevent this disease occurring at all. For the past nine years a group of doctors at Liverpool have been working on this problem, and they have now reached the point where the possibility of successful protection against rhesus haemolytic disease has been demonstrated and practical methods for making this protection available can be discussed. In his Lumleian lecture to the Royal College of Physicians printed on page 7 of this issue, Professor C. A. Clarke reviews the inception and development of this work in Liverpool and the information now available from other centres. It is an impressive story.

We now know that the cause of the disease is the development in the mother's blood of anti-Rh antibodies which pass the placenta and destroy the infant's red cells. The development of these antibodies in the mother's plasma is

¹ Heberden, W., (attrib.) 1759, Bill of Causes of Death, quoted from *Report of the County Medical Officer of Health, the London County Council, 1957*, p. 165, 1958.

² Rush, B., *Medical Inquiries and Observations upon the Diseases of the Mind*, 5th edition, 1835. Philadelphia.

³ *Brit. med. J.*, 1967, 3, 232.

⁴ Lindemann, E., *Amer. J. Psychiat.*, 1944, 101, 141.

⁵ Anderson, C., *Int. J. Psycho-Anal.*, 1949, 30, 48.

⁶ Parkes, C. M., *Brit. J. med. Psychol.*, 1965, 38, 1.

⁷ Cruse Clubs Counselling Service for Widows, 6 Lion Gate Gardens, Richmond, Surrey.

¹ Liley, A. W., *Brit. med. J.*, 1963, 2, 1107.

² Bevis, D. C. A., *Lancet*, 1950, 2, 443.

³ Bower, D., and Swale, J., *ibid.*, 1966, 1, 1009.

stimulated by the passage of Rh-positive red cells from the infant to the mother across the placenta during labour. Another possible cause is the previous transfusion of the mother before her pregnancy with Rh-positive blood, but such an event is rare today. It follows that it is the second and subsequent children that are at risk, and since the stimulation may produce increasing levels of Rh-antibody production the risk is greater for each succeeding child. But in practice only a small proportion of the children at risk actually develop signs of rhesus haemolytic disease. There are at least two reasons for this. Different individuals react differently to similar antigenic stimuli, so in some families the second child is affected, whereas in others of three or sometimes more children no cases have occurred. Secondly, we know that if mother and child have different ABO blood groups, Rh immunization rarely occurs, presumably because the incompatible red blood cells from the child are destroyed in the mother's blood before they can do any damage.

It was this protection afforded by ABO group incompatibility that suggested a possible line of approach to Professor Clarke and his colleagues. If a potent anti-Rh serum was available, would it protect mothers against Rh immunization and their children against risk of rhesus haemolytic disease? When Rh-positive red blood cells were given to Rh-negative male volunteers they produced Rh antibody in their plasma. It was found that antibody formation could be prevented by giving a potent anti-Rh (anti-D) plasma, provided the "incomplete" (albumin) antibody was used. The next step was to give to women at risk, within 48 hours of delivery, 5 ml. of gammaglobulin containing incomplete anti-D of suitable activity. The trial was limited to primiparous women who were found to have foetal red cells present in their own blood after delivery—a group known to be at risk. Alternate patients were given the serum. After six months none of the 78 treated women had developed immune antibody, whereas 19 of the 78 controls had done so. Results up to date from various centres collected by Clarke show that out of 559 control cases 75 (13%) had become immunized six months after labour, whereas out of 628 protected by anti-D gammaglobulin none was immunized—a result which Clarke calls "almost alarmingly successful." Further results have shown that the protective effect will persist through a further pregnancy when the foetus is Rh-positive and ABO compatible; combined results show that out of 66 women immunized during and after pregnancy none produced antibodies in the subsequent pregnancy, whereas out of 63 control cases 15 (24%) produced antibodies.

There is thus clear evidence that women at risk can be protected against Rh-immunization and their children against rhesus haemolytic disease. Professor Clarke deals then with two further questions that arise. What are the risks of the procedures? Can enough anti-D gammaglobulin be obtained? The risk to the mother is trivial; only minor local reactions have occurred and the risk of serum jaundice can be eliminated by appropriate methods of preparing the gammaglobulin. The male volunteer who is injected with Rh-positive blood risks being infected by the virus of homologous serum-jaundice. The risk can be minimized but not eliminated by following W.H.O. recommendations. A better way, proposed by Clarke, is to use a small number of donors made hyperimmune by small repeated injections of sensitizing antigen and to obtain plasma by plasmapheresis—that is, to take off plasma and return the red cells to the donor. Put against the possibility of eliminating unnecessary stillbirths, some

cases of mental deficiency, and the who exchange transfusion, Clarke considers that acceptable, though others may not agree.

To get enough protective anti-D gammaglobulin calculates that for every million of the population 15 immunized donors, willing to give 500 ml. of plasma once a month, would be needed. The organization of the immunization of donors, the collection of plasma, and the preparation of protective antibody will therefore require quite a large staff with necessary equipment, but it could also be found by proper expansion of the present national blood transfusion centres.

Metronidazole and Syphilis

Metronidazole (Flagyl) was introduced to therapeutics in 1959 after C. Cosar and L. Julou¹ had shown it to be active against *Trichomonas vaginalis* in vitro and in mice, and P. Durel and colleagues² reported on its efficacy in curing trichomoniasis in patients of both sexes. They gave combined oral and local treatment to their women patients, but in 1960 excellent results in women with oral treatment alone were reported from several centres.³⁻⁶ Metronidazole by mouth is now generally accepted as the drug of choice for the treatment of trichomoniasis.

The therapeutic range of the drug was increased in 1962, when D. L. S. Shinn⁷ found it to be highly effective in treating Vincent's gingivitis. This led to an investigation into any possible effect of the drug on *Treponema pallidum*. Many patients attending venereal disease clinics are treated for trichomoniasis, which is usually sexually transmitted. Some of these patients may be incubating syphilis, and it is obviously important to know if metronidazole in the dosage usually given can destroy *T. pallidum*.

M. Scott-Gray and M. Murrell⁸ had previously shown that metronidazole 1.8 g. in 48 hours had no effect on a patient with primary syphilis. In 1966 A. R. Yobs and colleagues⁹ found that relatively large doses had no effect on the course of syphilis in rabbits. Two recent papers cast further light on this important problem. A. H. Davies¹⁰ treated six patients with secondary syphilis with doses of metronidazole ranging from 13.5 g. in five days to 34 g. in nine days. The local lesions healed and material from these patients showed disappearance of *T. pallidum* on dark-field examination. A. E. Wilkinson and his colleagues¹¹ showed that sera from patients under treatment for trichomoniasis may immobilize *T. pallidum* (Nichols strain) in vitro, but treatment of a patient with primary syphilis (positive on dark-field examination) with 200 mg. metronidazole three times daily for seven days did not heal the lesions, and *T. pallidum* was still detected at the end of the course.

It seems that the ability of metronidazole to eliminate *T. pallidum* depends on the daily dosage level: the organism

¹ Cosar, C., and Julou, L., *Ann. Inst. Pasteur*, 1959, **96**, 238.

² Durel, P., Roiron, V., Siboulet, A., and Borel, L. J., *C. R. Soc. franç. Gynéc.*, 1959, **29**, 36.

³ Watt, L., and Jennison, R. F., *Brit. med. J.*, 1960, **2**, 902.

⁴ Rees, E., *ibid.*, 1960, **2**, 906.

⁵ Moffett, M., and McGill, M. I., *ibid.*, 1960, **2**, 910.

⁶ Rodin, P., King, A. J., Nicol, C. S., and Barrow, J., *Brit. J. vener. Dis.*, 1960, **36**, 147.

⁷ Shinn, D. L. S., *Lancet*, 1962, **1**, 1191.

⁸ Scott-Gray, M., and Murrell, M., *Practitioner*, 1961, **186**, 218.

⁹ Yobs, A. R., Clark, J. W., and Schroeter, A. L., *Brit. J. vener. Dis.*, 1966, **42**, 122.

¹⁰ Davies, A. H., *ibid.*, 1967, **43**, 197.

¹¹ Wilkinson, A. E., Rodin, P., McFadzean, J. A., and Squires, S., *ibid.*, 1967, **43**, 201.

will survive 600 mg. of the drug but will be destroyed by 2 g. Thus the dosage of metronidazole usually employed for trichomoniasis does not appear to be treponemicidal. However, until more investigations have been carried out it would be wise for the venereologist to withhold metronidazole from patients who may be incubating or in the early phase of syphilis, until that diagnosis has been confirmed.

More Retroperitoneal Fibrosis

Though first described over 60 years ago, interest in retroperitoneal fibrosis has grown since its reported association with the drug methysergide.¹⁻³ There are now reports of over 200 cases, and the evidence suggests that it is being increasingly recognized. For example, in a recent series of 14 patients encountered in as many years in Birmingham,⁴ no fewer than ten were seen after 1963. This may be due to better awareness of the protean manifestations of a curious disease or to the increased activity of some aetiological agent as yet unknown.

There is no general agreement on what constitutes the syndrome of retroperitoneal fibrosis, and some authorities would exclude localized plaques of fibrosis. But it might be defined as a chronic fibrosing process which usually starts in the pelvis or lumbar region, and in the majority of cases spreads to the ureters. The disease attacks their walls though patency is maintained. Mediastinal fibrosis⁵ can also occur, and discrete fibrous masses may be found at the hilum of the lung and even in the lung parenchyma. Arteries, veins, and lymphatic channels may be compressed by fibrosis, so that a wide variety of ischaemic and obstructive lesions result. The usual history is of vague abdominal pain and backache, often radiating into the groins, with sooner or later signs of impaired renal function and hypertension. Epididymal swelling, hydrocele, and leg oedema may result from obstruction of veins in the pelvis, and in some patients the arterial supply to the lower limbs may be jeopardized. Less commonly, mediastinal fibrosis may have such diverse consequences as facial oedema, coronary ischaemia, pericarditis, and pleurisy. In addition there are such indications of the generalized nature of the disease⁶ as loss of weight, anaemia, a raised erythrocyte sedimentation rate, and increased levels of γ -globulin in the serum. While no doubt most patients will be seen by genitourinary surgeons or by physicians concerned with renal disease and hypertension, it is clear that no one, whatever his specialty, can afford to ignore the syndrome, and this is borne out by the fact that two of the patients in the Birmingham series presented as orthopaedic problems.

Retroperitoneal fibrosis may be a self-limiting condition,⁷ and spontaneous remission has been recorded.⁸ But in some cases it is progressive and fatal. Recognition is all the more important because, once the condition is thought of, diagnosis in the average case is not difficult and treatment is often rewarding. Hypertension with a history of abdominal pain,

a raised blood urea and erythrocyte sedimentation rate, and abnormalities in the plasma proteins, especially if there are other seemingly bizarre clinical features, should suggest the need for pyelography, especially by the retrograde route. The features are characteristic¹: delayed excretion of dye, with hydronephrosis and hydroureter above an obstruction, which is commonly in the mid-lumbar region or at the pelvic brim, and medial deviation and irregularity of the ureter at the site of obstruction. In difficult cases lymphangiography may also be valuable. Operation to free the ureters is often strikingly successful, though further obstruction may occur, and in some patients an affected segment of ureter has had to be resected.

What is the nature of retroperitoneal fibrosis? Histological examination of excised tissue has shown a wide variety of cell types, and in some cases vasculitis has been a prominent feature. There seems little doubt that an immunological reaction to a variety of sensitizing agents is the likely mechanism, and in some cases an autoimmune type of response is probable.⁹ The association with methysergide suggests a drug sensitivity, but so far no other drug has been implicated. Sometimes the condition appears to have been initiated by local infection or by haemorrhage in association with blood diseases.⁴ In a few cases the fibrosis represents an intense fibrotic response to malignant disease.¹⁰ But most must still be labelled "idiopathic," and they represent a challenge which will no doubt be met by careful clinical appraisal of new cases and by the efforts of immunologists.

Mental Handicap and the Family

Most undergraduate and postgraduate teaching on mental subnormality concentrates on diagnosis and phenomenology and gives little time to the study of the families of subnormal children and the stresses to which they are exposed. However, the interested doctor is aware that despite the common sense and compassion he brings to bear on the family's situation he needs to be better informed. He feels the lack of a broader background of knowledge and of guidance when he seeks to alleviate the stresses inevitable within a family confronted by the tragedy of mental handicap. He needs to know how the handicapped child should be assessed and educated, how the services available are organized, and how to make use of them. Further, he should be aware of current opinion on how these services could be developed and improved. A number of recent publications^{1,2} have dealt with these matters, but what the practitioner requires is a succinct but comprehensive presentation of the information. A working party convened by the National Society for Mentally Handicapped Children has recently produced a short report which goes a long way to meeting these requirements.

In 1958 F. L. Masland and his colleagues⁴ came to the broad conclusion that many mentally subnormal children do better at home than in institutions, especially in the early years. Later J. Tizard and J. C. Grad suggested that, unless there were strong contraindications, "parents should be encouraged and helped" to care for mentally handicapped babies themselves. The working party accepted these views as a premise, but it was no doubt aware that beyond a certain point the burden of looking after a mentally handicapped child may threaten the well-being of the family, and in these cases institutional care may be the only answer. "For parents of older children the choice remains theirs. It is unfortunate

¹ Utz, D. C., Rooke, E. D., Spittell, J. A., and Bartholomew, L. G., *J. Amer. med. Ass.*, 1965, 191, 983.

² Graham, J. R., Suby, H. I., LeCompte, P. R., and Sadowsky, N. L., *New Engl. J. Med.*, 1966, 274, 359.

³ *Brit. med. J.*, 1966, 1, 755.

⁴ Webb, A. J., and Dawson-Edwards, P., *Brit. J. Surg.*, 1967, 54, 508.

⁵ Barrett, N. R., *ibid.*, 1958, 46, 207.

⁶ Kay, R. G., *Brit. J. Urol.*, 1963, 35, 284.

⁷ Ormond, J. K., *J. Urol. (Baltimore)*, 1965, 94, 385.

⁸ Benfield, J. R., Harrison, R. W., Moulder, P. V., Lyon, E. S., and Graff, P. W., *J. Amer. med. Ass.*, 1962, 182, 579.

⁹ Que, G. S., and Mandema, E., *Amer. J. Med.*, 1964, 36, 320.

¹⁰ Webb, A. J., and Dawson-Edwards, P., *Brit. J. Surg.*, 1967, 54, 505.

that, today, the parents who bring up a subnormal baby themselves are likely to have a hard time of it."³

The report examines the procedure whereby the school medical officer, acting on behalf of the local education authority, assesses children who may be subnormal at the age of about 5. It points out that no matter how skilfully this assessment is made the objective is primarily administrative and is directed at excluding the child from school rather than at making a constructive educational or therapeutic recommendation. The report also emphasizes the inadequacy of a single assessment at a single point in time. Child psychiatry has long recognized the value of the multidisciplinary team approach for the diagnosis, assessment, and management of childhood disorders. This important concept is adopted and extended by the working party. Its view is that the assessments should be undertaken by such a team working in a co-ordinating centre planned and staffed jointly by the local authority and the National Health Service. The staff of such a centre should include medical specialists, educationalists, psychologists, social workers, and possibly parents. The team should work in co-operation with general practitioners and hand on information to them. Such an arrangement would give a family access to a centre where they could obtain authoritative diagnosis and assessment of subnormality and other handicaps, and under the same roof the accumulated knowledge of social and personal problems could be applied for the benefit of individual cases.

The report describes how provisions for the care and management of handicapped children vary from area to area throughout Britain. Greater co-operation between local authorities, hospital authorities, and voluntary societies is necessary before services can be integrated and rationalized so that more effective use is made of existing resources. Essential services such as pre-school facilities for subnormal children, training centres, and accommodation for short-term residential care to cover holidays or family crises are missing or inadequate in some parts. Planning for the future should ensure that these gaps are filled.

However, comprehensive outside services of this kind supply only part of the help that families need. The report goes on to indicate what needs to be done nearer home to relieve the burden of those who have handicapped children. They need help in getting suitable living. Financial assistance, when applicable, should include increased grants from the National Assistance Board, income tax relief, grants for laundry or home nursing, and subsidized holiday care. In addition to short-stay residential units, crèches and day nurseries should be widespread.

Counselling is of crucial importance. In the hands of the uninformed it may tend only to increase distress. Disclosure is a painful and delicate task, and, however carefully conducted, it may lead to an unfavourable reaction in the parents. It has been shown that a proportion of parents are critical not only of the way in which the disclosure was conducted but of the subsequent advice and help they had received.^{5 6}

Parents need a patient and sympathetic hearing and well-informed answers to their questions. They need genetic counselling and advice about family planning. They will wish to know how they can help with play activities; they will want advice about education, speech development, and training in social behaviour. The family will also need help with its own adjustment to handicap, with its own attitudes and reactions. If the counsellor has both the training and judgement to know not only when but how to explain the child's condition and is also capable of offering informed advice on the problems outlined above, the family will be the more likely to accept the situation realistically and to deal with it effectively, while adverse reactions such as rejection, over-compensation, or overwhelming feelings of guilt and conflict within the family may be avoided or attenuated.

Visible Alternatives

What is the best treatment for the ailing Health Service? Should it be radical, symptomatic, or both? What other ways are there of finding money and administering the Service? Taking up Mr. Enoch Powell's contention that "what is necessary is a visible alternative,"¹ the *B.M.J.* has recently examined some of the possibilities. Experts in economics and related fields have discussed, among other solutions, a nationalized health corporation, decentralizing administration, a Parliamentary Committee on the Health Service, and the prospects for private health insurance. All the articles in this series, together with a medical summing up by Sir Robert Aitken, have now been collected into a booklet, which was published this week.²

Most of the contributors conclude that for various reasons the National Health Service cannot now be abandoned. Nevertheless, as Sir Robert Aitken points out in his thoughtful and provocative concluding essay, "some large and important practical improvements . . . lie to hand." The first of these should be a serious attempt to lessen central control over hospital boards. Boards should be given considerable responsibility for the design and construction of buildings and allowed to spend their recurrent grants as they wish. Sir Robert's second main proposal is for a Health Service Ombudsman, possibly associated with a Select Parliamentary Committee on Health, through which valuable and unbiased evidence would flow to Parliament. Sir Robert argues that the creation of an Ombudsman would take away the strain of the petty Parliamentary Question without lessening the standards and accountability inherent in a public service. Thirdly, experiments should be made in ending the tripartite structure of the Service—for example, by associating general practice with hospital practice. In this way "urban general practice would come alive again." Finally, he argues, more value must be got out of the same amount of money, both by sensible economies and by greater efficiency.

Unlike some of the alternatives proposed, this last suggestion would cost nothing and could be put into practice more or less immediately. Nevertheless, it is only one of several important changes that must be made if our Health Service is to compare with those in many other countries. All who are striving to improve the Service will find much useful guidance in this booklet.

³ Tizard, J., *Community Services for the Mentally Handicapped*. London, 1964.

⁴ — and Grad, J. C., *The Mentally Handicapped and their Families*. London, 1961.

⁵ *Stress in Families with a Mentally Handicapped Child*. Report of a working party set up by the National Society for Mentally Handicapped Children. London, 1967.

⁶ Masland, R. L., Sarason, S. B., and Gladwin, T., *Mental Subnormality: Biological, Psychological and Cultural Factors*. New York, 1958.

Koch, R., Galiker, B. V., Sands, R., and Parmelee, A. H. Sr., *Pediatrics*, 1959, 23, 582.

Jensen, R. A., *Amer. J. Psychiat.*, 1950, 106, 830.

¹ Powell, J. E., *A New Look at Medicine and Politics*, 1966. London.

² *Is There an Alternative?*, 1967, B.M.A., Tavistock House, Tavistock Square, London W.C.1. Obtainable from the Publishing Manager, B.M.J., price (including postage) 7s. 6d.

Papers and Originals

Prevention of Rh-Haemolytic Disease*

C. A. CLARKE,† M.D., SC.D., F.R.C.P.

[WITH SPECIAL COLOUR PLATE FACING PAGE 8]

Brit. med. J., 1967, 4, 7-12

The story of the Liverpool research to prevent Rh iso-immunization is a simple one, and its origins were unusual in that they stemmed from breeding Lepidoptera.

Single Gene Differences and the Origin of a Supergene in *Papilio* Butterflies

Plate 1 shows the Swallowtail butterfly *Papilio machaon*, which in this country flies in the Norfolk Broads. All that needs to be noted is that it is yellow. Plate 2 shows a related species, *Papilio asterias*, common in North

distasteful model, *Parides coon* (Plate 5b). In both model and mimic it should be noted that (1) tails are present, (2) the white "window" of the hindwing is small, and (3) the body is yellow. Plate 5c is a non-mimetic form (*agenor*) of *P. memnon*, and breeding data appear to show that *achates* is dominant to *agenor* and that there is a single gene difference between the two forms. However, the matter is not as simple as this, for occasionally rearrangements take place, and Plate 5d shows a bred *memnon* insect where, though tails are present and the "window" is small, yet the body is black. This suggests that crossing-over has occurred and that the single gene is in fact a supergene composed of several closely linked loci (Fig. A).

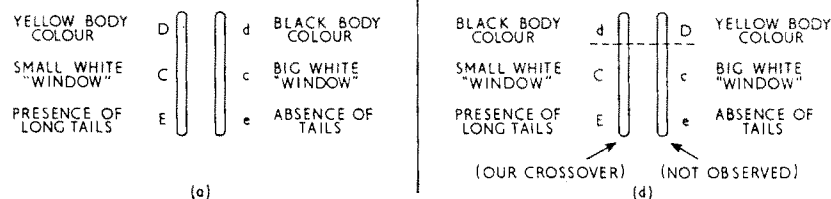


FIG. A.—Chromosomal arrangement of insects (a) and (d) in Plate 5.

America, and it will be seen that here the ground colour is black. In 1953, having earlier learnt how to hand-pair swallowtails (Clarke, 1952), hybridization between *P. machaon* and *P. asterias* was carried out (Clarke and Knudsen, 1953). The cross proved fertile, and in Plate 3 it will be seen that the F_1 hybrid was black and remarkably similar to the American parent. Though the hybrids were sterile *inter se*, yet it was possible to obtain back-crosses, and in the one to *P. machaon* there was clear-cut segregation (Plate 4), indicating a single gene difference as regards ground colour between the two species, black being dominant to yellow. During this study I met P. M. Sheppard, and it was decided to use the hand-pairing technique to investigate the phenomenon of mimicry, first in an African species, *P. dardanus* (Clarke and Sheppard, 1956, 1958, 1959, 1960), and later in a South-east Asian species, *P. memnon* (Clarke *et al.*, in press).

In mimicry certain butterflies, particularly tropical ones, resemble others, the models (often belonging to quite different families), which are distasteful to predators, particularly birds. Models and mimics usually fly together, and birds which have sampled the distasteful models tend to leave the mimics alone even though these are highly palatable. Plate 5a shows a mimetic form (*achates*) of *P. memnon* together with the

It was this type of finding (originally in *P. dardanus*) and the many examples of genic interaction in the *Papilio* species which directed our attention to the rhesus blood group system, where crossovers probably account for the rarer genotypes and where there is a marked interaction between the Rh and ABO systems.

Rh and ABO Interaction

Levine (1943) first pointed out that there is a deficiency of ABO incompatible matings—that is, those where the wife cannot safely be transfused with her husband's blood—in families where children with Rh-haemolytic disease have occurred. This is because ABO incompatibility as between mother and foetus markedly protects against Rh immunization. The original observation has since been amply confirmed, and the most reasonable explanation is that ABO incompatible foetal red cells are destroyed in the maternal circulation by the naturally occurring anti-A or anti-B before they can sensitize the mother against the D antigen (the elimination probably taking place in the liver). This theory has support from the experimental work of Stern *et al.* (1956). They injected Rh-positive blood into Rh-negative male volunteers and found much higher titres of anti-D when compatible ABO blood was injected than when incompatible blood was used. Another observation made by them (Stern *et al.*, 1961) which turned out later to be very relevant to our research was that when Rh-negative ma-

* Lumleian Lecture delivered at the Royal College of Physicians of London on 3 May 1967.

† Professor of Medicine, University of Liverpool; Consulting Physician, Liverpool Royal Infirmary and Broadgreen Hospital, Liverpool. Director, Nuffield Unit of Medical Genetics, University of Liverpool.

volunteers were injected with Rh-positive red cells coated with complete anti-D the men did not form immune anti-D.

To test further Levine's original observation, in 1958 we carried out in Liverpool a family study in order to determine the ABO group of the sensitizing foetus in families where there was Rh-haemolytic disease (Clarke *et al.*, 1958). The number of families investigated was 91, and of these the parents of 23 are incompatible on the ABO system. In 14 of these 23 families we were able to determine the sensitizing foetus with certainty and all were compatible with the mother on the ABO system. The probability of this occurring by chance alone is less than 1 in 500. Additional support for protection by ABO compatibility, derived from this same series, was the marked deficiency of matings where the mother was O and the father was A (16 as against 33 where the mother was A and the father was O), whereas a 1:1 ratio would be expected if no protection existed. Nevertheless protection is not invariable—in a different study we did find one ABO incompatible sensitizing foetus, and it has also been described by other authors (and in Table II).

Shortly after this 1958 paper it occurred to us that it might be possible to mimic the protection afforded by ABO incompatibility by giving the mother anti-D after delivery, thereby destroying any Rh-incompatible foetal cells (which we assumed had at some time crossed the placental barrier) before they had time to sensitize her. This idea was put forward at a meeting of the Liverpool Medical Institution by Finn (1960), and by this time we had already begun work to test the hypothesis. This involved injecting Rh-negative male volunteers with chromium-tagged Rh-positive cells and later giving high titre anti-D as an infusion of plasma (Finn *et al.*, 1961). It was found that when complete (saline) antibody was given enhancement of immune antibody was produced in the "treated" compared with the controls, but that when incomplete (albumin) anti-D was used then significant protection was obtained (Clarke *et al.*, 1963). Though protection in men therefore seemed possible it was still uncertain whether the technique would work in mothers, but this problem was made much easier when it became possible to detect foetal cells in the maternal circulation, and this is next discussed.

Foetal Cells in the Maternal Circulation

Kleihauer *et al.* (1957) showed by means of an acid elution technique that it was possible to demonstrate and count foetal cells among a population of adult red cells, the latter appearing as ghosts and the former as dark refractile bodies. Goursky *et al.* (1959) first used this method to detect foetal cells in the blood of women after delivery, and it was their paper which decided us to use the technique in our work. Our investigations showed that, while foetal cells can be demonstrated occasionally in the maternal circulation throughout pregnancy, they occur much more often and in greater numbers near or after delivery. Again, and most important from the protection point of view, the number of foetal cells found in the maternal circulation near or just after delivery correlated well with the frequency of the formation of immune anti-D in the mother six months later (Woodrow *et al.*, 1965; Woodrow and Finn, 1966). It was these findings together with our results in the volunteers which strengthened our view that giving anti-D to mothers after delivery might be effective. We therefore decided to carry out clinical trials, but before discussing these it is necessary to mention some important points relating not only to our work but also to that of others.

(1) Counting of Foetal Cells and Accuracy of the Acid Elution Technique

In most of our work the foetal cell score has been the number of foetal cells found in 50 low-power fields, and very roughly

we assess that a score of 1-4 implies less than 0.25 ml. of foetal blood in the maternal circulation, a score of 5-60 means approximately 0.25-3 ml., and a score of over 60 means more than 3 ml. of foetal blood (Clarke *et al.*, 1963; Woodrow *et al.*, 1965). In this paper the term "significant bleed" means either of the last two.

A more accurate method of scoring is to relate the number of foetal to the number of adult cells, and Table I shows the result in our laboratory of a test carried out "blind" from material sent to us by Professor P. L. Mollison in which varying proportions of adult and foetal cells (samples A-E) were mixed. It will be seen that though our results (Mollison, personal communication) are not particularly impressive, yet the findings are in the right order of correctness though we failed to detect any cells in the most highly dilute mixture (sample D).

TABLE I.—Accuracy of the Acid Elution Technique in Our Laboratory (See Text)

	A	B	C	D	E
No. of foetal cells observed (two observers)	3+4	0+0	60+58	0+0	0+0
Ratio of total foetal cells to total number of adult cells scanned (our estimate) ..	1/50,000	—	1/3,000	—	—
Correct result	1/17,000	0	1/1,070	1/37,000	0

(2) Difficulties in Scoring

There are several inherent difficulties in the interpretation of the slides, because the acid elution technique does not distinguish between maternal and foetal Hb F. Maternal Hb F levels are increased in thalassaemia and in some other haematological disorders, and there may also be an increase in maternal Hb F during pregnancy. False positive results may also occur in association with a marked reticulocytosis. With experience it is usually, though not invariably, possible to identify those conditions with a high maternal Hb F, because the latter is usually unevenly distributed among many cells rather than concentrated in a few, as it is in a true transplacental haemorrhage (Woodrow and Finn, 1966). In a few cases this distinction is, however, not possible (see W.H.O. Report, in press).

(3) Foetal Cell Count and ABO Incompatibility

Table II shows well the effect of ABO incompatibility in reducing the foetal cell count in 1,000 Rh-negative primigravidae, the information kindly being supplied by Dr. C. C. Bowley, of Sheffield, who has been working with us in the group project (see *Brit. med. J.*, 1966). The reason why foetal cells survive in some of the ABO incompatible cases is because destruction is not always complete, and also because in certain cases the blood has been examined so quickly after delivery that there has not been time for the cells to be eliminated.

TABLE II.—Comparison of Foetal Cell Counts in Foeto-maternal ABO Compatibility and Incompatibility (See Text)

Foetal Blood	Significant Bleeds		Insignificant Bleeds		No Bleed		Total
	No.	%	No.	%	No.	%	
ABO compatible: D-positive	85	18.6	184	40.2	189	41.2	458
D-negative	70	20.2	147	42.2	131	37.6	348
ABO incompatible: D-positive	5	4.2	28	23.5	86	72.3	119
D-negative	3	4.0	20	26.7	52	69.3	75
Total ..	163		379		458		1,000

(4) Similar Research in the U.S.A.

Gorman, Freda, and Pollack, who started experimental prevention of Rh-haemolytic disease independently of the Liverpool group, were not seeking ways and means of eliminating foetal

C. A. CLARKE: PREVENTION OF Rh-HAEMOLYTIC DISEASE

Plates 1-5 and Fig. A show the genetic investigations in *Papilio* butterflies which led to the Rh research.



PLATE 1
*Papilio
machaon.*

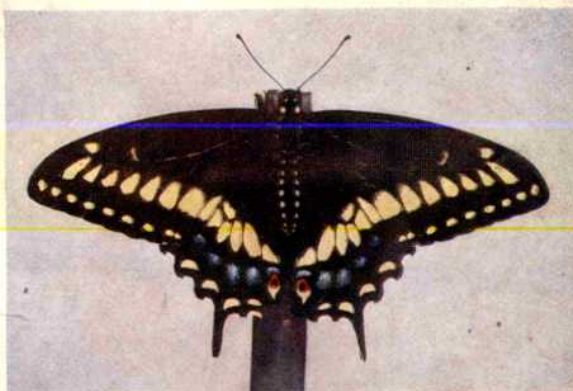


PLATE 2
*Papilio
asterias.*



PLATE 3
F¹ hybrid.



PLATE 4
Back-cross to
P. machaon.



PLATE 5a
*P. memnon
f. achates.*

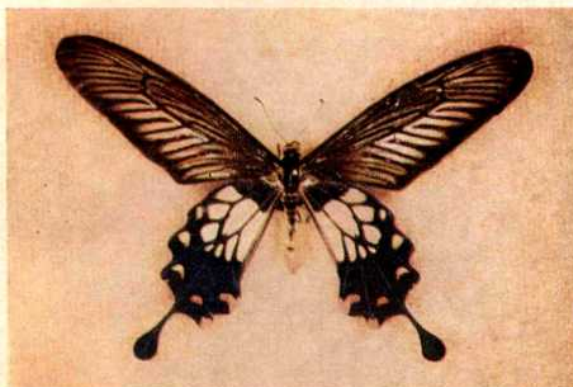


PLATE 5b
P. coon.



PLATE 5c
*P. memnon
f. agenor.*



PLATE 5d
Bred insect
showing
cross-over of
gene
controlling
body colour
(see Fig. A).

cells (Freda and Gorman, 1962; Freda *et al.*, 1964). Rather they tried to put to practical use the finding of Smith (1909) that mixtures of diphtheria toxin and antitoxin, with antibody in excess, did not immunize when injected. Later it had been shown that if specific antibody is given passively to an individual subsequent injections of antigen completely fail to immunize, provided that there is a state of antibody excess at all times. Because of this, in the early New York experiments with male Rh-negative volunteers, the antibody injection was given before the Rh-positive cells were injected (Gorman *et al.*, 1963; Freda *et al.*, 1964) (see McConnell, 1966, and also Clarke, 1966).

There may, in fact, be no very great difference between our rationale and theirs, but the important contribution which the U.S.A. workers made was the introduction of anti-D gammaglobulin rather than plasma. Anti-D gammaglobulin carries no risk of jaundice, and being given intramuscularly is a much more convenient preparation to administer, and as soon as we knew of the U.S.A. advance we switched over to gammaglobulin, which has been made for us from the plasma of our hyperimmunized male volunteers by Dr. W. d'A. Maycock, Mr. L. Vallet, and their colleagues at the Lister Institute.

Clinical Trials

In May 1964 we decided to give, within 48 hours of delivery, 5 ml. of gammaglobulin containing incomplete anti-D (usually with a titre of between 1 in 1,280 and 1 in 4,096 in albumin with R_{17} cells). This was given intramuscularly to alternate primiparae in whom the foetal cell score was 5 or more, and we decided to analyse this trial when about 70 controls and 70 treated had been followed up for at least six months. The results were highly satisfactory and were reported last year (*Brit. med. J.*, 1966). Of the 78 treated none had for certain produced immune antibody whereas 19 of the 78 controls had done so.

Similar trials, though not restricted always to primiparae and to "high risk" cases, have been in progress in U.S.A. and Germany, and Table III gives the overall results, so far as we know them, up to July 1967. It will be seen that at six months only one woman has become immunized in the treated group, a much better result than in our male volunteers. However, the controls pose some problems. It will be seen that in the various centres there is considerable heterogeneity among them and we do not know for certain the cause of this. While the figure in the "Liverpool group" is explicable because high-risk cases only were treated, yet this was not so elsewhere; but it may be that different obstetrical practices are responsible for greater or less foeto-maternal bleeding. In this connexion it is of interest that Worledge (1966) has shown in Nigeria that the Rh-immunization rate is only about one-third of what it is in this country, and this is probably not to be explained by the lack of antigenicity of the common R^0 antigen, since the

TABLE III.—Combined Results from Various Centres. Immune Antibody Results Six Months and Later in Controls and After Injection of Anti-D Gammaglobulin

	Control				Treated			
	Total	Imm.	Not Imm.	% Imm.	Total	Imm.	Not Imm.	Total in Study
Liverpool group (first trial)	136	29	107	21	131	1*	130	267
Germany ¹	76	3	73	4	76	0	76	152
Columbia, New York ²	113	14	99	12	163	0	163	276
Long Beach, California ³	176	21	155	12	176	0	176	352
Cornell, New York ⁴	58	5	53	9	41	0	41	99
Edinburgh ⁵	40	3	37	8	41	0	41	81
Totals	559	75	524	13	628	1	627	1,227

¹ Schneider and Preisler (1966) and Schneider (personal communication).

^{2,3,4,5} Robertson (personal communication).

* Though there is no doubt about the complete failure in this case, it may be instructive. The patient developed a sharp local reaction to the anti-D gammaglobulin, and we then learnt that she had received early in pregnancy a prophylactic dose of anti-rubella gammaglobulin. Whether this has any bearing on the failure is being investigated. (See Wilson and Steinberg, 1965.)

immunization rate after transfusion with Rh-positive blood is about the same as it is here.

Persistence of Injected Anti-D Gammaglobulin

The U.S.A. group have carried out tests to see how long the passive antibody can be detected and Table IV shows their results. We also seldom find passive antibody after six months, but occasionally traces have been detected for longer by an enzyme technique. For example, at the time of the original analysis of our Liverpool group clinical trial (*Brit. med. J.*, 1966) there were three cases among the 78 treated where it was uncertain whether it represented only the remains of the injected anti-D. This in fact turned out to be the case since in all three mothers the antibody eventually disappeared, though in one case it was thought to have lasted for as long as 13 months.

TABLE IV.—Post-delivery Passive Rh-antibody Titres. New York Series (Pollack *et al.*, 1967)

Antibody Titre	Weeks Post-injection and Number of Patients in Each Category		
	5-7 Weeks	12-16 Weeks	24-26 Weeks
0	0	24	77
1	1	15	1
2	3	29	
4	15	18	
8	48	11	
16	58	2	
32	17		
64	3		
Totals	145	99	78

Subsequent Pregnancies (all Centres) up to June 1967

Though the six months' results were highly satisfactory there was always the possibility that the anti-D was only masking immunization and that in the next pregnancy the treated women would produce overt antibodies and "catch up" with the controls. The data in Table V strongly suggest that this is not the case, because none of the women who received the anti-D gammaglobulin after their previous preg-

TABLE V.—Combined Results. Subsequent Pregnancies (All Centres) Up to June 1967. Rh-positive ABO Compatible Infants

	Control				Treated		
	Total	Imm.	Not Imm.	% Imm.	Total	Imm.	Not Imm.
Liverpool group (first trial)	26	4	22	15	21	0	21
Germany ¹	7	3	4	43	9	0	9
Columbia, New York ²	14	4	10	29	21	0	21
Long Beach, California ³	14	3	11	21	13	0	13
Cornell, New York ⁴	1	1	0	100	2	0	2
Edinburgh ⁵	1	0	1	0	0	0	0
Totals	63	15	48	24	66	0	66

¹ Schneider and Preisler (1966) and Schneider (personal communication).

^{2,3,4,5} Robertson (personal communication).

nancy has, in fact, produced immune rhesus antibodies after having had a subsequent Rh-positive ABO compatible baby, whereas 15 further cases in the controls have done so. Nevertheless, larger numbers of second pregnancies are needed before concluding that the prophylaxis is really of the very high order it appears to be at present.

Second Liverpool Trial

Having determined that 5 ml. of anti-D gammaglobulin protected the high risk cases, we decided in June 1966 to start a second trial, using only 1 ml. of anti-D, this again being given to alternate primiparae, but now only to those who had a foetal cell score of 0-4 cells, inclusive. Using these criteria, we knew

we should get many more cases, and it seemed highly likely that the immunization rate would be much lower. The indications are that this is so, since at the time of writing (July 1967) 3 out of the 54 controls have become immunized compared with one out of 51 treated, these all having been followed up for six months or more. The treated woman who produced the antibody did so between the fourth and seventh month of a second pregnancy. Whether this means that 1 ml. of the Liverpool anti-D gammaglobulin is too small a dose (see below), or whether the mother is one of the rare cases where antibody is produced in the first "at risk" pregnancy (to which this pregnancy approximates), remains to be seen. If the former is the case more antibodies will develop in the treated in this trial.

Because of the good results from the five Liverpool maternity units in the first trial, all primiparae in these hospitals where the cell score is 5 or more are now being given 5 ml. of anti-D gammaglobulin.

Indications for Prophylaxis in Rh-haemolytic Disease

The feasibility of a procedure is no indication for carrying it out, and, though there seems little doubt that the giving of anti-D is prophylactic, yet it has been suggested that the treatment is not without risk, and that the immunization of large numbers of volunteers and the mass inoculation of Rh-negative women is not justified. The critics feel that this is particularly so because only a small proportion of women at risk become immunized, and, even if they do, modern methods of treatment mean that the majority of children are saved. This clearly needs consideration and the risks must first be assessed.

Risks to the Mothers

In our experience the initial injection is safe. We have observed very occasionally local reactions, sometimes associated with fever, for 24 hours, but these are most exceptional and usually there is no upset of any kind. With anti-D gammaglobulin there appears to be no risk of causing homologous serum jaundice, since if the virus is present it is eliminated in gammaglobulin prepared by the alcohol or other fractionation procedure (Mollison, 1967). We have twice given it in error to women who were later found to be weakly Rh-positive (D^u) and no reaction of any kind was observed, and probably there would be no serious trouble if the injection were given to women who were of the more usual Rh-positive types. There remains the question of the possibility of the mother becoming immunized to the gammaglobulin itself. We have investigated this with the help of Dr. Sylvia Lawler, who has tested the Gm groups in 20 of our treated women and in 20 controls, both matched approximately for the size of foeto-maternal "bleed." No anti-Gm was found in the controls, but it was in one treated case and the details of this are as follows:

Anti-Gm Study.—Mrs. N., a treated mother, has anti-Gm antibody, of Gm^{a+} specificity, in her serum not present before delivery. She herself is Gm^{a-} and so is her husband. Her mother, however, is Gm^{a+}, and Mrs. N. may have been originally sensitized from her mother, our gammaglobulin acting as a secondary stimulus.

It seems certain that here the gammaglobulin was responsible for the development of the overt anti-Gm, though it is possible that the primary stimulus was derived from the mother of the treated woman. However, the risks of a serious anaphylactic reaction if gammaglobulin needed to be given again in a subsequent pregnancy appear to be small, severe anaphylaxis being likely to occur only if the patient is hypogammaglobulinaemic (Grubb *et al.*, 1965).

When considering risks it seems right to take into account the views of patients. They in general are in no doubt about

wanting prophylaxis, and it is in fact our controls who sometimes complain of being guinea-pigs.

Risks to the Volunteers

Deliberate immunization of Rh-negative volunteers carries the slight risk of homologous serum jaundice, but this can be minimized by injecting washed Rh-positive cells and always deriving these from a donor who has been known to have given blood to at least 10 recipients all of whom have been kept under supervision for a period of six months and not developed jaundice (see W.H.O. Report, in press). Nevertheless, the hazard remains and there is a genuine difference of opinion about the advisability of immunizing men on a large scale at this stage. The view of many is that supplies of anti-D from women who have been naturally immunized, or from men and women who have developed antibodies as the result of transfusion, should be used first. This is reasonable, but there are often difficulties in tapping these supplies, and they are in any case a dwindling source. The contrary view is that if protection can be obtained by the use of small quantities of anti-D when this is hyperimmune (donors repeatedly restimulated) then it would be preferable to have small numbers of Rh-negative volunteers in each region and the necessary supplies obtained by plasmapheresis. The extent of the problem if this were the procedure adopted is as follows. If it is assumed that for every million of a Caucasian population 1,600 Rh-negative women will give birth each year to an Rh-positive ABO compatible infant and that the suppressive dose of anti-D gammaglobulin is 1 ml. (but see below), then about 90 litres of anti-D antibody-containing plasma will be needed annually. Using plasmapheresis and assuming that each donor gives half a litre of plasma 12 times a year, 15 donors with acceptable anti-D antibody titre would be required per million of the population.

We think that the risks outlined above are very small and should be accepted. In all prophylactic inoculations large numbers of people are injected unnecessarily, but one of the chief functions of a clinician is to allay anxiety, and the evidence strongly suggests that Rh-negative women need no longer be anxious about their blood group. Also, though many babies are saved by medical care, yet the stillbirths remain a problem, and in general there is a great deal of distress in a not inconsiderable number of families and it seems likely that this can be avoided.

Lastly, the fact that exchange transfusion is feasible (though expensive, time-consuming, and not always successful) is no indication for preferring it to stopping the trouble at the source.

Problems Remaining to be Solved

(1) Latest Time at Which Gammaglobulin can Effectively be Given

In our trials the anti-D has been given within 48 hours of delivery and in the U.S.A. up to 72 hours. Since, for a variety of reasons, "at risk" patients might not be identified quickly, it is important to find out how long after delivery an injection of gammaglobulin is effective, and we are at present planning a trial in volunteer men to see if it is still protective when given a week after the injection of Rh-positive cells.

(2) Prophylaxis During Pregnancy

The results of the clinical trials to date giving the injection after delivery have been better than anticipated. It may, however, be that on occasion an effective immunizing dose of Rh-positive cells crosses the placenta during pregnancy. Zipursky *et al.* (1965) have shown that it is a safe procedure to give anti-D gammaglobulin during pregnancy, and while

we do not know whether this is protective yet it does not cause anaemia in the baby, though the Coombs test is occasionally positive. If failures with the conventional treatment after delivery do occur, their work would have great practical importance.

(3) Duration of Protection

The length of time during which injected anti-D affords protection is uncertain, but Chown (1966, personal communication) gives details of an interesting experiment which is summarized here. Three groups of six men in a local penitentiary were injected with 2 ml. of foetal Rh-positive blood. Then, 48 hours later: group (a) received 5 ml. of anti-D, group (b) received 1 ml. of anti-D, and group (c) received 1 ml. of commercial gammaglobulin.

Immune antibody production six months later was: group (a) 0/5 (1 man released), group (b) 0/6, and group (c) 3/6. At this time a further 2 ml. of Rh-positive foetal cells was given to each man.

Immune antibody production 10 months later was: group (a) 0/1, group (b) 0/3, and group (c) 5/5 (9 men released).

Chown and his colleagues interpreted these results as supporting the concept of a suppressive effect on the potential specific antibody-forming cellular system, and as being in line with the experimental work of Finkelstein and Uhr (1964) and Rowley and Fitch (1964). The Canadian workers go further and think that the protection may last even after the antibody is no longer detectable.

On the other hand, Freda *et al.* (1966) showed that two out of eight of their previously protected male volunteers were still (10 months after their last injection of anti-D) capable of producing immune antibody when given a fourth and fifth antigenic stimulus *without* the anti-D gammaglobulin cover. The matter therefore remains open, but is of great current interest not only in this field but also in others such as in the prevention of autoimmune disease and in tissue transplantation.

(4) Optimal Dose of Anti-D Gammaglobulin

This is the most important current problem. Clearly it is meaningless to talk of 5 or 1 ml. of gammaglobulin and its strength must be assessed in some way. Titre has generally been used in the past, but this for technical reasons varies greatly in different laboratories, and, moreover, it only measures the amount of antibody which is combined with antigen on the red cell. Since the reaction between antibody and antigen is reversible, there is always some free antibody present in the plasma, of which titre takes no account. Nevertheless, this fraction may be important if central inhibition of the antibody-forming cells is of more account in preventing immunization than the blocking of the antigen sites on the red cells (see above). Therefore the total amount of anti-D in $\mu\text{g. per ml.}$ is probably the most reliable measure, and it can be estimated by various labelling procedures (Hughes-Jones, 1967; Goldsmith *et al.*, in press).

However, for the present, since the precise method of protection is unknown, it seems best to estimate where possible both the titre *and* the total amount of anti-D present.

It is uncertain how the dose of anti-D in $\mu\text{g. per ml.}$ has been related to its effectiveness in suppressing immunization, but some information is available. In the first clinical trial carried out by the Liverpool group, 5 ml. of gammaglobulin containing incomplete anti-D with a titre of usually between 1 in 1,280 and 1 in 4,096 in albumin with R_{2r} cells were used. Though the concentration of this is not known, it is believed to have been similar to later ones that have been estimated, and if so the 5 ml. contained about 1,000 $\mu\text{g.}$ of anti-D, and this dose

appears to be nearly always protective. (For this and other assessments of anti-D in $\mu\text{g. per ml.}$ I am indebted to Dr. N. C. Hughes-Jones.)

However, both the New York and Winnipeg groups (W.H.O. Report, in press) have experimental evidence that a smaller amount is also effective. The former found that 0.1 ml. of their anti-D preparation protected four volunteers when given after 10 ml. of blood on six occasions, and the latter report that 1.5 ml. of another anti-D preparation protected 12 volunteers when injected with 2 ml. of blood. The anti-D concentrations of these two gammaglobulins, though also unknown, are thought to be of similar potency to later ones from the same centres, and if this is so the amount injected was of the order of 150 $\mu\text{g.}$ of anti-D in the New York experiments and 300 $\mu\text{g.}$ in those of Zipursky and his colleagues in Winnipeg. On the other hand, we have to remember that in her second pregnancy an immune antibody appeared in a woman in our second trial who had been given 1 ml.—that is, about 200 $\mu\text{g.}$ —of anti-D.

At lower doses it would seem from work carried out in Germany and New York (see also W.H.O. Report, in press) that a dose of the order of 10 $\mu\text{g.}$ of anti-D antibody is insufficient to prevent immunization. While these are only interim results they may serve as a basis for further experiments, but one fact is quite clear—namely, that the U.S.A. gammaglobulin is considerably stronger than that which we are using. Additional evidence that this is so is found when testing for passive antibody about 48 hours after a 1-ml. injection. Robertson (personal communication), using this dose of U.S.A. gammaglobulin, often finds a titre of 1 in 8, while, on the other hand, our 48-hour antiglobulin test with 1 ml. of the Lister product is always negative, the passive antibody being detected only by an enzyme technique. On using 5 ml. of the Lister preparation, as in the first Liverpool trial, our 48-hour antiglobulin titre is usually about 1 in 4. A particular case met with recently also gives some preliminary information about dosage (Gilliver, 1967).

A 21-year-old primigravida, blood group A rhesus (D) negative with no antibodies detectable at 34 weeks, was admitted to hospital on 12 September 1966.

After 54½ hours, an 8 lb. 5 oz. (3,770 g.) male infant was born by assisted breech delivery. His condition was satisfactory at birth but later the respirations became shallow and grunting and convulsions began, first right-sided and later generalized. About 24 hours after birth the infant's haemoglobin was 9.8 g./100 ml. and a blood film showed intense erythroblastosis. The baby's blood group was A Rh-positive and the direct Coombs test was negative.

Maternal blood was found to contain vast numbers of foetal cells, and this was confirmed by mixed-field agglutination with a saline anti-D serum. In a blood sample sent to Liverpool it was estimated that there were roughly 3,400 foetal cells per 50 low-power fields, and this was probably equivalent to about 170 ml. of foetal blood.

Seventy-two hours after delivery 5 ml. of gammaglobulin obtained from Liverpool was given, and 36 hours later the volume of foetal blood had fallen to about 80 ml., and at this time the Coombs test was positive. Free antibody at a titre of 1 in 4 was still present nine days after the injection, but the foetal cell score was 3 (representing less than 0.25 ml. of foetal blood) and the direct Coombs reaction had become negative.

Three and seven months later the follow-up revealed no antibodies detectable by the saline, albumin, Coombs, or enzyme techniques.

The baby improved satisfactorily after a transfusion of 85 ml. packed cells.

It will be interesting to see what happens in a subsequent pregnancy, but 5 ml. of the Liverpool gammaglobulin is evidently effective in clearing a very large T.P.H., and if this is, as we think, important in protection then it may well be that 5 ml. is an unnecessarily large dose in the majority of cases (see also Mollison and Hughes-Jones, 1967). But it must be remembered that in mismatched transfusions only about 50% of Rh-negative individuals are immunized by giving 1 pint (570 ml.) of Rh-positive blood (Mollison, 1967).

Until the mechanism of suppression of primary immunization is more precisely known, factors other than anti-D concentration and titre may be important. Thus it is possible that there may be variation in the biological activity of anti-D antibody obtained from different donors, and anti-D preparations are now made from pools of at least 10 donors. It will be interesting to see the results of clinical trials where the relative effectiveness of anti-D antibody derived from mothers who have had severely affected babies but who have not been deliberately restimulated is compared with that from donors who have been.

Summary

Genetic studies in *Papilio* butterflies, particularly those concerned with the evolution of mimicry, led to our interest in the Rh blood groups. Here, as in the mimetic butterflies, the various phenotypes are controlled by a series of closely linked genes (a supergene) and, again as in the butterflies, there are marked genetic interactions. The most important of these, described by Levine in 1943, is that ABO incompatibility as between mother and baby is nearly always protective against rhesus immunization of the mother. The mechanism of this is uncertain, but the most reasonable explanation is that any rhesus-positive foetal cells which have crossed into the maternal circulation are destroyed by the mother's naturally occurring anti-A or anti-B before they have had time to stimulate the production of Rh antibodies.

It occurred to us that it might be possible to imitate this by giving anti-D to Rh-negative mothers in the far more usual situation where mother and baby were compatible on the ABO system, and the idea was first put forward in 1960 at a symposium on medical genetics at the Liverpool Medical Institution.

Experiments on rhesus-negative blood-donor volunteers showed that protection could be achieved provided incomplete anti-D was given, and in these early experiments plasma was used from artificially immunized males. Concurrently with this research, the acid elution technique for the detection of foetal cells in an adult red cell population was used to show that transplacental haemorrhage was commoner at or near delivery, and, furthermore, that the greater the number of foetal cells in the maternal circulation just after delivery the more likely the mother was to produce immune Rh antibodies.

Similar work in the U.S.A., using anti-D in the form of gammaglobulin, which was much safer and more convenient, was first published in 1962, and after this we too used only anti-D gammaglobulin.

Details are given of several successful clinical trials carried out in this country, the U.S.A., and Germany, in which soon after delivery the mother is given an intramuscular injection of gammaglobulin containing a high titre of incomplete anti-D.

Definite proof that Rh immunization can be prevented by this technique will rest on the immunological state of the treated women, just after they have had a subsequent Rh-positive ABO compatible baby. To date the results in these subsequent pregnancies are very encouraging, and the evidence indicates that nearly all cases of maternal Rh immunization can be prevented.

The risks to mothers and to the male volunteers are discussed and mention is made of the problem of supplies of anti-D gammaglobulin if the prophylaxis is to be made generally available. Other problems which remain to be solved, particularly the optimal dose of gammaglobulin, are outlined.

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Mortality of Bereavement

W. DEWI REES,* M.B., B.S., M.R.C.G.P.; SYLVIA G. LUTKINS,† B.SC.

Brit. med. J., 1967, 4, 13-16

"He first deceased; she for a little tried
To live without him; liked it not, and died"
—Sir Henry Wootton.

That bereavement is associated with an increased mortality rate for close relatives is an old concept that has only recently begun to receive statistical confirmation.

In 1959 Kraus and Lilienfeld reported that married people had a lower death rate at every age group than those who were widowed, single, or divorced and that there was a particularly high excess risk of mortality for young widowed people. Young *et al.* (1963) then tried to assess the "duration effect" of widowhood on the mortality of 4,486 widowers aged 55 and over and found that widowhood increased the mortality rate by about 40% in the six months following bereavement. Cox and Ford (1964) analysed data about 60,000 women awarded widows' pensions in 1927 and concluded that the mortality of widows is probably not exactly the same in each of the five years following bereavement and seems to be higher in the second year after bereavement. The need for further studies in this field was stressed by Kraus and Lilienfeld (1959) and by Young *et al.* (1963), and a survey was therefore made to assess the effect of bereavement on the mortality of close relatives in a small semirural community. This survey differed from those previously made in that it included close blood relatives as well as the widowed and because a total community study was made in an area where the investigator (W.D.R.) possessed a close personal knowledge of the people included in the survey.

Method

The survey was made in a defined area, centred upon the small market town of Llanidloes (pop. 2,350). The area was so defined that with very few exceptions all residents were patients of a single group practice. A small cottage hospital, a chronic sick unit, and an old people's residential home are situated within the area.

The name, sex, age, address, certified cause of death, and place of death of all those people normally resident in the area who died in the six-year period following 1 January 1960 were obtained from the county medical officer of health. The marital state of these people and the identity of those of their close relatives who also lived in the area were determined with the help of the practice secretaries and the secretary of the local cottage hospital. Those people were considered close relatives who were either a spouse, parent, child, or sibling. Those people who had no close relatives alive when they died were excluded from the survey. The remainder were matched by age, sex, and marital state with a similar control group known to have relatives living in the area. This was done by arbitrarily selecting alternate names from the relevant age/sex lists of the practice age/sex register. It was not found possible to match all the paired couples exactly for age or marital state, and five widowed people were paired with people still married. The identity of the close relatives of the control group was determined in a similar way for that of the survey group. In determining the subsequent mortality of close relatives in this

control group the assessment was made in each case from the time of death of the individual with whom the control had been paired.

Results

A total of 5,184 patients lived in the defined survey area; their age and sex distribution is given in Table I. During the period under review 488 residents died; 404 residents died within the survey area and 84 other residents died in hospitals or private homes outside the area; the age and sex distribution of these people is given in Table II. Of the 488 residents who died, 108 had no close relatives living in the area and they, together with the nine recorded as neonatal deaths, were excluded from the survey. The remaining 371 (76%) form the survey group; the age and sex distribution of this group is given in Table III. When the 371 residents forming the survey group died they had a total of 903 close relatives living in the area; the comparative figure for the control group is 878. The number and type of close relatives extant at the time of real or hypothetical death for both the survey and control groups are given in Table IV. The number of each type of relative who died in the years following bereavement is

TABLE I.—Age/Sex Distribution of Patients Resident Within Survey Area

Age	Male	Female	Total
0-9	375	358	733
10-19	349	303	652
20-29	296	284	580
30-39	329	297	626
40-49	313	354	667
50-59	345	357	702
60-69	288	367	655
70-79	157	228	385
80-89	65	101	166
90-99	5	13	18
Total	2,522	2,662	5,184

TABLE II.—Age/Sex Distribution of People Who Died

Age	Male	Female	Total
Neonates	5	4	9
0-9	1	1	2
10-19	3	—	3
20-29	2	1	3
30-39	3	2	5
40-49	6	4	10
50-59	29	9	38
60-69	48	35	83
70-79	67	75	142
80-89	70	93	163
90-99	10	20	30
Total	244	244	488

TABLE III.—Age/Sex Distribution of Deceased Patients (Excluding Neonates) With Close Relatives in Area

Age	Male	Female	Total
0-9	1	1	2
10-19	3	—	3
20-29	2	—	2
30-39	3	2	5
40-49	6	4	10
50-59	27	7	34
60-69	43	32	75
70-79	57	57	114
80-89	50	57	107
90-99	6	13	19
Total	198	173	371

* General Practitioner, Llanidloes, Mont.

† Research Officer, Department of Statistics, University College of Wales, Aberystwyth.

shown in Table V, and this distribution is expressed as a percentage of those at risk in Table VI.

TABLE IV.—Close Relatives Alive at Time of Actual Death (Survey Group) and Hypothetical Death (Control Group)

	Male	Female	Total
<i>Survey Group</i>			
Spouse ..	51 (5.7%)	105 (11.6%)	156 (17.3%)
Parent ..	16 (1.8%)	19 (2.1%)	35 (3.9%)
Children ..	201 (22.3%)	235 (26.0%)	436 (48.3%)
Sibling ..	123 (13.6%)	153 (16.9%)	276 (30.5%)
Total ..	391 (43.3%)	512 (56.7%)	903 (100%)
<i>Control Group</i>			
Spouse ..	51 (5.8%)	115 (13.1%)	166 (18.9%)
Parent ..	9 (1.0%)	20 (2.3%)	29 (3.3%)
Child ..	222 (25.3%)	188 (21.4%)	410 (46.7%)
Sibling ..	132 (15.0%)	141 (16.1%)	273 (31.1%)
Total ..	414 (47.2%)	464 (52.8%)	878 (100%)

Statistical Method

The following test was used to determine whether the proportion of deaths in the survey group was significantly greater than the proportion of deaths in the control group.

For large samples u is approximately normally distributed with zero mean and unit variance, where

$$u = \frac{p_1 - p_2 - \frac{1}{2}}{\left[pq \left(\frac{1}{N_1} + \frac{1}{N_2} \right) \right]^{\frac{1}{2}}}$$

which is algebraically equivalent to

$$u = a - \frac{rA}{N} - \frac{1}{2} \left[\frac{ABr(N-r)}{N^3} \right]^{\frac{1}{2}} = \sqrt{\chi^2}$$

using the customary notation for a 2×2 contingency table, and a correction for continuity.

A one-tail test is appropriate here, so a value of u greater than or equal to 1.64 will be significant at the 5% level. For

the 1% level the value of u is 2.33. For very small values of A and B exact values for the probabilities were obtained from *Tables of the Hypergeometric Probability Distribution* by Lieberman and Owen, but none of these small sample tests were significant.

The statistical significance of the differences in mortality recorded between close relatives in the survey and control groups during the first year of bereavement is given in Table VII.

All Close Relatives

The number of close relatives who died each year following bereavement is given in Table V. This shows that there is a considerable difference between the number of deaths recorded in the survey and control groups and that the difference is

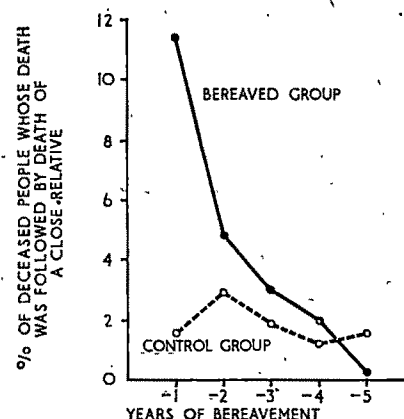


FIG. 1.—Percentage of deceased people whose death was followed each year by the death of a close relative.

greatest during the first year of bereavement. During the first year 43 (4.76%) bereaved close relatives died compared with 6 (0.68%) in the control group. This difference in risk between the two groups was found to be highly significant at the 0.001% level. During the second year the comparative figures for the bereaved and control groups were 18 (1.99%)

TABLE V.—Distribution of Relatives who Died Following Bereavement

	-1 Year			-2 Years			-3 Years			-4 Years			-5 Years			-6 Years		
	♂	♀	Total	♂	♀	Total	♂	♀	Total	♂	♀	Total	♂	♀	Total	♂	♀	Total
<i>Survey Group</i>																		
Spouse ..	10	9	19	2	7	9	3	—	3	1	2	3	2	—	2	—	—	—
Parent ..	3	—	3	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Child ..	6	1	7	1	1	2	1	1	2	—	1	1	—	1	1	—	—	—
Sibling ..	6	6	12	1	4	5	1	1	2	3	1	4	—	1	1	—	2	2
Total ..	25	18	43	6	12	18	6	4	10	4	4	8	2	2	4	—	2	2
<i>Control Group</i>																		
Spouse ..	2	—	2	1	4	5	2	—	2	—	—	2	—	4	4	—	—	—
Parent ..	1	—	1	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—
Child ..	—	—	—	3	—	3	—	—	3	—	—	—	—	1	1	—	—	—
Sibling ..	1	2	3	2	1	3	—	—	3	2	1	3	1	—	1	1	—	1
Total ..	4	2	6	6	5	11	2	5	7	4	1	5	2	4	6	1	—	1

TABLE VI.—Distribution of Relatives who Died Following Bereavement Expressed as a Percentage of those at Risk each Year

	-1 Year			-2 Years			-3 Years			-4 Years			-5 Years			-6 Years		
	♂	♀	Total	♂	♀	Total	♂	♀	Total	♂	♀	Total	♂	♀	Total	♂	♀	Total
<i>Survey Group</i>																		
Spouse ..	19.6	8.5	12.2	4.9	7.1	6.6	7.7	—	2.5	2.8	2.2	2.4	5.7	—	1.6	—	—	—
Parent ..	18.8	10.5	14.3	14.3	—	6.7	9.1	11.6	10.7	—	6.6	3.6	—	7.1	4.2	—	—	—
Child ..	3.0	0.4	1.6	0.5	0.4	0.5	0.5	0.4	0.5	—	—	—	—	—	—	—	—	—
Sibling ..	4.8	3.9	4.3	0.9	2.7	1.9	0.9	0.7	0.8	2.4	0.7	1.6	—	0.7	0.4	—	0.7	0.4
<i>Control Group</i>																		
Spouse ..	3.9	—	1.2	2.0	3.5	3.0	4.2	0.9	1.9	4.3	—	1.3	—	3.6	2.6	—	—	—
Parent ..	11.0	—	3.4	—	—	—	—	12.5	3.6	—	—	—	—	—	—	—	—	—
Child ..	—	—	—	1.3	—	0.7	—	—	—	—	—	—	0.5	—	0.2	—	—	—
Sibling ..	0.8	1.4	1.1	1.5	0.7	1.1	—	2.6	1.1	1.6	0.7	1.1	0.8	—	0.4	0.8	—	0.4

and 11 (1.25%); the difference between these figures was not significant.

The difference between the groups is exemplified further by Fig. 1; this shows the percentage of deceased people whose death was followed each year by the death of a close relative. It shows that close relatives of 11.6% (43) of the survey group died within a year of bereavement and that the corresponding figure for the control group was only 1.6% (6). It also shows that while the mortality rate for the control group shows a relatively small fluctuation over the six-year period there is an apparent change in pattern for the survey group, and the mortality rate for the bereaved group remains higher than that of the control group for the first three or four years following bereavement.

The risk for male relatives was found to be greater than for female relatives. During the first year of bereavement 6.4% of the 391 male relatives at risk died, compared with 3.5% of the 512 female relatives. This difference in risk between the sexes was significant at the 5% level.

Widows and Widowers

During the first two years of bereavement the mortality rate for widowed people in the bereaved group was higher than for those in the control group. The difference between the two groups is shown in Tables V and VI. Of recently widowed people, 12.2% died during the first year of bereavement, 6.6% of those at risk died during the second year, and 2.5% during the third year. Though 12.2% of widowed people in the bereaved group died during the first year of bereavement only 1.2% of the control group died. This increase in risk for widowed people during the first year of bereavement was significant at the 0.01% level.

The mortality rate for widowers was considerably higher than the mortality rate for widows. During the first year of bereavement 19.6% of widowers and 8.5% of widows in the bereaved group died. This difference in risk between the widowers and widows was significant at the 5% level.

Of the bereaved widowers, 13.7% died during the first six months of bereavement, 5.9% died during the second six months, and 4.9% died during the following 12 months. This different mortality rate for widowers during the first and second six months of bereavement was significant at the 1% level and confirms the findings of Young *et al.* (1963) that the mortality rate of widowers is particularly high during the first six months of bereavement. Conversely, the suggestion by Cox and Ford (1964) that the mortality of widows is higher than average in the second year of bereavement was, in this survey, found to be not significant at the 10% level and therefore not confirmed.

Close Relatives Excluding Widowed People

Apart from widowed people, there were 747 close relatives in the bereaved group and 712 in the control group. During the first year of bereavement 3.21% of these close relatives died in the survey group compared with 0.56% in the control group. This increase in risk for bereaved relatives was significant at the 0.1% level.

The mortality rates for the bereaved parents, children, and siblings are shown in Tables V and VI. These show an increase in mortality during the first and sometimes the second year of bereavement for each type of relative and that in each case the increase in mortality for the bereaved male relative is greater than for the female relative. The statistical significance of the differences in mortality determined for these various groups is shown in Table VII.

TABLE VII.—Statistical Significance of the Differences in Mortality Recorded During the First Year of Bereavement

	Total	Male	Female
All relatives	0.001	0.01	0.1
Parents	N.S.	N.S.	N.S.
Widowed	0.01	5.0	1.0
Children	5.0	5.0	N.S.
Siblings	5.0	N.S.	N.S.
All relatives (excluding widowed people)	0.1	1.0	N.S.

N.S. denotes that the levels were not found to be statistically significant.

Place of Death

An assessment was made to determine whether the place at which people die is related in any way to the subsequent mortality of close relatives. The various places at which death occurred and the number of deaths which occurred at each site are given in Table VIII. This shows that in this area, though little difficulty is experienced in admitting the old, the chronic sick, and the dying into hospital, a very high proportion of people die at home. Because the place of death is often chosen by the patient, his family, or the people caring for him, the fact that 25.9% of the people without close relatives die at home is noteworthy.

TABLE VIII.—Places at Which People Died

	Home	Hospital	Chronic Sick Unit	Old People's Home	Other Sites	Total
<i>Original Sample</i>						
Male	108	86	24	12	14	244
Female	104	70	57	8	5	244
Total	212	156	81	20	19	488
%	43.4	32.0	16.6	4.1	3.9	100
<i>No Close Relatives</i>						
Male	10	9	12	9	2	41
Female	18	12	29	6	1	67
Total	28	21	41	15	3	108
%	25.9	19.4	38.0	13.9	2.8	100
<i>Those with Close Relatives</i>						
Male	98	78	12	3	12	203
Female	86	57	28	2	4	177
Total	184	135	40	5	16	380
%	48.4	35.6	10.5	1.3	4.2	100

Table IX gives the percentages of people who died each year, at the sites listed, whose death was followed by the death of a close relative. Close relatives of 13 (7.1%) of the 184 people who died at home died within the ensuing year, compared with the relatives of 17 (12.6%) of the 135 people who died in a general hospital and 7 (17.5%) of the 40 people who died in a chronic sick unit. Close relatives of 24 (13.7%) of the 175 people who died in hospital died within the following year. It seems, therefore, that the risk to a bereaved close relative of dying within one year of bereavement is determined, in part, by the place of death of the first relative. If the first relative dies in hospital the bereaved close relatives carry twice the risk of dying within a year of bereavement than if the first relative had died at home. This increase in risk for bereaved close relatives when the original death occurred in hospital compared with at home was significant at the 5% level.

TABLE IX.—Percentages of People Who Died Each Year, At the Sites Listed, Whose Death was Followed by the Death of a Close Relative

	Years of Bereavement					
	-1	-2	-3	-4	-5	-6
Died at home	7.1	5.0	1.2	2.5	0.6	0.6
Died in hospital	12.6	3.7	3.8	4.0	2.0	1.0
Died in chronic sick unit	17.5	9.1	6.7	—	—	—
Died in old people's home	—	—	20.0	—	—	—
Died at other sites	37.5	—	20.0	—	—	—

Similarly, a difference in risk was found to occur when the original death occurred at some site other than at home or hospital. It was found that 19 people died at sites other than hospital or home and that 16 of these people had close relatives living in the area. The "other sites" included roads, fields, a cemetery, chapel, shop, wood, bowling-green, and pond. Deaths at these sites were invariably sudden and the shock to relatives consequently great. Their grief was often increased by the need for a necropsy and inquest. Six (37.5%) of these deaths at other sites were followed within one year by the death of a close relative, and of the close relatives at risk during this period 11.6% (6) died.

Close relatives of 13.7% of the people who died in hospital and of 37.5% of those who died at other sites died within one year of bereavement. This increase in risk for the relatives of people who died at other sites compared with those who died in hospital was significant at the 5% level.

Close relatives of 7.1% of the people who died at home and of 37.5% of those who died at other sites died within one year of bereavement. This increase in risk for the relatives of people who died at other sites compared with those who died at home was significant at the 0.01% level.

Age of Relatives who Die Following Bereavement

The age distribution of all the people resident in the area who died during the six-year period is given in Table II. The mean age of death for this group was 73.35 ± 13.8 . The mean age of those people whose death was followed within one year by the death of a close relative was 70.9 ± 13.2 . The mean age of the relatives who died during the first year of their bereave-

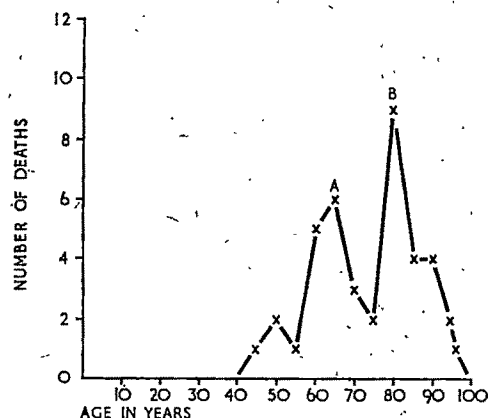


FIG. 2.—Age distribution of relatives who died within one year of bereavement.

ment was slightly lower at 69.75 ± 14.7 . These figures suggest that people who die following bereavement are on average slightly younger than the relatives who predeceased them and that they die at an earlier age than is usual for the community in which they live. Fig. 2 shows the age distribution of relatives who died within one year of bereavement. This chart is biphasic, with two modes, A and B. Histograms (not shown) of the age distribution of all the people who died in the area and of those people whose death was followed within one year by the death of a close relative each have only one mode, and these occur in the same general age distribution as mode B in Fig. 2. The presence of mode A in the chart suggests that a

significant number of relatively young people are particularly at risk during the first year of bereavement.

Summary

A survey was made in a semirural area (pop. 5,184) to determine whether bereavement produced an increased mortality among bereaved close relatives—these being defined as a spouse, a child, a parent, or a sibling. During a six-year survey period 488 residents died; 371 of these people had close relatives living in the survey area, and the subsequent mortality of their 903 close relatives was compared with that of a control group; this control group was composed of the 878 close relatives of 371 people matched by age, sex, and marital state with the people who had originally died.

It was found that 4.76% of bereaved close relatives died within one year of bereavement compared with 0.68% in the control group. This sevenfold increase in risk between the bereaved and control group was significant at the 0.001% level, and indicates that bereavement carries a considerably increased risk of mortality. This risk was found to be greater for male than for female relatives: 6.4% of the 391 male relatives at risk died, compared with 3.5% of 512 female relatives. This difference in risk between the sexes was significant at the 5% level.

The increase in risk was particularly great for widowed people and least for female children. During the first year of bereavement 12.2% of widowed people died, compared with 1.2% in the control group. This increase in risk for widowed people was significant at the 0.01% level. Of the remaining close relatives in the survey group, 3.21% died during the first year of bereavement, compared with 0.56% in the control group. This increase in risk for bereaved close relatives, excluding the widowed, was significant at the 0.1% level.

There is a relation between the place at which a person dies and the subsequent mortality of bereaved relatives. The risk of close relatives dying during the first year of bereavement is doubled when the primary death causing bereavement occurs in a hospital compared with at home. This difference in risk was significant at the 5% level.

If the primary death occurs at some site—for example, a road or field—other than at home or hospital, the risk of a close relative dying during the first year of bereavement is five times the risk carried by the close relatives of people who die at home. This difference in risk was significant at the 0.01% level, though the small size of the sample reduces the significance that can be attributed to the result.

People who die following a bereavement are on average slightly younger than the relatives who predeceased them, and they die at an earlier age than is usual for the community in which they live.

We are grateful to Dr. Felix Richards for providing data used in the survey and to Miss Kathleen Vaughan for her considerable help in identifying the close relatives resident in the area.

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Severe Outbreak of Surgical Sepsis Due to *Staphylococcus aureus* of Unusual Type and Origin

RICHARD W. PAYNE,* M.A., M.D., M.C.PATH.

Brit. med. j., 1967, 4, 17-20

Outbreaks of staphylococcal infection in hospital due to infection arising in the operating-theatre are probably less rare than reports in the literature would suggest. There are many possible explanations for this natural reticence. However, it is felt that the following outbreak should be recorded since there are a number of features of general interest.

Outbreak in Outline

The outbreak occurred at St. Albans City Hospital—a 400-bedded provincial general hospital—in January 1963. Each surgical ward has for some years maintained a wound infection register and it has been the practice of the clinical pathology department to keep a record of all coagulase-positive staphylococci (*Staphylococcus aureus*) isolated from patients in the hospital; a record is also kept of the antibiotic sensitivity pattern of each organism. In January 1963 the number of patients from whom *Staph. aureus* was isolated began to rise (Fig. 1). Nearly all these organisms were resistant to penicillin, streptomycin, and tetracycline when tested by a routine Multidisk diffusion method. This was a pattern of antibiotic resistance that was uncommon in the hospital at the time.

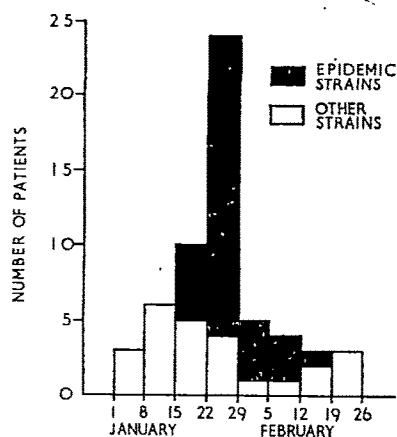


FIG. 1.—Weekly number of patients with *Staph. aureus* infections in January and February 1963.

Early in the outbreak it became apparent that all the affected patients had staphylococcal wound infections and that patients in many separate wards were involved. The patients were under the care of six consultant surgeons. It was therefore felt that the most probable source of infection lay in the operating-theatres.

Subsequently, *Staph. aureus* was shown to be widely distributed throughout the theatre suite. It was also found that an anaesthetist (A) was not only a nasal and skin carrier but also a "disseminator" of *Staph. aureus* of the same antibiotic-sensitivity pattern as the affected patients.

* Consultant Clinical Pathologist, Mid-Herts Group of Hospitals. Present address, Department of Haematology, The Victoria Infirmary, Glasgow S.2

The theatres were closed and washed down with hypochlorite solution. This was not effective, so the theatre suite was washed down again much more thoroughly with hypochlorite solution followed by fumigation with formalin vapour and finally shown to be bacteriologically clean.

Organism

Coagulase-positive staphylococci (*Staph. aureus*) of two phage patterns were involved in this outbreak: (a) phage type 80 and (b) phage untypable (Holt, 1963). The antibiotic sensitivity patterns of these two different phage types of *Staph. aureus* were the same, as shown by a Multidisk plate diffusion method (Table I).

TABLE I.—Results of Antibiotic Sensitivity Tests (Disc Diffusion Method)

Antibiotic	Amount in Disc	Sensitive (S) Resistant (R)
Ampicillin	10 µg.	R
Chloramphenicol	10 "	S
Erythromycin	10 "	S
Methicillin	10 "	S
Neomycin	10 "	S
Novobiocin	5 "	S
Penicillin	1.5 "	R
Phenethicillin	1.5 units	R
Cloxacillin	5 µg.	S
Streptomycin	10 "	R
Sulphafurazole	100 "	R
Tetracycline	10 "	R

The phage "untypable" strain was further investigated in the Department of Bacteriology at the Leeds School of Medicine. Their report stated "This strain is typical of our yellow isolates. It forms bright yellow pigment on glycerol monoacetate agar, is non-proteolytic, and multiple-resistant (resistant to penicillin, streptomycin, tetracycline, and mercury). It falls into phage group III, subdivision 77w (1,000 R.T.D.)" (Jacobs, Willis, Ludlam, and Goodburn, 1963; Willis, 1963).

Carrier

Swabs taken from the anterior nares, the dorsum of each hand, and the forehead of the anaesthetist (A.) on 24 January all yielded a heavy growth of *Staph. aureus*. The organisms had the same antibiotic sensitivity pattern as those isolated from the affected patients (Table I) and were subsequently shown to be of the same phage patterns (phage type 80 and phage untypable).

In retrospect it was discovered that A. had been found to be a nasal carrier of *Staph. aureus* three years previously at another hospital. During the ensuing three years he had been actively associated with clinical work in other hospitals, but had not to his knowledge been associated with an outbreak of staphylococcal infection previously. He had had psoriasis for eight years. In December 1962 he had suffered an acute exacerbation of his skin condition necessitating hospital admission and local and systemic treatment with corticosteroids. This acute exacerbation had settled fairly rapidly, leaving many

large desquamating but not overtly infected areas of skin. A. returned to his anaesthetic duties on 7 January 1963 and continued to work until 24 January.

Exposure plates were placed on the floor of a room for 20 minutes prior to A.'s entry and then for 20 minutes, during which time A. entered the room, removed his clothes, and dressed again at a distance of 10 feet (3 metres) from the plates. The plates exposed while A. undressed and dressed showed a heavy contamination with *Staph. aureus* (Fig. 2) of the two phage patterns, described above.

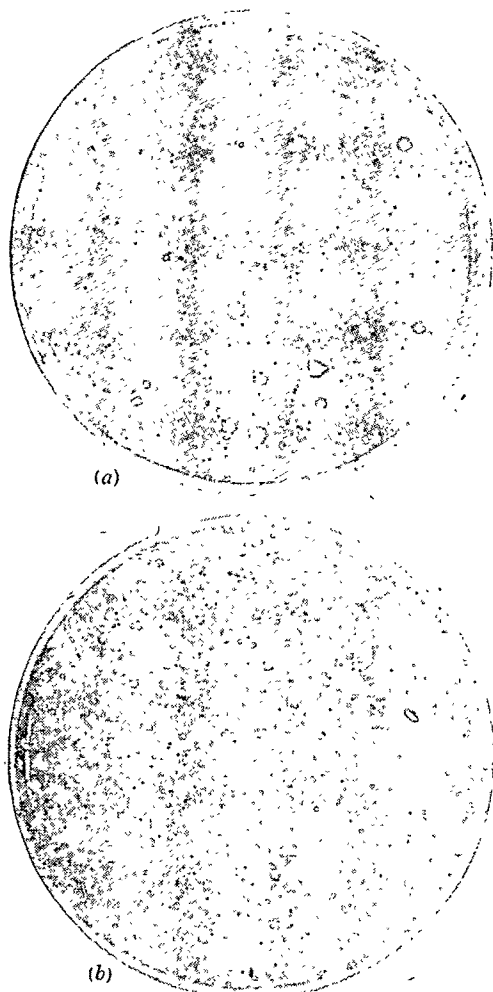


FIG. 2.—Twenty-minute exposure plates (blood-agar) taken (a) before A.'s entry into room and (b) after A.'s dressing and undressing in room.

Theatre Suite

The theatre suite is modern, having been in use since November 1959. There is a plenum system of ventilation, with adiabatic cooling and humidification, which gives about 17 changes of air per hour in the theatres. Exposure plates placed at seven sites in the theatres and also swabs taken direct from six random sites showed the widespread presence of *Staph.*

TABLE II.—Sites of Origin and Phage Types of *Staph. aureus*

Source	Total	Phage Untypable	Phage Type 80	% Phage Untypable
Carrier	5	3	2	60
Theatres	9	5	4	56
Patients	33	29	4	88
Complications:				
Pneumonia	5	5	0	100
Peritonitis	2	2	0	100
Deaths:				
Pneumonia 2, peri-				
tonitis 2	4	4	0	100

aureus. The total colony counts on these exposure plates varied from 10 to 28 colonies per plate per hour of exposure (mean 17 colonies per plate per hour) and a total of six colonies of *Staph. aureus* were isolated (5% of total colonies isolated). *Staph. aureus* was also isolated from swabs taken direct from three of the six random sites. These organisms were of the same antibiotic sensitivity patterns and same phage type as those isolated from the carrier (Table II). No staphylococci were isolated from the filters or air-ducts of the ventilating plant.

Patients

A total of 33 patients were involved in this outbreak; in all of them surgical wounds were the primary site of infection. *Staph. aureus* phage type 80 was isolated from wound swabs from 4 of the patients, while the phage-untypable strain was isolated from the other 29 patients' wound swabs (Table II). The patients' ages ranged from 8 months to 88 years; 15 were male and 18 female.

Patients in 11 wards and under the care of six surgeons were involved in this outbreak. The distribution of patients according to wards and to surgical teams is given in Tables III and IV respectively.

TABLE III.—Distribution of Patients with Staphylococcal Wound-sepsis by Wards

Ward	No. of Cases
Male surgical 1	8
" 2	6
Female " 1	6
" 2	3
Gynaecological	4
6 other wards (1 case in each)	6
Total	33

TABLE IV.—Distribution of 33 Patients with Staphylococcal Wound-sepsis by Surgical Teams

Surgeon	Specialty	No. of Cases
A	General surgery	11
B	"	6
C	Orthopaedics	6
D	Obstetrics and gynaecology	5
E	General surgery	3
F	"	2

All the patients were operated on in the theatres in the operating-suite described above during the period 9–28 January. Thirteen were operated on in theatre 1 and twenty in theatre 2. These details are summarized in Table V, together with the total number of operations performed in each theatre during the above period. Out of a total of 217 patients operated on 33 (15.2%) developed staphylococcal wound infections.

TABLE V.—Distribution of Patients with Staphylococcal Wound-sepsis by Operating-theatre

	No. of Infected Cases	Total No. of Operations	% Wound Infections
Theatre 1	20	115	17.4
" 2	13	102	12.7
Total	33	217	15.2

The interval between the time of operation and of clinical presentation of wound infection ranged from 2 to 20 days (mean 9.6 days) (Fig. 3).

In Fig. 4 an attempt has been made to correlate the subsequent occurrence of wound sepsis in a patient with A.'s presence in the theatre at the time of the operation. Staphylococcal wound infections continued to occur for five days after A.'s last attendance in the theatre suite and for 10 days after his last known attendance in theatre 2.

Complications

In addition to wound sepsis and its surgical sequelae staphylococcal pneumonia occurred in five patients, and staphylococcal peritonitis in two. All of them were infected with the phage-untypable strain of *Staph. aureus* (Table II).

Mortality

In spite of intensive treatment there were 4 deaths among the 33 patients (mortality rate 12.1%). These deaths occurred in patients in whom complications had developed—two had

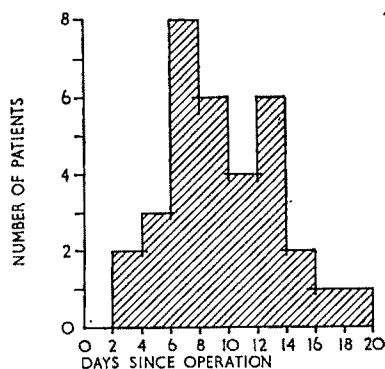
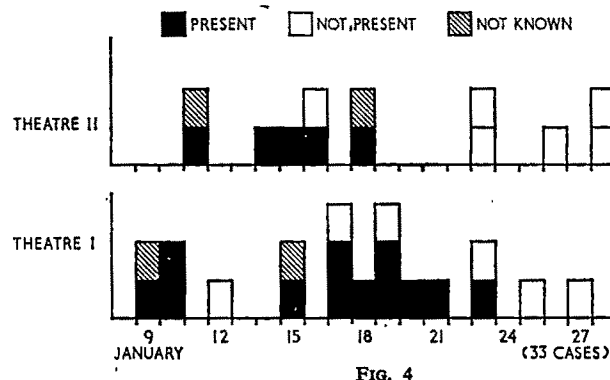


FIG. 3.—Time interval between operation and isolation of *Staph. aureus* from wound swabs. FIG. 4.—Retrospective analysis of the carrier's presence or absence in the theatre at time of operation.



developed pneumonia and two peritonitis, due in all cases to the phage-untypable strain of *Staph. aureus* (Table II).

Management

On 24 January it became apparent that the theatre suite was contaminated with *Staph. aureus* and that the most likely source of these organisms was the anaesthetist, A. At the time it was decided, firstly, to suspend A. from duty; secondly, to close and cleanse the theatre suite (using another operating theatre for emergency surgery); thirdly, to suspend elective surgery; and, fourthly, to regard any ward in which a patient had developed a staphylococcal wound infection as contaminated.

The theatre suite was closed on 24 January and washed down with 1:80 sodium hypochlorite solution. The theatres were reopened after 36 hours, but subsequently it was discovered that staphylococci were still present. The suite was therefore closed again, and every part (including ceilings, cupboards, and loose apparatus) was scrupulously washed with 1:80 sodium hypochlorite solution by hand, while all dressings and linen were laundered and autoclaved. Finally, the whole theatre suite was fumigated with formalin vapour produced from the Formitas outfit (Sanitas & Co. Ltd.) and kept sealed for four hours; during this procedure the ventilating plant was stopped. Twenty-four hours later no staphylococci were isolated on prolonged (12-hour) exposure plates or direct swabs taken at many sites in the theatres.

Because of the large number of patients affected in this outbreak, the normal facilities for isolation soon became inadequate. Therefore it was decided to segregate infected and non-infected patients in separate "dirty" and "clean" wards respectively. As soon as a patient was discharged from a "dirty" ward, his bedding and surrounding curtains were "formalin-stoved" and laundered. After the last patient had been discharged each "dirty" ward was cleaned in the same careful way as in the theatres on the second occasion (washing down with a 1:80 solution of sodium hypochlorite, followed by formalin fumigation).

Discussion

Different strains of *Staph. aureus* show wide variation in virulence (Barber, Dutton, Beard, Elmes, and Williams, 1960). In particular, phage type 80/81, first isolated in Australia by Rountree and Freeman (1955) has subsequently been associated with severe outbreaks of staphylococcal infection throughout the world. More recently a newly recognized strain of *Staph. aureus*, designated phage type A, has been associated with a series of severe staphylococcal outbreaks in six hospitals in the Glasgow area (Temple and Blackburn, 1963) and also in hospitals in the Leeds area (Jacobs, *et al.*, 1963). In the present outbreak, 4 cases were associated with phage type 80 infections

and 29 with the phage-untypable strain. This untypable strain was isolated from all the patients in whom staphylococcal pneumonia or peritonitis occurred. This may imply that the untypable strain was more virulent or more infective to patients than phage type 80 (it is of interest that the observed incidence of both strains in the theatre was almost equal). It is therefore felt that attention should be drawn to the occurrence of the outbreak, though it is impossible to foretell the future importance of this strain.

In the outbreak under review circumstantial evidence strongly suggests that the patients' wounds became infected in the theatre at the time of the operation. Other workers have also concluded that suppuration in surgical wounds is most likely to have arisen from infection in the theatre (Gillespie, Alder, Ayliffe, Bradbeer, and Wypkema, 1959; Howe and Marston, 1962). An anaesthetist (A.) appears to have been the source of staphylococcal contamination of the theatre suite. It is of interest to note that this individual had in the past been a nasal staphylococcal carrier, and had had psoriasis which remained quiescent until December 1962, when he suffered an acute exacerbation of his skin condition. However, at the time of his return to duty, in January 1963, his skin was desquamating over wide areas. The increased liability of patients with certain skin lesions to be disseminators of staphylococci has been demonstrated by Hare and Cooke (1961), while Davies and Noble (1962) have demonstrated the importance of desquamated skin-scales in the carriage of bacteria. It is possible that A. was transformed from a relatively harmless nasal carrier into a highly dangerous staphylococcal disseminator by the presence of desquamating psoriatic lesions colonized by staphylococci. In this context the part played by topical and systemic corticosteroid therapy on the change in A.'s skin: bacteria relationship remains unknown.

It was not possible to determine the aerial density of staphylococci in the theatre suite during this outbreak, but an impression of the numbers of organisms disseminated by A. has been given in Fig. 2. Wound infections continued to develop in patients operated on during the five days after A.'s last attendance in the theatre suite, the most probable explanation being the continued survival of staphylococci in the theatres, for Noble

(1962) has shown that these organisms can survive for up to seven days in ward air. Though it has been shown that efficient theatre ventilation will greatly reduce the concentration of air-borne bacteria (Shooter and Williams, 1961) it is quite apparent that modern plenum ventilation was unable to prevent theatre infection in these circumstances.

Considerable doubt has been cast on the value of "routine" washing down of theatres with 1:80 sodium hypochlorite solution, since it has been shown that staphylococci survived this procedure during the first closure of the theatre suite. However, the combined use of the same strength of hypochlorite solution applied to literally every part of the theatre suite and its contents, followed by formalin fumigation, has been shown to have been effective, since staphylococci could no longer be isolated and no further wound infections occurred. It is not possible to define the relative importance of the thorough washing down with hypochlorite solution in relation to the importance of formalin fumigation. Hare, Raik, and Gash (1963) have, however, shown under experimental conditions that 1:80 sodium hypochlorite solution was highly efficient in killing *Staph. aureus* whereas formalin was much less effective. The dangers of relying on "routine" cleansing of contaminated theatres have been inadvertently demonstrated in this outbreak, and it is my view that such theatres must remain out of use until full bacteriological results are available.

The policy of segregation of patients into "clean" and "dirty" wards in an outbreak of this type appears to have been justified, since no obvious cases of cross-infection in the wards were detected. This, in addition, reflects great credit on the nursing staff.

Noble (1962) found six disseminators of staphylococci in 3,675 surgical patients. The incidence of disseminators among those working in operating-theatres is not known, but the outbreak under review emphasizes the grave hazards of the presence of such an individual in the theatre.

The *Lancet* (1963) stated: "Without dependable statistics it is impossible to assess the size of the staphylococcal problem or to determine the value of control measures. . . . The detection and recording of *all* infections, trivial and serious, the identification of important sources of cross-infection, the correlation of clinical and laboratory findings, and the supervision of special precautions all take more time than can be spared by busy doctors and nurses." From personal experience I would wholeheartedly support these views, for during this outbreak it was impossible to attend to any other duties or commitments. It is felt that the suggestion, made by Gardner, Stamp, Bowgen, and Moore (1962) and quoted in the same *Lancet* editorial, of overcoming these difficulties by appointing a full-time sister to work with the team in control of infection is one that should be carefully considered by many hospitals.

Considering this outbreak in retrospect it is felt that three points, which though obvious are nevertheless of fundamental importance, should be stressed: (1) the value of keeping a central register of *all* staphylococcal infections occurring in a

hospital; (2) the importance of the co-operation of the medical staff in formulating a comprehensive collective plan of action at the earliest possible stage; and (3) the importance of the co-operation of medical, nursing, and administrative staffs in rapidly implementing this plan.

Summary

A severe outbreak of staphylococcal infection involving 33 surgical patients in a general hospital is described.

Two strains of *Staphylococcus aureus* were involved: phage type 80 (4 cases, no deaths) and phage untypable (77w (1,000 R.T.D.)) (29 cases, 4 deaths).

An anaesthetist suffering from psoriasis was found to be carrying and disseminating staphylococci of these two strains, which were found to be widely distributed in two operating-theatres.

The findings, and the management of the outbreak, are described and discussed.

ADDENDUM.—Since this paper was submitted for publication a similar but smaller outbreak of surgical wound infection has been reported by Ayliffe and Collins (G. A. J. Ayliffe and B. J. Collins, *J. clin. Path.*, 1967, 20, 195). These infections were probably also acquired in the operating-theatre, from an orderly who had generalized dry eczema and who was both a nasal and skin carrier and a disseminator of another unusual strain of *Staph. aureus*.

I am greatly indebted to all who were involved in investigating and controlling this outbreak, whether medical, nursing, laboratory, or administrative staff. I also wish to thank Drs. Holt, Jacobs, and Willis for permission to quote the results of their investigations.

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Glucose Tolerance and Serum Insulin in Unaffected Identical Twins of Diabetics

D. A. PYKE,* M.D., F.R.C.P.; K. W. TAYLOR,* M.A., PH.D., M.B., B.CHIR.

Brit. med. J., 1967, 4, 21-22

Since diabetes mellitus is partly inherited a study of the unaffected identical twin of a diabetic may yield useful information regarding both its genetics and its metabolic abnormalities.

About half of the pairs of identical twins so far reported have been concordant—that is, both twins were diabetic (Joslin *et al.*, 1959; Harvald and Hauge, 1963). If diabetes is transmitted by a single gene then all the twins ought eventually to become diabetic, unless “penetrance” is incomplete. Glucose-tolerance tests may reveal abnormalities in such apparently unaffected twins.

In addition the insulin response to glucose of a series of twins of diabetics has not so far been reported. Such studies might reveal whether these apparently normal twins show antagonism to insulin or impairment of the response of the beta cell to glucose. Thus increased blood insulin levels with normal glucose tolerance might indicate antagonism to insulin, and lower levels after glucose might reflect a diminished insulin secretion.

We report here the results of glucose-tolerance tests performed on nine apparently healthy identical twins of diabetics. Blood insulin was determined during the tolerance tests.

Present Investigation

Subjects.—The clinical characteristics of the twins are shown in Table I. In six cases the twins were female and in three male. The age at diagnosis of diabetes in the affected twin varied from 5 to 52; in all but two it was under 45 years. The mean interval from diagnosis in the affected twin to the time of testing the unaffected twin was five years. In pair 3 both twins were fat (50% overweight), but in the other pairs neither the diabetic nor the non-diabetic twin was significantly overweight—that is, none was 10% overweight. In seven of the nine pairs there was a family history of diabetes; in pair 2 both parents were diabetic.

TABLE I.—Clinical Details of Identical Twins Studied

Pair No.	Sex	Age at Test	Age at Diagnosis of Diabetes in Affected Twin	Familial Relationship with Other Members of Family with Diabetes
1	F	23	13	Grandfather, 2 great aunts, 1 uncle. (All maternal)
2	M	55	52	Mother. Father. Daughter
3	M	55	50	Father
4	F	23	20	None
5	M	30	28	Uncle
6	F	43	43	Mother
7	F	43	43	Sister
8	F	56	44	Great aunt.
9	F	14	5	Great uncle (maternal)

Normal Persons.—The normal group for comparison of serum insulins consisted of 24 individuals (8 male, 16 female) aged between 18 and 75. None of the normals differed from their expected weight by more than 10% and none was known to have a family history.

Procedure.—In some cases the tests were done at King's College Hospital, and in others one of us carried out the test

* Diabetic Department and Department of Medicine, King's College Hospital, London S.E.5.

in the patient's home. All subjects took a full carbohydrate diet for at least three days before the test. Venous blood was taken from a forearm vein after an overnight fast. Then 50 g. of glucose was given by mouth, and blood samples were taken 30, 60, and 120 minutes later. Determinations were made of glucose and insulin. For determination of insulin the blood was allowed to clot and the serum was separated by centrifugation. Serum was stored at -20°C . Insulin was measured by immunoassay; Hales and Randle's (1963) method being used with certain modifications, the most important being the use of 0.01 M disodium diethyltetracetic acid in the reaction mixture (Morgan *et al.*, 1964; Sheldon and Taylor, 1965), to avoid interference from complement. Results on human serum were compared with the response to ox insulin standards prepared from a recrystallized specimen kindly provided by Wellcome Laboratories, Beckenham, Kent. Glucose was determined by an oxidase method (Huggett and Nixon, 1957).

Confirmation that twins were identical was obtained by determining blood groups ABO, MN, S, P, Lu^a, Le^a, Le^b, Fy^a (through the kind help of the Blood Group Reference Laboratory, Lister Institute).

Results

Normal Persons.—Blood glucose and serum insulin levels in normal persons are shown in Table II. These results do not show marked differences from those of many other workers who have employed a test of this type. The blood glucose results, for example, are very slightly lower than those of Welborn *et al.* (1966) for 45 normal volunteers in whom blood glucose was determined by a ferricyanide method after 50 g. of oral glucose. Serum insulin values obtained by various

TABLE II.—Glucose Tolerance and Serum Insulins in Unaffected Identical Twins of Known Diabetic Patients

	Glucose Tolerance (mg./100 ml.)				Insulin ($\mu\text{u.}/\text{ml. Serum}$)			
	0 min.	30 min.	60 min.	120 min.	0 min.	30 min.	60 min.	120 min.
Normals*	67 $\pm$ 2	98 $\pm$ 4	80 $\pm$ 3	67 $\pm$ 3	21 $\pm$ 2	64 $\pm$ 5	57 $\pm$ 6	31 $\pm$ 6
Patient:								
1	77	133	137	118	24	65	63	53
2	80	162	183	125	9	22	29	22
3	95	145	162	125	27	26	50	50
4	67	71	65	55	10	11	16	13
5	78	114	59	63	29	100	45	11
6	94	147	154	71	13	41	43	18
7	76	145	185	123	—	16	32	2
8	86	129	136	38	11	14	10	11
9	92	122	163	110	18	25	26	6
Mean $\pm$ S.E.M.	83 $\pm$ 3	133 $\pm$ 10	137 $\pm$ 16	92 $\pm$ 4	18 $\pm$ 3	36 $\pm$ 10	35 $\pm$ 5	21 $\pm$ 6

* Thirty-four normal individuals were tested for glucose tolerance and 25 for serum insulin.

immunoassay methods which differ considerably in detail have been remarkably uniform from one group of workers to another (see Taylor, 1967). Moreover, our results in normal subjects differ only slightly from values in an earlier series obtained in 10 normal people in this department (Rudnick and Taylor, 1965). As has been noticed by Welborn *et al.* (1966) serum insulin levels did not differ with age.

Twins.—Serum insulin and blood glucose values in the nine twins of diabetics are shown in Table II. It will be seen that

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glucose tolerance is abnormal by comparison with the control group. Blood glucose levels are significantly different in the twins from those in the controls in the fasting state and after glucose. In only two curves did all the points lie within two standard deviations of normal values. The others showed high values, especially one and two hours after glucose. The two subjects with normal glucose tolerance results were from the only pairs without a family history of diabetes. Serum insulin levels in the fasting state did not differ between the groups. However, insulin levels were lower than normal half an hour and one hour after glucose in the twins.

Discussion

The significance of these abnormal blood glucose levels is increased by the fact that the subjects are young. High blood glucose values after oral glucose are rare in early life (Butterfield, 1964). Despite these high blood glucose levels serum insulin levels are low, particularly after glucose.

There are a number of possible explanations for this reduced response to glucose. It might be that not all the insulin in the blood is being measured. At present there is no conclusive evidence to suggest that immunological methods fail to measure all the available insulin in the blood. When attempts are made to extract insulin from blood proteins by various acid-ethanol methods there does not appear to be any release of insulin previously associated with other proteins (Karam *et al.*, 1963). When higher values for blood insulins have been obtained by bioassay methods their significance is doubtful. It has always been difficult to measure blood insulin levels with precision by the rat diaphragm technique (Taylor and Randle, 1959), and the biological significance of adipose tissue assays for blood insulin is uncertain (Kipnis and Stein, 1964; Rasio *et al.*, 1965).

It might be that insulin was being more rapidly broken down in the twins of diabetics. However, serum insulin levels tend to rise after glucose less than in normal persons, though fasting levels are not different in the two groups. This is not the pattern of response which would be expected if there were a uniformly enhanced rate of insulin destruction throughout the glucose-tolerance test. Neither do these studies give any evi-

dence of antagonism to endogenous insulin, which would lead to raised levels of blood insulin in the presence of a normal glucose tolerance. It seems much more likely that the response of the beta cell to a rise of glucose concentration is less than normal. The diminished glucose tolerance of some of these non-diabetic twins may be a consequence of diminished insulin response to oral glucose.

The clinical significance of these findings is not known. In particular, we do not know whether the abnormalities will progress to frank clinical diabetes. We intend to observe the present group and collect data on other identical twins of diabetics.

Summary

Glucose tolerance and serum insulin levels have been examined in nine apparently normal twins of diabetics and compared with the results in normal people.

Mean glucose tolerance was significantly less than that of normals and serum insulin levels after sugar were also low.

It is suggested that the impairment of glucose tolerance in some of these twins is a consequence of a diminished response of the beta cell to glucose.

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Glucose Tolerance and Serum Insulin in the Unaffected First-degree Relatives of Diabetics

K. W. TAYLOR,* M.A., PH.D., M.B., B.CHIR.; JOANNA SHELDON,* M.D., M.R.C.P.; D. A. PYKE,* M.D., F.R.C.P.
W. G. OAKLEY,* M.D., F.R.C.P.

Brit. med. J., 1967, 4, 22-24

In the preceding paper the effects of oral glucose on blood glucose and serum insulin levels were examined in the identical twins of known diabetics, and abnormalities of glucose tolerance and serum insulin levels in some of them were shown. It seemed of interest to determine whether these abnormalities were present in other first-degree relatives of diabetic patients. In addition, serum insulin and glucose tolerance were examined in a small group of relatives of diabetic patients who gave clinical evidence of hypoglycaemia.

Methods and Subjects

Blood glucose and serum insulin were measured by methods identical to those in the preceding paper. The results have been compared with the same control series.

Six children of conjugal diabetic couples were studied and studies were made of a family of nine children derived from an additional conjugal pair of diabetics.

Nine other first-degree relatives of diabetics were studied. None of them was previously known to have diabetes. As in the preceding paper, subjects were tested after an overnight fast and after at least three days on a normal carbohydrate diet. All but one of these patients were aged under 45.

Results

Values for Glucose and Insulin in Relatives of Diabetics.—When oral glucose-tolerance tests were performed in the off-

* Diabetic Department, Department of Medicine, King's College Hospital, London S.E.5.

TABLE I.—Glucose Tolerance and Serum Insulin in Relatives of Diabetics (not exhibiting hypoglycaemia).

Case No.	Age and Sex	Relationship to Patient	Blood Glucose (mg./100 ml.)				Serum Insulin (μ u./ml.)			
			0 min.	30 min.	60 min.	120 min.	0 min.	30 min.	60 min.	120 min.
1	47 F	Both parents	84	137	128	92	2	16	20	2
2	25 F	" "	70	99	85	63	10	39	33	6
3	26 M	" "	89	158	148	89	10	18	25	21
4	44 M	" "	65	119	117	103	17	72	120	78
5	— F	" "	71		95	67		19	21	5
6	— F	" "	71	157	90	60	5	205	89	
		Mean $\pm$ S.E.M.	75 $\pm$ 3	134 $\pm$ 9	110 $\pm$ 11	79 $\pm$ 7	10 $\pm$ 3	62 $\pm$ 31	51 $\pm$ 17	22 $\pm$ 11
7	30 F	Mother					7	24	30	10
8	25 M	Father					6	28	25	4
9	54 F	Sister	82	137	152	64	28	94	81	34
10	7 F	"					18			
11	30 F	3 children	93	118	126	130	16	35	144	170
Normals (as in preceding paper)			67 $\pm$ 2	98 $\pm$ 4	80 $\pm$ 3	67 $\pm$ 3	21 $\pm$ 2	64 $\pm$ 5	57 $\pm$ 6	31 $\pm$ 6

Results are expressed as means $\pm$ S.E.M.

spring of conjugal diabetics blood glucose values were somewhat higher than those obtained in the control series (Table I). This is particularly noticeable half to one hour after glucose. By contrast, serum insulin levels in the offspring of the conjugal group were similar to those obtained in the normal series. A similar pattern of insulin and glucose is observable in the other first degree relatives tested. In the instance where the subject was obese (Case 11) rather high serum insulin values were obtained. This result is in line with other observations which suggest that elevated blood insulin levels are characteristic of obesity whether diabetes is present or not (Karam *et al.*, 1963). Studies were also made on nine offspring of a single pair of conjugal diabetics. Values for blood glucose and serum insulin are shown in Table II. One subject (E) was

insulins were usually increased at those times. These values were significantly greater than those in normal people.

Discussion

These results (like those in the preceding paper) suggest that glucose tolerance is often abnormal in the close relatives of diabetic patients. This is so in all the groups tested, but is especially noticeable in the nine children of a single conjugal pair of diabetics. There have so far been few studies of glucose tolerance in large families. Fajans (1964) has drawn attention to some similar results obtained by glucose-tolerance tests in another family study. Thus when 10 apparently healthy children of a diabetic father were tested seven were found to be diabetic.

Despite the abnormal levels of blood glucose recorded in this paper (with the exception of those with hypoglycaemia) blood insulin values have been relatively low. These values confirm those obtained by a number of other workers who have found normal or reduced levels of blood insulin in close relatives of diabetics (Grodsky *et al.*, 1965; Colwell and Lein, 1966). The insulin response to intravenous glucose has also been reported to be reduced (Cerasi and Luft, 1963) or normal (Soeldner *et al.*, 1966) in a number of relatives of diabetic patients. There now seems to be general agreement among workers who have used various types of immunological techniques for measuring insulin that blood insulin levels are relatively low in the relatives of diabetics.

A different type of response had earlier been found by Steinke *et al.* (1963), who used an adipose-tissue method to measure insulin in the blood of a large group of the offspring of conjugal diabetics. Increased insulin-like activity was found in the serum of many, though not all, such subjects. The authors were careful to point out that the physiological significance of blood-insulin activity measured in this way is uncertain.

The results shown both in this paper and in the preceding one suggest that in close relatives of diabetics there may be an impairment in the response of the islet cells to glucose. It is at present not known whether this defective response extends to other stimuli for insulin secretion such as amino-acids, glucagon, or sulphonylureas. If it is a defective response only to sugars that is being measured, then the defect could lie either with the phosphorylation of glucose, within the beta cell or in

TABLE II.—Serum Insulin and Blood Glucose Concentrations in Nine Children of a Pair of Conjugal Diabetic Patients

Subject	Age and Sex	Blood Glucose (mg./100 ml.)				Serum Insulin (μ u./ml.)			
		0 min.	30 min.	60 min.	120 min.	0 min.	30 min.	60 min.	120 min.
A	58 M	86	194	215	35	11		48	25
B	57 F	89	145	171	123	11	20	36	
C	55 M	80	200	196	129	15	19	28	19
D	55 M	80	162	183	125	9	22	29	22
E	53 F	308	349	377	284	20	25	25	20
F	49 F	92	175	167	38	18	<250	<250	35
G	47 M	87	183	206	115	11	24	49	30
H	45 F	72	156	42	66	10	60	45	23
I	41 F	111	201	151	44	10	14	26	15

found to be frankly diabetic, and abnormalities of glucose tolerance were discovered in several of the other offspring. Again serum insulins were relatively low, apart from one patient (F) who showed an extreme rise after glucose. The pattern of serum insulin response after glucose is characterized by a normal fasting level and slow rise in insulin, suggestive of a delayed and inadequate response of the beta cells to stimulation by sugars.

Blood Insulin and Glucose in Patients with a Clinical History of Hypoglycaemia.—Glucose-tolerance tests were carried out and serum insulin values were measured in four patients with symptoms of hypoglycaemia, all with first-degree relatives with diabetes. Results are shown in Table III. Relatively low blood sugars were obtained two hours after taking glucose, though values at 30 and 60 minutes were high, and serum

TABLE III.—Glucose Tolerance and Serum Insulin in Relatives of Diabetic Patients with Clinical Evidence of Hypoglycaemia

Patient	Age and Sex	Relationship to Patient with Diabetes	Blood Glucose (mg./100 ml.)				Serum Insulin (μ u./ml.)			
			0 min.	30 min.	60 min.	120 min.	0 min.	30 min.	60 min.	120 min.
I	45 M	Father	99	159	213	30	14	21	47	28
II	16 M	"	74	99	100	72	20	100	205	45
III	45 M	"	78		154	56	9	124	211	20
IV	26 F	Mother	61	133	117	42	11	148	160	10
		Mean $\pm$ S.E.M.	78 $\pm$ 6	131 $\pm$ 17	146 $\pm$ 23	50 $\pm$ 9	14 $\pm$ 2	98 $\pm$ 27	158 $\pm$ 38	26 $\pm$ 9

worker in a previous study of 80 healthy subjects (40 males, 40 females)—mean percentage adhesive platelets 40.3, standard error ± 0.9). For the purpose of this study, therefore, these group 1 patients have been regarded as controls, and differences in means have been analysed against them.

Those subjects found to have benign tumours (group 2) did not differ in their mean adhesiveness from those in group 1, though the mean initial platelet count in this group was significantly lower than in the others. In patients with invasive

patients could account for the variation in platelet adhesiveness shown. There appears to be no explanation for the low mean initial platelet count in the group of patients with benign tumours, but the number in this group was small.

Nathanson and Savitsky attributed the increased platelet stickiness found in patients with cerebral tumours to a non-specific effect of malignancy. Yet the occurrence of similar changes in platelet adhesiveness in patients with active multiple sclerosis and rapidly growing brain tumours suggests an alter-

Platelet Stickiness in Intracranial Tumours

	Group 1	Group 2	Group 3	Group 4
No.	15	9	10	18
Proportion of males to females	11:4	5:4	3:7	12:6
Mean age	44.0 $\pm$ 3.2	40.7 $\pm$ 3.9	40.5 $\pm$ 5.2	53.9 $\pm$ 3.3 (P < 0.05)
Mean initial platelet count per cu. mm. $\times 10^9$	250 $\pm$ 10.3	206.3 $\pm$ 13.5 (P < 0.01)	315.1 $\pm$ 36.5	259.2 $\pm$ 15.9
Mean % adhesive platelets	39.8 $\pm$ 1.8	39.9 $\pm$ 2.6	41.5 $\pm$ 2.7	49.4 $\pm$ 2.0 (P < 0.01)

Standard errors follow $\pm$ sign.

P values are given where means differ significantly from those in Group 1.

Group 1: No space-occupying lesion found. Group 2: Benign tumours. Group 3: Invasive tumours; clinical history of more than three months' duration. Group 4: Invasive tumours; clinical history of three months or less.

tumours platelet stickiness was increased. The increase was small and did not reach significance in those with a longer clinical history (group 3), but became more striking and was significant in group 4 patients with a presenting history of three months' duration or less (P < 0.01). The mean age for this group was, however, significantly higher than that of the control patients (P < 0.05).

The mean percentage of adhesive platelets did not differ significantly between patients with cerebral metastases and those with primary brain tumours.

Discussion

These findings support Nathanson and Savitsky's (1952) observation that platelet adhesiveness is increased in brain tumours. In this larger series raised stickiness was found to occur most often in those patients with invasive tumours and a short history of disease, while platelet adhesiveness in patients with benign tumours lay within the normal range. It is recognized that the length of a patient's history may be influenced by many factors, but in general most rapidly growing brain tumours cause the patient to present for investigation within a few weeks of the onset of symptoms, and it is these tumours which are associated with a relatively rapid destruction of neural tissue.

The group of patients showing increased platelet adhesiveness while matched for sex were significantly older than the control patients with negative investigations. However, the effect of age upon platelet adhesiveness is not yet clear. In a previous study (Millac, 1967b) no significant effect of age, within a similar range, on adhesiveness was found in 80 healthy subjects and 82 patients with multiple sclerosis. It is thought unlikely that the difference in age between these two groups of

native explanation. In both these clinical situations there is acute destruction of neural tissue, and it seems possible that degradation products may enter the circulation and bring about the alteration in platelet behaviour.

Summary

Platelet adhesiveness has been measured in 52 patients admitted with suspected brain tumours. Compared with those patients whose investigations turned out to be negative or in whom the neurological diagnosis was other than brain tumour, patients with invasive tumours and a clinical history of three months' duration or less had a significantly increased platelet adhesiveness. In view of the similarity in alterations of platelet adhesiveness in patients with rapidly growing brain tumours and multiple sclerosis it is suggested that these platelet changes are consequent on acute degradation of neural tissue.

I wish to thank Professor Henry Miller and the physicians and surgeons of the Regional Neurological Centre, Newcastle upon Tyne, for permission to study patients under their care.

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Impedance Spirometry in Clinical Monitoring*

J. V. FARMAN,† M.B., F.F.A.R.C.S.; D. A. JUETT,† B.Sc.

Brit. med. J., 1967, 4, 27-29

There are certain places, such as the operating-theatre and the intensive therapy unit, where it is impossible to keep a finger always on a patient's pulse or a constant watch on his breathing. In these circumstances it is customary to employ various types of monitor. Ideally, by using such a machine, one should be able to tell at a glance that the patient is breathing and his heart is beating, even if he cannot be directly observed. Most of the apparatus in common use falls short of this ideal. We have therefore been examining changes in the electrical impedance across the chest as a method of monitoring patients.

Methods of Respiratory Monitoring

Many methods of respiratory monitoring have been employed. The anaesthetic reservoir bag gives a useful qualitative indication of spontaneous respiration, but it cannot be calibrated and it is in any case seldom used in the artificially ventilated patient. Thermistors and pressure transducers placed in the airway also give an indirect indication of respiration. Some mechanical ventilators have calibration marks which purport to measure the tidal volume; these tend to be inaccurate, difficult to read, and in any case capable only of measuring the volume leaving the machine. Only the spirometer and the pneumotachograph can measure accurately the volume of respiration. All these methods share the disadvantage of being placed in the airway, where they will fail to detect disconnection of a ventilator, if this is of the type which continues to function in the presence of a leak. The external strain-gauge pneumograph lacks this drawback but it tends to slip and has not proved popular. Pressure transducers placed in the oesophagus give an even less direct indication of respiration.

For the heart beat the E.C.G. is the best way of detecting arrhythmias and disturbances of conduction, but it is capable of giving a fairly normal-looking trace in the absence of any significant forward flow of blood. Peripheral pulse monitors, apart from their tendency to produce artifacts, err in the other direction by indicating no-flow under conditions of skin vasoconstriction when the cardiac output may be little disturbed.

In any event it is undesirable to have a multiplicity of monitors attached to a patient. They can be such a nuisance to the medical and nursing staff that they may not be used in situations where they might otherwise be helpful. The time needed to apply and adjust them may be too long to be acceptable, particularly in the theatre or recovery room. A variety of leads and transducers attached to the chest and arms may cause dangerous confusion to the attendants and alarm to the patient.

A less obvious disadvantage of many currently available monitors lies in the way in which the information is displayed. Dial displays are difficult to understand if they show rapidly changing variables such as respiration or the arterial pulse, and for this reason the information they impart can only be

of a qualitative nature. In such a case a blinking light will often be more appropriate. Pen recorders are essential for the proper interpretation of the E.C.G., the pneumotachograph, and spiograms, but it is inconvenient and expensive to use them for continuous display purposes at any useful paper speed. For this reason an oscilloscope is best for continuous monitoring purposes. Most oscilloscopes used for this purpose have screens of 3-5 in. (7.5-12.5 cm.) diameter and are far too small to be seen at any distance.

We believe that for any method of monitoring the form of display must be appropriate to the information displayed. Rapidly changing variables should be appreciated as they occur, and for this reason an oscilloscope or a chart recorder is needed to show individual waves. For less rapidly changing variables, such as respiration rate, heart rate, or mean arterial pressure, a meter or digital display is more appropriate. For slowly changing variables such as body temperature a meter can also be used. In addition to this the display should be easily visible from a distance—for example, from across the patient's bed—particularly in the case of the most rapidly changing variables. Lastly, we feel it is important that the criteria which are monitored should be easy to comprehend. This is important when the monitor is to be watched by nurses who may not, for example, understand the significance of changes in rather indirect measurement such as the digital pulse wave.

Impedance Spirometer

Atzler (1935) attempted to measure cardiac activity by following changes in electrical impedance across the chest. He noted at the same time that the transthoracic impedance varied with respiration. Other workers later attempted to record respiration by this means, but modern interest in the method is due largely to the work of Geddes *et al.* (1962b). They passed a small high-frequency current through the chest and were able to demonstrate the relation between changes in the volume of air breathed and changes in electrical impedance. Later work (Kubicek *et al.*, 1964; Pallet and Scopes, 1965; Baker *et al.*, 1965) confirmed that, though the calibration varied, this relation was more or less linear. The slope of the line varied between individuals and depended, moreover, on the position of the skin electrodes, the frequency of the current applied, and the posture of the subject.

Most writers have noted small variations in the tracing synchronous with the heart beat. While this has generally been treated as an artifact we regard it as indicative of pulsatile changes in the volume of blood in the thorax. It is not necessary to assume that this variation is due to change in the size of the heart during each beat. Kubicek *et al.* (1966) concluded that it was probably due to the pulsating pulmonary blood flow. In some of our subjects, however, complex wave-forms have been observed which might be due to changes in heart size (see Fig. 2).

Geddes *et al.* (1962a) showed that it was possible, by the employment of suitable filtering circuits, to record the electrocardiogram from the electrodes used to measure transthoracic impedance. We therefore employ this technique in order to display the E.C.G. at the same time as impedance changes.

* This work was supported by a grant from the Joint Research Committee, United Cambridge Hospitals and East Anglian Regional Hospital Board.

† Addenbrooke's Hospital, Cambridge.

The apparatus we are using consists of a 100 kc./s. oscillator that supplies a constant current of 200 μ A to two electrodes attached to the chest wall. The signals across these electrodes are separated into E.C.G. and 100 kc./s. components. The E.C.G. is fed to a conventional display system and the 100 kc./s. is amplified and rectified to d.c. and then subtracted from a reference potential to give the respiration signal required. We have found it preferable to employ three skin electrodes for long-term monitoring because the addition of an indifferent electrode considerably reduces artifacts on impedance and E.C.G. displays caused by contact with the patient. The electrodes are stainless-steel discs of 2.3 cm. diameter coated with Cambridge electrode jelly. They are attached to the skin by adhesive paper tape.

The outputs of the impedance spirometer and E.C.G. amplifier are displayed on a large screen oscilloscope (Lan Electronics L S 19). The tracings may also be recorded on magnetic tape or on a paper chart recorder. The impedance trace appears as a line of small waves, due to the heart beat, with larger waves due to respiration superimposed (see Figs. 2-6).

Clinical Use

For monitoring purposes the measuring electrodes are attached to the patient's chest at the level of the sixth rib in the mid-axillary line (Fig. 1). At this level the maximum impedance change is seen during respiration (Geddes *et al.*, 1962). The indifferent electrode is placed on the manubrium sterni. Use of a standard arrangement makes it easy for nurses to remember the position. It also allows the conscious patient a good deal of freedom of movement, and, perhaps more important, he is not aware of the presence of the electrodes once they have been applied. The electrodes can be

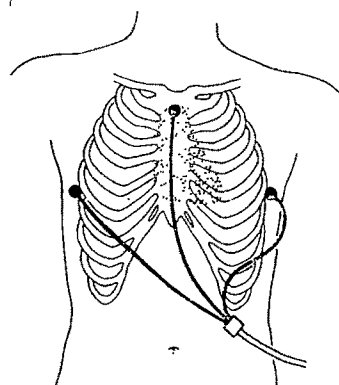


FIG. 1.—Position of electrodes on patient's chest. The measuring electrodes are in the mid-axillary line and the indifferent electrode on the manubrium sterni.

applied quickly without too much disturbance of the patient. We have found that they can be left on for up to a week without causing irritation to the skin. However, we have experienced difficulty in keeping them attached to the skin in very obese subjects and are at present considering alternatives.

After a few minutes the tracing settles down to the pattern shown in Figs. 2-6. Baseline stability is good so long as the patient remains still. Movement and postural changes, such as lying on one side, alter

the basal impedance, but the baseline can be restored by altering the high-frequency gain (Pallett and Scopes, 1965) or by means of an automatic baseline-restoring circuit. In practice this represents little disadvantage because the patients we monitor are usually immobile for one reason or another. We have occasionally encountered tracings which appeared inverted, and this has been found to result from wrong positioning of the electrodes or from poor skin contact. It is noticeable that in children the cardiac component of the tracing is much more prominent than in adults.

Our intensive therapy unit nurses have little difficulty in understanding the significance of the tracings. They recognize the E.C.G. immediately, and, after seeing the position of the electrodes, soon decide that the other tracing shows respiration. The cardiac component of the impedance tracing is less often recognized immediately, but is understood once it

has been explained. As the height of the respiratory waves is proportional to the tidal volume the system is meaningful, unlike a tracing of airway or oesophageal pressure. This enables the observer to form the same appreciation of the patient's respiration as can be obtained by close observation of the movement of the chest.

Calibration is carried out by measuring the height of the tracing at the same time as the breath is measured with a spirometer. For monitoring purposes we use either a Wright spirometer or a calibrated concertina bellows which can be used to give a breath of known volume to an apnoeic patient. These methods are accurate enough for clinical purposes, in spite of the relatively large standard deviations of the impedance changes reported by Kubicek *et al.* (1964). For adults we normally employ a sensitivity of 1 cm./100 ml. volume change, but in children we usually increase this to 2 or 3 cm./100 ml.

We have found, as we had originally hoped, that changes in tidal volume and upper airway resistance are immediately apparent. We regard the display of these changes as an essential property of any respiratory monitoring system. Fig. 2 shows the effect of clamping the endotracheal tube connexion in a spontaneously breathing anaesthetized patient. Fig. 3 shows the same procedure in a fully relaxed anaesthetized patient receiving artificial ventilation. In both these cases the small cardiac waves are seen to persist while the

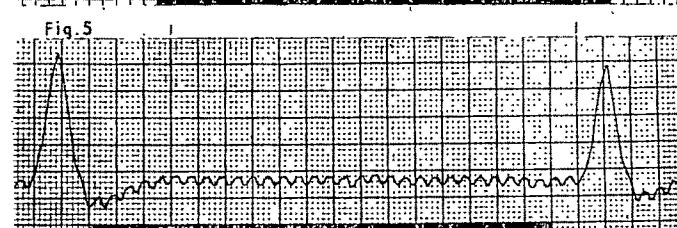
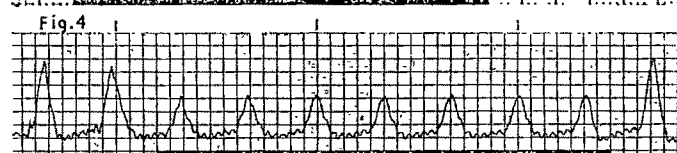
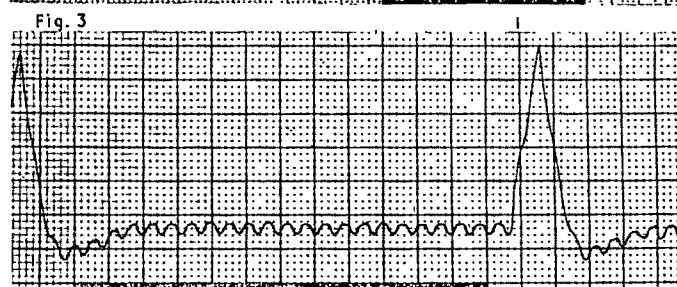
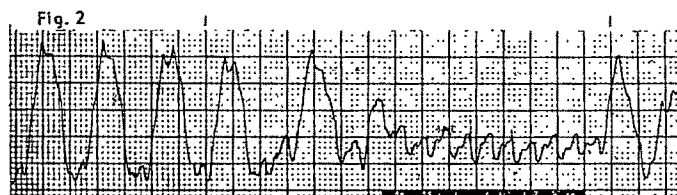


FIG. 2.—Tracing taken from a spontaneously breathing anaesthetized patient. The larger variations are due to respiration and the smaller to the heart beat. The black line shows when the endotracheal connexion was clamped, causing a complete obstruction to respiration. The respiratory wave disappeared in spite of the patient's efforts to breathe, but the cardiac wave remained. (Paper speed 5 mm./sec.) FIG. 3.—Tracing taken from the same anaesthetized patient during artificial ventilation after receiving a relaxant. Only the cardiac waves could be seen when the airway was clamped for 12 seconds (black line). (Paper speed 5 mm./sec.) FIG. 4.—Recording from the same patient when the airway was partially clamped (black line) during artificial ventilation. The tidal volume fell to about half its previous value. (Paper speed 5 mm./sec.) FIG. 5.—Tracing showing the effect, again in the same artificially ventilated patient, of disconnecting the ventilator (black line). As in Fig. 3, only the cardiac waves can be seen. (Paper speed 5 mm./sec.)

respiratory waves are absent. In Fig. 4, recorded from the same relaxed patient, the airway is only partially obstructed, resulting in an obvious reduction of tidal volume. Fig. 5 shows the effect, again in the same apnoeic patient, of disconnecting the ventilator. This pattern is indistinguishable from that shown in Fig. 4, demonstrating that this technique reveals the essential point—namely, that ventilation of the lungs has ceased. So far as we know this is the only method of monitoring which cannot give a wrong indication in these circumstances.

It is also possible to study the shape of the respiratory wave-form with the impedance spirometer. The tracing follows closely all changes in the volume of air in the lungs, so that it is possible to measure not only the tidal volume but the rate of change of volume, both in inspiration and in expiration. Fig. 6 was recorded on a patient ventilated with a Barnet Mark III ventilator. This machine, though theoretically a constant pressure generator, in practice operates as a

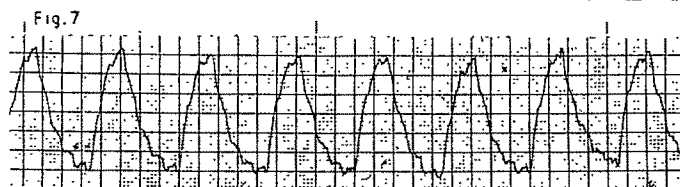
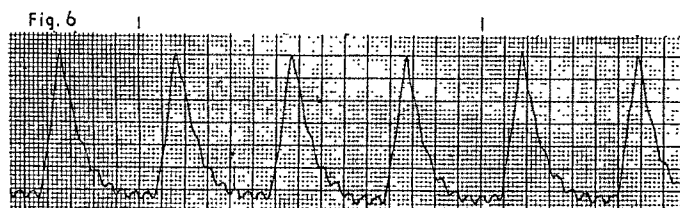


FIG. 6.—Tracing showing the respiratory wave-form when using a Barnet Mark III ventilator. This machine functions as a constant flow generator and the upstroke of the respiratory wave shows the expected straight line. The downstroke, as the patient expires to atmosphere, is exponential. (Paper speed 5 mm./sec.) FIG. 7.—Tracing showing the wave-form when using an East-Radcliffe ventilator to produce the same tidal volume as in Fig. 6. In this case both the upstroke and the downstroke are exponential. This wave-form is typical of a constant pressure generator. (Paper speed 5 mm./sec.)

constant flow generator (Mapleson, personal communication) and the tracing shows the expected straight line during the inspiratory phase. Fig. 7 was recorded when the same patient was being ventilated with an East-Radcliffe ventilator at approximately the same rate and tidal volume. In this case the tracing shows the exponential curve expected of a constant pressure generator. In both these tracings the expiratory portion is identical, being an exponential decay as the patient expires to atmosphere. The technique may therefore prove helpful in the treatment of asthmatics in whom this decay is prolonged because of the increased lower airways resistance.

Summary

A technique for monitoring respiration is described which is simple to use and simple to understand. Three electrodes are attached to the patient's chest and changes in trans-thoracic electrical impedance are displayed on an oscilloscope. This tracing reflects the volume of air in the lungs so that the tidal volume, respiratory rate, and respiratory wave-form can be immediately appreciated by those attending the patient.

Additional advantages are that an E.C.G. can be obtained from the same electrodes and that the impedance tracing shows small variations in time with the heart beat. It therefore gives a valuable indication of the function of the heart as well as of respiration. The display provides direct, reasonably accurate, and conceptually simple indications of these two vital factors, important points where nurses are concerned. We feel that this technique is worthy of further trial.

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Haemoglobin E and α -Thalassaemia*

P. WASI,[†] M.B., PH.D.; M. SOOKANEK,[†] M.B.; S. POOTRAKUL,[†] M.B., M.S.; S. NA-NAKORN,[†] M.D.
 A. SUINGDUMRONG,[†] M.B.

Brit. med. J., 1967, 4, 29-32

Haemoglobin Bart's was first described by Ager and Lehmann (1958). The fast-moving haemoglobin earlier reported by Fessas and Papaspyrou (1957) is believed to be identical with Bart's (Fessas, 1959). This haemoglobin has been found by Hunt and Lehmann (1959) to consist entirely of γ -polypeptide chain, thus having the molecular formula of γ_4 ; Hbs A, F, and A_2 are $\alpha_2\beta_2$, $\alpha_2\gamma_2$, and $\alpha_2\delta_2$ respectively.

Hb Bart's, in extremely variable amount, has been found in conditions ranging from the asymptomatic newborns (Tuchinda *et al.*, 1959; Lie-Injo, 1959; Vella, 1959; Hendrickse *et al.*, 1960; Fessas, 1960; Lie-Injo and Ti, 1961; Schneider and Haggard, 1961; Minnich *et al.*, 1962; Silvestroni and Bianco, 1962; Weatherall, 1963) to the lethal Hb Bart's hydrops foetalis

syndrome (Lie-Injo *et al.*, 1962; Banwell and Strickland, 1965; Diamond *et al.*, 1965; Wong, 1965; Pootrakul *et al.*, 1967). Apart from its presence in minute amount in the cord blood of apparently every newborn, the occurrence of Hb Bart's is believed to be a result of α -thalassaemia gene. The latter depresses α -chain synthesis, resulting in excessive γ -chains, which then polymerize to the tetrameric form- γ_4 .

In Thailand Hb E, β -, and α -thalassaemias are prevalent (Na-Nakorn *et al.*, 1956; Flatz *et al.*, 1965; Wasi *et al.*, 1967). These genes, in different combinations, give rise to various conditions and diseases, such as β -thalassaemia homozygosity (Hbs A+F), β -thalassaemia-Hb E disease (Hbs E+F), and Hb H disease (Hbs A+H). Beginning from 1961, we have frequently encountered another disease characterized by the presence of three haemoglobins, A, E, and Bart's. Genetical data indicate that individuals with this disease inherit three abnormal genes—namely, a classical or α -thalassaemia, a milder

* Supported by U.S. Public Health Service Research Grant AM 09805-01 from National Institute of Arthritis and Metabolic Diseases.

[†] Division of Haematology, Department of Medicine, Siriraj Hospital Medical School, Bangkok, Thailand.

or α -thalassaemia₂, and Hb E genes. We wish here to present the clinical and haematological data of this α -thalassaemia₁/ α -thalassaemia₂-Hb E disease in 21 patients.

Materials and Methods

Standard haematological techniques were employed. The counting of red blood cells in the latter patients was done in Coulter's electronic counter; quantitative osmotic fragility of the red cells was also switched from the standard method (Dacie, 1960) to Danon's (1963) automatic fragiligraph. Red cell inclusion bodies were demonstrated according to the technique previously described (Na-Nakorn, *et al.*, 1965). The acid elution method of Betke and Kleihauer (1958) was used to demonstrate individual cells containing Hb F.

Haemolysate was prepared according to Singer *et al.* (1951). Originally haemoglobin types were determined by paper and cellulose acetate electrophoreses, and the relative amount of each fraction was obtained by starch block electrophoresis (Kunkel and Wallenius, 1955; Gerald and Diamond, 1958). Later all the haemoglobin typings were done in starch-gel tris-borate-E.D.T.A. buffer, pH 8.6 (Smithies, 1959). Haemoglobin fractions were quantitated by electrophoresing on cellulose acetate in tris-borate-E.D.T.A. buffer pH 8.6 for one hour, each haemoglobin type being eluted with water from the cut strip, the optical density being read in Beckman B spectrophotometer. Alkali-resistant haemoglobin was measured with the one-minute method (Singer *et al.*, 1951).

Results

General and Clinical Description.—Table I summarizes the general and clinical data. The patients were 5 to 38 years old,

those younger than 13 having been seen in the department of medicine only through family investigation. Ten were males. All had Thai ethnic background with mixed Chinese and Mon, each in one instance. They were from central or north-eastern Thailand. Retardation of development was observed in eight cases, being most pronounced in Case 21. "Thalassaemic mongoloid" facies (Fig. 1) was definite in two and suggestive in 12. All were anaemic, and 17 were mildly to moderately jaundiced when first seen. The liver was not palpable in four cases, being 5 to 8 cm. below the right costal margin in the rest. Splenomegaly was noted in all except Case 14, and varied from being just palpable to 18 cm. below the left costal margin.

Haematological Findings.

—These are summarized in Table II. The means of the haemoglobin concentration, red blood cell count, and haematocrit in the 21 patients were 6.9 (S.D. 1.6) g./100 ml., 4.29 (S.D. 1.14) million/cu. mm., and 27 (S.D. 6) % respectively. Both red cell indices and morphology showed hypochromicity and microcytosis; anisocytosis, poikilocytosis, nucleated red cells, polychromasia, and leptocytosis were always observed (Fig. 2). Reticulocyte counts were 3–17%. Quantitative red cell osmotic fragility, either with the



Fig. 1.—Case 21. 22-year-old man showing mongoloid facies.

TABLE I.—General and Clinical Data

Case No.	Age and Sex	Races	Anaemia	Jaundice	Hepatomegaly (cm.)	Splenomegaly (cm.)	Retardation of Development	Mongoloid Facies	X-ray Bone Changes
1	5 F	Central Thai	+	+	5	1	+	—	Not done
2	33 F	N.E. Thai	+	+	5	>8	—	—	—
3	37 M	Central Thai	+	+	5	5	—	—	—
4	31 F	" "	+	+	5	5-8	—	Suggestive	Suggestive
5	6 F	" "	+	—	0	5	+	"	Not done
6	22 F	" "	+	+	0	5	—	—	—
7	22 F	" "	+	+	5	5-8	—	Suggestive	Not done
8	38 F	N.E. Thai + Chinese	+	+	5	5	—	"	—
9	17 F	Central Thai + Mon	+	—	5	5-8	+	"	Suggestive
10	28 M	Central Thai	+	+	5	>8	—	Suggestive	—
11	17 M	" "	+	+	5-8	5-8	—	—	Not done
12	26 F	N.E. Thai	+	+	5	5	—	—	"
13	16 F	" "	+	+	5	5	+	Suggestive	"
14	9 M	" "	+	—	0	0	+	"	—
15	28 M	Central Thai	+	+	5	5	+	"	—
16	38 M	N.E. Thai	+	+	5-8	8	+	+	—
17	27 M	" "	+	+	0	5	—	Suggestive	—
18	5 M	" "	+	—	5	5	+	"	—
19	34 F	Central Thai	+	+	5	5	—	"	—
20	25 M	" "	+	+	5	5	—	"	—
21	22 M	" "	+	+	5	18	+	+	+

TABLE II.—Haematological Data

Case No.	Hb (g./100 ml.)	R.B.C. $\times 10^6$ /cu. mm.	Hct %	M.C.V. cu. μ	M.C.H. μ	M.C.H.C. %	R.B.C. Morphology					Retic %	R.B.C. Inclusion %	Hb E %	Hb Bart's %	Alkali R-resistant Hb %
							Hypo.	Micro.	Anis.	Poik.	Target					
1	6.6	4.34	27	63	15	24	+++	+	++	++	+++	8	10	14.7	11.2	3.2
2	8.1	4.95	34	69	16	24	+++	+	+++	+++	+++	10	8	14.9	7.8	3.8
3	8.6	5.54	30	55	16	29	+++	+	++	++	+++	—	—	13.3	8.4	2.4
4	4.7	2.10	18	86	22	26	+++	+	+	+	+++	9	7	13.2	6.9	5.0
5	6.6	4.37	26	60	15	25	+++	+++	+++	+	+++	9	—	18.7	4.8	4.0
6	7.5	4.47	29	66	17	26	++	+	++	++	+++	17	—	13.6	8.3	4.8
7	5.7	3.35	27	79	17	22	+++	+++	+++	+++	++	—	—	18.9	3.4	—
8	6.6	3.76	22	59	18	30	++	+	++	+	+	6	17	14.5	8.0	2.5
9	6.7	3.79	29	77	18	23	+++	+	++	+++	+	—	—	15.4	8.0	1.6
10	8.9	3.85	29	75	23	31	++	+	+	+	+++	10	2	18.8	4.7	2.8
11	5.9	4.46	26	47	10	20	+++	+++	+++	+++	+++	4	0	13.2	7.7	—
12	7.0	5.21	28	54	13	25	+++	+	++	+	+++	5	3	14.6	7.1	4.6
13	4.8	3.10	18	58	16	27	++	+	+++	++	+++	3	12	12.5	9.4	1.5
14	8.4	5.90	32	55	14	26	+++	+	++	++	+++	4	16	14.7	18.0	—
15	7.0	4.88	29	59	14	24	++	+	+	+	+++	10	5	14.5	9.2	4.7
16	8.4	4.43	32	72	19	26	++	+	++	++	+++	10	3	13.1	8.7	4.2
17	9.8	6.01	39	65	16	25	++	+	++	++	+++	6	3	13.4	8.3	4.8
18	7.1	5.40	23	43	13	31	+++	+	++	++	+++	10	5	12.6	11.5	5.2
19	6.0	4.25	25	59	14	24	++	+	++	++	+++	4	10	13.6	8.6	4.1
20	7.2	4.61	30	65	16	24	++	+	++	++	+++	8	1	12.2	—	1.8
21	3.2	1.41	11	78	18	21	+++	+++	+++	+++	+++	3	2	14.4	7.0	4.2

— = not estimated.

standard technique or with Danon's automatic fragiligraph, was constantly decreased. On mixing the blood with methylene blue solution inclusion bodies, unlike those in Hb H disease, were always seen but only in very few red cells (Fig. 3). Acid elution and counterstaining according to Betke's technique showed a few cells retaining haemoglobin (Fig. 4). ^{51}Cr red cell half-lives† in Cases 7, 9, 13, 16, and 21 were 3.5, 10, 8.5, 12, and 4 days respectively. The bone marrow examination in four cases showed marked erythroid hyperplasia and haemosiderosis.

Haemoglobin Types.—The major haemoglobin types in starch gel (Fig. 5) were A+E+Bart's. The level of Hb E fell in a

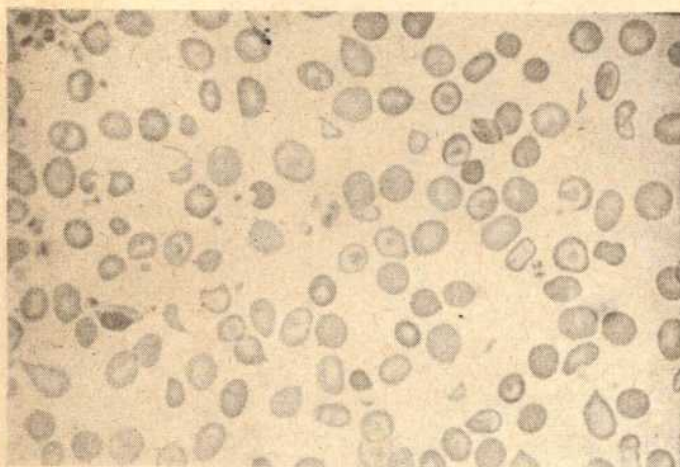


FIG. 2.—Case 16. Peripheral blood smear. (Wright's stained. $\times 1,280$.)

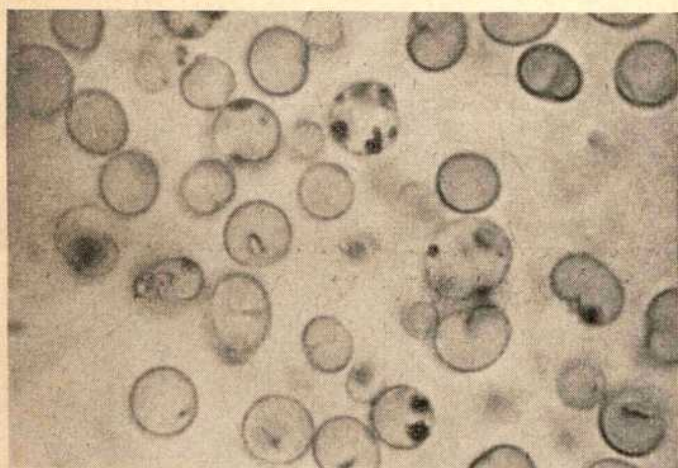


FIG. 3.—Case 18. Methylene blue fresh preparation ($\times 3,200$) showing characteristic presence of a few cells with inclusion bodies.

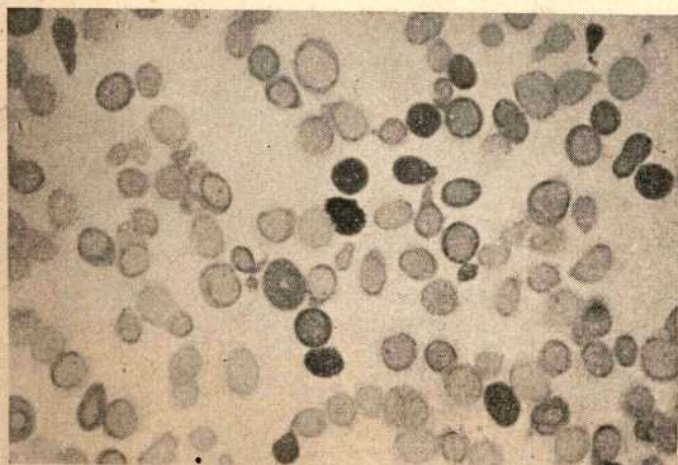


FIG. 4.—Case 21. Acid elution staining ($\times 1,280$) showing a few acid-resistant red cells.

rather narrow range between 13 and 15%, in most cases, the extreme values being 12.2 and 18.9%. Hb Bart's constituted 3.4 to 18.0, averaging 8.4%. Alkali-resistant haemoglobin, as determined by Singer's one-minute method, was slightly raised (Table II). A band of presumably Hb F was seen behind that of Hb A in both starch-gel and cellulose acetate electrophoreses; with the latter technique the amounts in Cases 10, 12, 13, 19, and 21 were 4.4, 3.9, 4.0, 3.9, and 7.0% respectively. With both starch-gel and cellulose acetate electrophoreses a faint band of haemoglobin was seen cathodal to Hb E at pH 8.6 (Fig. 5). The amount of this slow-moving haemoglobin was 0.53–1.30%. Occasionally a faint band of haemoglobin at Hb H position was observed.

Other Findings.

X-ray examination of the skulls and long bones in 17 cases showed widening of the medulla typical of thalassaemic diseases in one case, and in two cases the pictures were suggestive. Serum iron was raised in most cases. Conjugated bilirubin level was normal, but the total value was

raised up to 5.5 mg./100 ml. Serum globulin was above 4 g./100 ml. in three out of nine patients, and serum electrophoresis showed gammaglobulin of 25% or over in five out of eight cases. Serum flocculation tests were often positive. The fasting blood sugar, serum alkaline phosphatase, transaminases, cholesterol, and sulphobromophthalein excretion, determined in five cases, were within normal limits.

Clinical Course.—The patients remained anaemic all the time, though the haemoglobin level may fluctuate considerably. Folic

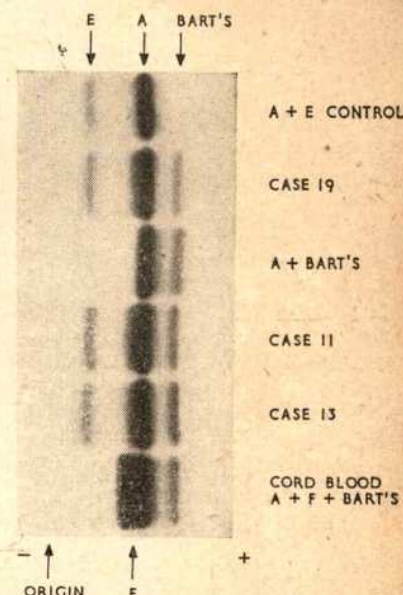


FIG. 5.—Horizontal starch-gel electrophoresis in tris-borate-E.D.T.A. buffer, pH 8.6, stained with ortho-dianisidine.

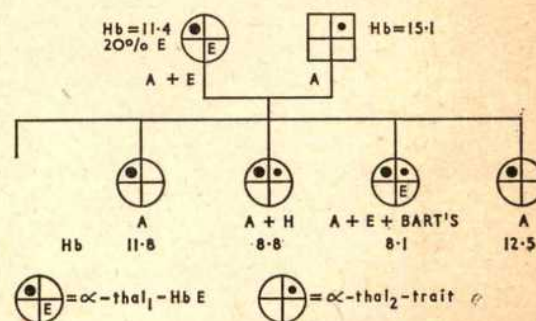


FIG. 6.—Family of Case 2. Detailed genetical data will be described elsewhere.

acid orally did not seem to alleviate the anaemia. Hypersplenism was noted in Case 21. Splenectomy had been performed in Cases 2, 3, 4, 10, 14, and 21, with a slight improvement of anaemia in Cases 14 and 21.

Genetical Findings.—Family members of the patients were examined, but the results are not presented here. Only representative findings from the family of Case 2 are condensed into Fig. 6.

† Done by Dr. V. Viranuvatti and others, of the Faculty of Medical Technology.

• Discussion

That this Hb A + E + Bart's disease is connected with thalassaemia is evident from thalassaemic stigmata in the patients themselves and in their parents, siblings, and offspring. This type of thalassaemia is the low Hb A₂ or α -chain variety of thalassaemia. Two forms of α -thalassaemia have been identified in the Thai population (Wasi *et al.*, 1964): α -thalassaemia₁ (α -thal₁) is the classical or the most severe form, and α -thalassaemia₂ (α -thal₂) is the mildest type which cannot be identified in heterozygotes. Those homozygous for the α -thalassaemia₁ gene die during intrauterine existence with the clinical findings of the Hb Bart's hydrops foetalis syndrome (Pootrakul *et al.*, 1967). The α -thal₁/ α -thal₂ combination results in Hb H disease. Genetic analysis of the families reported here will be presented in detail elsewhere. They indicate that the patients with Hb A + E + Bart's disease are carrying the Hb E gene and those for α -thal₁ and α -thal₂. This condition has been reported as well by Tuchinda *et al.* (1964), who discussed the interaction of two different α -thalassaemia genes and Hb E as one of the possible aetiologies.

Clinically this disease cannot be differentiated from β -thalassaemia homozygosity, β -thalassaemia-Hb E, and Hb H diseases, much prevalent in Thailand. The severity of the already recognized disease forms appears to be in the following order: α -thalassaemia₁ homozygosity (Hb Bart's hydrops foetalis), β -thalassaemia homozygosity, β -thalassaemia-Hb E, α -thal₁/ α -thal₂-Hb E, and α -thal₁/ α -thal₂.

Haemoglobin phenotype of A + E + Bart's is the hallmark of the disease under present discussion. In contrast to Hb H disease, in which inclusion bodies are demonstrable in the majority or all of the red cells, in α -thal₁/ α -thal₂-Hb E disease only a few red cells show inclusion bodies. The non-overlapping numbers of red cells containing inclusion bodies in these two conditions have led us to correct diagnosis previous to electrophoresis in all instances. These scanty inclusion bodies in the red cells of the patients with Hb A + E + Bart's probably represent Hb H, which is present at too low concentrations to be readily detected by electrophoresis. Hb E, which in heterozygotes is present in about 30% of total haemoglobin, represents about 14% of the total haemoglobin in this disease. Three reasons for the reduced quantity of Hb E in this circumstance may be considered. Firstly, the α -thal₁/ α -thal₂ combination, in addition to suppressing α -chain synthesis, has an inhibitory effect upon Hb E production (Tuchinda *et al.*, 1964). Secondly, unequal distribution of haemoglobin types among red cells may be associated with differential survival as found in Hb H disease (Gabuzda *et al.*, 1965). Finally, β_2 subunits may compete for α_2 subunits more successfully than β_2 E subunits. In view of insufficient data it is not appropriate to discuss these possibilities at length here.

In this disease both Hbs F and Bart's are raised irrespective of the patient's age. The increased amount of alkali-resistant haemoglobin is due to both types of haemoglobin, since Hb Bart's is partially alkali-resistant. According to Betke's technique, cells containing Hb F are relatively resistant to acid elution. In Hb A + E + Bart's disease a few cells are obviously resistant. Whether they represent cells containing only Hb F or Hb Bart's as well is not yet known.

The apparent decrease in β -chain synthesis in α -thalassaemia has been previously discussed (Rucknagel, 1964; Pootrakul *et al.*, 1967). As judged by the amount of Hbs F and Bart's found in α -thal₁/ α -thal₂-Hb E disease the quantity of γ -chain produced in this condition is obviously greater than that in Hb H disease. This suggests that the amount of β -chain synthesis in the former is less than in the latter, since the quantity of γ and β chains is reciprocally related. This would indicate that, for reasons not yet clear, when the Hb E gene is present in addition to the α -thal₁ and α -thal₂ genes a reduction in β -chain synthesis occurs. Thus very little Hb H is found in this disease, despite the α -thal₁/ α -thal₂ genotype which is identical to that in Hb H disease.

The haemoglobin band slower than Hb E has not yet been identified. Its absence in both parents suggests that it is not a result of primary mutant gene action. It is most likely δ_1 , as found in Hb H disease (Dance *et al.*, 1963) and/or β_2 E. Further investigation is in progress.

The patients with this disease seem to benefit only from blood transfusion, and from splenectomy when hypersplenism is present. Liver damage often handicaps the victims. The patients with these various combinations of thalassaemias and Hb E, about 100,000 in number as estimated from gene frequencies, present a socio-economic problem to Thailand.

Summary

The clinical and haematological study of 21 patients in Thailand with a new disease is described. It is similar to a thalassaemia major disease clinically. Hepatosplenomegaly was almost consistently detected, the mean haemoglobin concentration was 6.9 g./100 ml., the red cells showed strong stigmata of thalassaemia, and the erythrocytic life-span was shortened. This disease is characterized by the presence of inclusion bodies in very few red cells, and haemoglobin phenotype of A + E + Bart's with about 14% Hb E and 8% Hb Bart's. Elevation of Hb F was demonstrated electrophoretically, morphologically, and by the alkali denaturation test. Small amounts of an unidentified haemoglobin slower than E, probably δ_1 and/or β_2 E, were also detected. Genetical data suggest that this disease is a result of a combination of three abnormal genes—namely, the more usual type of α -thalassaemia or α -thalassaemia₁ gene, a milder or α -thalassaemia₂ gene, and Hb E. Anaemia in these patients was, although fluctuating in degree, perpetual. Splenectomy had been done in six patients, with a slight improvement of anaemia in two—one with hypersplenism.

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Medical Memoranda

Cantharides Intoxication

Brit. med. J., 1967, 4, 33

Preparations containing cantharides, commonly known as "Spanish fly," have been used since the time of Hippocrates for conditions such as dropsy and amenorrhoea, and for the aphrodisiac properties that it is wrongly thought to possess. Cantharides is the active component contained in the ovaries, soft tissues, and blood of the blister beetle *Cantharis vesicatoria*. It contains not less than 0.6% of cantharidin (3:6-epoxy-1:2-dimethylcyclohexane-1:2-dicarboxylic anhydride), which is the active principle. The fatal dose of cantharidin is described as being less than 60 mg. (Nickolls and Teare, 1954).

Only four cases (*Pharm. J.*, 1963; Nickolls and Teare, 1954; Craven and Polak, 1954; Lécuyer, 1954), all terminating in death, have been reported in the English medical literature in the past 25 years. In the world literature 30 cases have been described since 1900.

CASE HISTORY

A man aged 42 was admitted to hospital at 2.15 a.m. on 9 August 1966. He had previously been in good health, except for two episodes of "nephritis" when aged 10 and 22 years.

At 5.30 p.m. he had taken a teaspoonful of liquor epispaeticus, which he knew contained cantharidin (approximately 20 mg.) to increase his libido, even though he had read of the man who caused the death of two typists by concealing cantharides in coconut ice (Nickolls and Teare, 1954; Craven and Polak, 1954).

One hour after taking the mixture symptoms started with the onset of frequency of micturition and severe dysuria. Approximately two hours later he felt nauseated and vomited. He micturated five times between 9 and 10 p.m., each specimen becoming progressively more blood-stained. Half an hour later he was passing pure blood, and had abdominal discomfort accompanied by bouts of diarrhoea. He continued to have haematuria and developed priapism; a few hours later he became worried and decided to seek medical advice.

On examination he was pale and extremely anxious. There was no pyrexia and his blood pressure was 120/80. The mucous membranes and throat were reddened, but blistering was not evident. Generalized tenderness was present over the abdomen and the bladder was palpable. The penis was erect and blood was present at the tip of the urethra. The central nervous, respiratory, and cardiovascular systems were normal.

The urine was loaded with protein (300 mg./100 ml.) and blood was visible macroscopically; pus, red blood, and scanty epithelial cells were seen on microscopy. No casts were present.

Laboratory Investigations.—Serum urea was 41 mg./100 ml., serum sodium 133 mEq/l., potassium 4.4 mEq/l., and bicarbonate 22 mEq/l. Total protein 6.7 g./100 ml. His haemoglobin was 13.8 g./100 ml., and the white blood cell count was 16,300/cu. mm. E.C.G., chest, and straight abdominal x-ray films were normal.

It was thought that a stomach wash-out performed nine hours after ingestion would be of no value. He was therefore treated with a high fluid intake of milk, a magnesium sulphate enema, analgesics, and sedation.

The next day ulceration and blistering of the mucous membranes of both cheeks, the tongue, and palate were observed. These responded well to hydrocortisone pellets. His blood pressure was maintained, and the daily urinary output remained at approximately 2 litres per 24 hours. The priapism subsided spontaneously and within four days the urinary abnormalities had resolved.

When seen as an outpatient one month later he was extremely fit. His haemoglobin was 13.4 g./100 ml. and serum urea 35 mg./100 ml., and his urine showed no abnormality.

DISCUSSION

Liquor epispaeticus contains: cantharidin 400 mg., castor oil 2.5 ml., colophony 1.2 g., plus acetone to 100 ml.

Acute renal damage after cantharides poisoning was documented as long ago as 1913 (Pearce). Dérobert and Le Breton (1957) described the case of a 77-year-old man who died from cantharidin poisoning, and at necropsy the most significant findings were those of acute tubular necrosis. Nickolls and Teare (1954) showed that microscopically there was haemorrhage into the tubules, producing tubular epithelial damage. Lécuyer (1954) stated that the acute tubular necrosis is due to the direct toxic action of the drug. It is possible, however, that the toxic action is aggravated by shock, which results in diminished renal blood flow. Powell (1907) reported chronic renal disease with associated contracted kidneys after cantharides ingestion.

No specific treatment is available. Csiky (1958) described four cases of pure cantharides poisoning; all the patients lived. His treatment was similar to ours, but he stated that oil, milk, and alcohol should not be taken as they aid absorption of the drug.

Management of the renal disorder and the associated fluid and electrolyte imbalance is probably the most important aspect of cantharides ingestion. As diminished renal blood flow and a reduced glomerular filtration rate are well described, acute tubular necrosis must be anticipated. Treatment will depend on urinary output, specific gravity, and the signs and symptoms of dehydration.

In none of the reported cases was there any evidence of an increase in libido. The myth that cantharides is an aphrodisiac should be destroyed, as its use for this purpose is fraught with danger and it is this property alone that perpetuates its illegal sale.

My thanks are due to Professor M. D. Milne for permission to publish this case, and to Drs. J. D. Swales and D. G. Gibson for their helpful advice.

R. D. ROSIN, M.B., B.S.,

Formerly House-physician, Professorial Medical Unit,
Westminster Hospital, London S.W.1.

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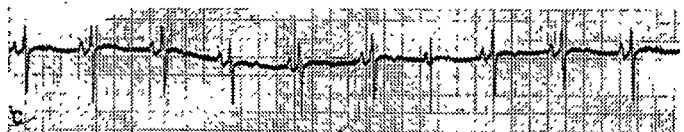
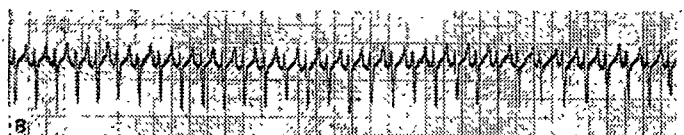
Dangerous Consequence from Use of Phenytoin in Atrial Flutter

Brit. med. J., 1967, 4, 34

Phenytoin sodium (Epanutin)* has been used successfully in various ventricular and supraventricular arrhythmias (Leonard, 1958; Dreifus *et al.*, 1964; Conn, 1965) and has been recommended for the treatment of digitalis-induced tachycardias (Conn, 1965; Lang *et al.*, 1965; Ruthen, 1965; Smith, 1966). It would therefore appear to be a suitable drug for patients who require immediate termination of a rapid arrhythmia in the face of an unclear history of digitalis, diuretic, and potassium intake. For this reason we wish to record a dangerous complication of this drug—namely, the conversion of paroxysmal atrial flutter with 2:1 block to 1:1 conduction with a ventricular rate of 300 per minute. The decision to use phenytoin was made because this patient was in acute pulmonary oedema and required urgent treatment; she had been treated for many years with digitoxin and a thiazide diuretic without potassium supplements, and digitalis intoxication could not be excluded.

CASE REPORT

A 38-year-old Negro woman with chronic rheumatic heart disease was admitted to Cook County Hospital in acute pulmonary oedema.



Electrocardiographic tracing showing paroxysmal atrial flutter with 2:1 conduction (A). The administration of phenytoin led to the establishment of 1:1 conduction with a ventricular rate of 300 a minute (B). The patient later reverted to sinus rhythm after administration of digitalis (C).

She had had a mitral commissurotomy nine years before admission; in recent years symptoms recurred and she had become progressively incapacitated by exertional dyspnoea. One day before admission she developed palpitations, haemoptysis, and severe breathlessness at rest. She had been treated with digitoxin 0.1 mg. a day, thiazide diuretics, but no potassium supplements up to the day of her admission.

Physical examination revealed a woman in acute distress. The pulse rate was 150 a minute and was not affected by carotid sinus pressure. Blood pressure was 110/80 mm. Hg. The heart was not enlarged, but she had the physical signs of mitral valve disease and pulmonary oedema. An electrocardiogram showed atrial flutter at a

rate of 300 and a ventricular rate of 150, with a 2:1 atrioventricular block (see Fig.).

With electrocardiographic monitoring a slow intravenous injection of phenytoin sodium was begun. After two minutes, when approximately 150 mg. had been injected, the heart rate increased to 300 and 1:1 conduction was observed. Deslanoside (Cedilanid) 0.4 mg. was given intravenously and after five minutes she reverted back to her previous rhythm. An additional 0.4 mg. of deslanoside was subsequently given and she converted to sinus rhythm at a rate of 78. The serum potassium level at the time of admission was later reported to be 3.8 mEq/l.

Clinical evaluation at a slow heart rate revealed signs of tight mitral stenosis. The results of cardiac catheterization in February 1965 were later obtained; the mitral valve area was 0.6 sq. cm. Operation was refused at that time.

COMMENT

Phenytoin, while effective in stopping aconitine-induced atrial flutter in experimental animals, has been found to be generally ineffective in treatment of this arrhythmia in man (Conn, 1965; Ruthen, 1965). Nevertheless, Friedberg (1966) has referred to one patient in whom the drug may have been effective in converting atrial flutter to sinus rhythm. Our patient was in acute distress due to pulmonary oedema, and the possibility of digitalis intoxication, though rarely presenting as atrial flutter, was seriously considered; hence the decision to give intravenous phenytoin. The patient responded by the establishment of 1:1 conduction with an extremely rapid heart rate.

The mechanism of action of phenytoin in cardiac arrhythmias is not clear. Evidence has been presented that it decreases intracellular sodium content in cardiac muscle (Dreifus *et al.*, 1964; Ruthen, 1965). Clinically, the action of phenytoin is similar to that of quinidine and antazoline—that is, depression of excitability, conductivity, and contractility of cardiac muscle (Friedberg, 1966). Production of 1:1 conduction has been reported with both quinidine and antazoline (Dreifus *et al.*, 1964) and perhaps might also be expected to occur with phenytoin. We believe that the above case shows that intravenous phenytoin should not be used in atrial flutter with block, unless there is overwhelming evidence of digitalis intoxication.

JAMES H. GRISSOM, M.D.,

Fellow in Cardiology, Cook County Hospital, Chicago.

BENITO G. SY, M.D.,

Chief Resident, Chicago Medical School Service, Cook County Hospital.

JOHN P. DUFFY, M.D., M.R.C.P.,

Staff Physician, Cook County Hospital; Instructor in Medicine, Loyola University Stritch School of Medicine.

GEORGE DUNEA, M.B., M.R.C.P., M.R.C.P.E.D.,

Chief, Chicago Medical School Service, Cook County Hospital; Assistant Professor of Medicine, Chicago Medical School.

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* Known in U.S.A. as diphenylhydantoin sodium (Dilantin).

Cardiac Involvement in Psittacosis

Brit. med. J., 1967, 4, 35-36

Involvement of the heart during the course of psittacosis is extremely rare if one is to judge from the few reports in the literature. This prompted us to record the following case.

CASE REPORT

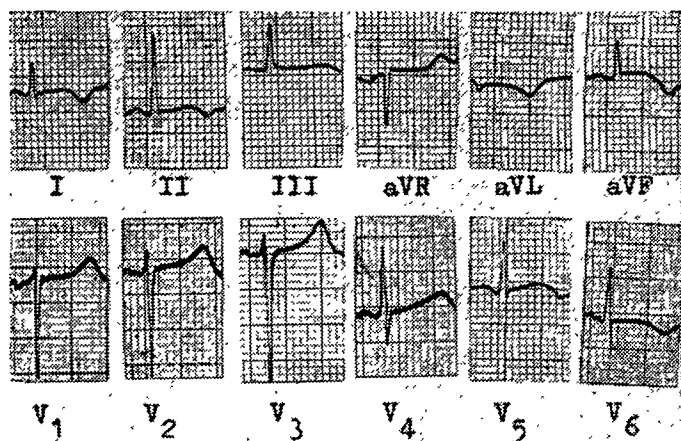
An 18-year-old youth was admitted to hospital on 16 July 1965. Five years previously he had been in hospital because of typhoid. He said that he often caught and handled wild birds only to release them soon after. The last occasion on which he had done this was two weeks before taking ill.

His illness began two weeks before admission with the appearance of severe headache and fever, the latter persisting till admission and varying between 37 and 38° C. Soon after taking ill he experienced pain in his throat and a burning sensation in the retrosternal area, which caused great difficulty in swallowing. In addition, he developed such severe pain in the muscles of both legs that he was unable to stand unassisted.

On examination he appeared to be mildly ill and pale. Oral temperature was 38.8° C., blood pressure 110/80, and radial pulse 90 a minute and regular. The heart was normal in size. Neither cardiac murmurs nor a pericardial friction rub were heard. All peripheral pulses were palpable and equal.

Numerous white shallow ulcers were visible on the soft palate and on the fauces. A few ulcers were seen on the oropharynx. There was no lymphadenopathy. Lungs were clear to percussion and auscultation. The liver and spleen were not palpable. His calf muscles were exquisitely tender on palpation and the slightest movement evoked severe pain. There were no signs of thrombophlebitis. Neurological examination was unrevealing.

The erythrocyte sedimentation rate was 11 mm. an hour (Wintrobe), haemoglobin 12.0 g./100 ml.; leucocyte and platelet counts were normal. Blood urea, electrolytes, bilirubin, alkaline phosphatase, and aspartate aminotransferase were normal. Blood lactic dehydrogenase was 220 units (normal range 83-185), hydroxybutyric



Electrocardiogram taken soon after admission. Negative T waves are seen in leads I, II, aVL, V₅, and V₆.

dehydrogenase 198 units (normal range 55-150), and aldolase 4.2 units (normal range 2.3-6.4). Thymol turbidity, thymol flocculation, and Lugol's test were normal. Serum iron was 30 µg./100 ml. Plasma protein was 8.5 g./100 ml. (albumin 3.5 g., globulin 5 g.); electrophoresis on starch gel showed slight hypergamma-globulinaemia. The Wassermann reaction was positive, but reverted to normal five weeks later. Psittacosis complement-fixation test was positive in a titre of 1:320 on 7 July, 1:480 on 25 July, 1:240 on 23 August, and 1:160 on 9 September. Urinalysis was normal. The 24-hour urinary creatine excretion was 154 mg.

Chest x-ray examination on admission showed a normal heart and lungs. Fluoroscopy of the heart five days later was normal.

Electrocardiograms, repeated several times during his stay in hospital, showed sinus rhythm at a regular rate of 80 a minute. Negative T waves were seen in leads I, II, aVL, aVF, V₅, and V₆; the Q-T interval was prolonged to 0.42 second (see Fig.). An E.C.G. performed during his previous admission was normal.

The patient's symptoms and signs subsided gradually during a two-weeks stay in hospital. Results of the serological tests were received after complete clinical recovery. Three weeks after discharge he was completely symptom-free, and an E.C.G. showed similar findings to those during his stay in hospital.

COMMENT

The diagnosis of psittacosis in this case is based on the serological findings, for a titre of 1:16 is regarded as positive (Rivers, 1952). The threefold rise in titre level to a peak of 1:480 is adequate evidence of active infection. The known limitations in interpreting the positive serology can be excluded rather readily. Both cat-scratch fever and lymphogranuloma venereum can produce false-positive reactions (Rivers, 1952; Kryslar and Altman, 1961), but the clinical picture in our case confidently excludes these diseases. False-positive serological reactions for syphilis have been described during the course of psittacosis (Allison and Dick, 1954; Grist and McLean, 1964).

The finding of cardiac involvement is the most interesting aspect of this case. This was clearly shown by the electrocardiographic changes in the T waves and prolongation of the Q-T interval. Such changes are indicative of myocarditis. The complaint of retrosternal burning made by our patient suggests that pericarditis may have been present as well, but an unequivocal diagnosis of pericarditis cannot be made in the absence of a friction rub or evidence of effusion.

Clinical accounts of cardiac involvement in psittacosis are few in the literature. The case has been reported of a patient with serologically proved psittacosis who manifested signs of pneumonitis, encephalitis, and myocarditis (Vosti and Roffwarg, 1961). The outcome was fatal. Electrocardiogram showed T-wave inversion in leads I, II, aVL, and V₁₋₆ and prolongation of the Q-T interval. Fatal myocarditis in a child was reported, in which serological proof of psittacosis was sought (Jannach, 1958). The diagnosis was established after examining tissue preparations obtained from two pet parrots that died three weeks after the child's illness. Characteristic Levinthal-Cole-Lillie inclusion bodies were seen in tissues of mice infected with suspensions of the parrots' tissues, and in the myocardium of the dead child. A case of psittacosis in which myocarditis could be inferred from the clinical picture has been reported, but electrocardiographic evidence was not presented (Valero, 1953).

In addition to the few clinical descriptions of myocarditis some cases have been described in which only pathological evidence of psittacosis myocarditis was presented (Lyon, 1956). In three other cases the mild T-wave changes are not convincing evidence of myocarditis, and the associated manifestations may well have been due to pneumonic involvement. Psittacosis pericarditis is similarly rare and only one case was encountered in the literature of recent years (Schoenemann and Gläsel, 1965).

When admitted to hospital our patient was bothered by two additional symptoms—namely, difficulty in swallowing and inability to stand because of exquisite muscle pain. The dysphagia can be explained by the mucosal lesions in the mouth, and if pericarditis was indeed present it may have contributed as well. The occurrence of oral ulcers has been described in psittacosis (Rivers, 1952). The pronounced calf tenderness was compatible, clinically, with a diagnosis of myositis. However, neither muscle biopsy nor electromyography was performed. The possibility of thrombophlebitis (Rivers, 1952)

seems unlikely in view of the patient's age, the symmetrical involvement, and the severity of the subjective manifestations in contrast with the paucity of the objective findings.

RAYMOND COLL, M.B., B.CH.,
ISRAEL HORNER, M.B., B.CH.,

Residents in Medicine, Department of Internal Medicine,
Tel-Aviv University Medical School and Tel-
Hashomer Hospital, Israel.

Urticaria after Insertion of Smith-Petersen Vitallium Nail

Brit. med. J., 1967, 4, 36

The cause of chronic urticaria is usually elusive. The following case report suggests that the nickel contained in a cast cobalt-chromium alloy (Vitallium) was responsible for symptoms of immediate type allergy.

CASE REPORT

On 11 January 1965 a woman of 65 sustained a fracture of the right femoral neck. The next day a Smith-Petersen Vitallium nail was inserted under halothane anaesthesia. On the day after operation pruritus and generalized urticaria developed, and these symptoms persisted for the next 10 months. During this time there was radiological healing of her fracture, but there was little weight-bearing on the limb on account of anginal congestive cardiac failure and three episodes of cerebral thrombosis. A right-sided hemiplegia followed one of these strokes.

On 8 December she was admitted to the Norfolk and Norwich Hospital for investigation of urticaria. Her major physical findings were right-sided flaccid hemiplegia, generalized urticaria, and dermatographism. Laboratory findings were as follows: haemoglobin 13.4 g./100 ml.; W.B.C. 5,600/cu. mm. (neutrophils 70%, lymphocytes 22%, monocytes 5%, eosinophils 3%); E.S.R. 11 mm. in one hour (Westergren); direct Coombs test negative; blood urea 25 mg./100 ml.; total serum proteins 6.62 g./100 ml. (albumin 4.6 g., globulin 2.02 g.). X-ray picture of chest and urinalysis were normal.

Discontinuation of current treatment (barbiturates, digitalis, and diuretics) produced no lessening of urticaria, and challenge with the drugs she had received before operation—Omnopon and scopolamine—led to no exacerbation. Routine patch testing showed an eczematous response to a solution of 2% nickel sulphate at 48 hours. A similar response was produced by a Vitallium nail strapped to the thigh for 48 hours. During patch testing there was no increase in severity of urticaria, but severe non-eczematous peri-orbital oedema developed at 48 hours and resolved within the following 12 hours. A scratch test with 2% nickel sulphate solution resulted in an itching weal (3 cm.) at 10 minutes, and was associated with patchy erythema and swelling of the same forearm for one hour. A passive transfer (Prausnitz-Küstner) test performed on a volunteer was positive. Patch and scratch tests with the other constituents of a Vitallium nail were negative.

Since the patient was bedfast and her fracture had healed clinically, the nail was removed on 10 January 1966 under local anaesthesia. Within 24 hours spontaneous urticaria resolved but dermatographism persisted. Exquisite and troublesome dermatographism was still present one year after removal of the nail.

COMMENT

At first this patient's urticaria was thought to represent an allergic reaction to drugs given postoperatively. It was she

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who, for the wrong reason, suggested the correct line of investigation. She reported that during early married life she was said to be "metal sensitive," and that reports about her had appeared in the *British Medical Journal* and the daily press. A search through the *British Medical Journal* of the 1930s showed that she was referred to in a "Queries and Answer" series under the heading of "The Sympathetic Ring" (Jones, 1936). Her practitioner questioned the mechanism involved when the patient's gold ring became the colour of platinum when on her finger but reverted to a golden colour when placed on the mantelshelf overnight. Subsequent editorial comment (*Brit. med. J.*, 1936) summarized correspondence which suggested contact with mercury contained in soaps, ointments, and lotions. The patient had noted no skin change under her ring or other metal object.

Classically, the separate nature of immediate and delayed type allergy has been stressed. However, clinical experience and various reports in the literature suggest that these two types of allergy may exist in the same individual. Calnan (1956) noted the presence of urticaria in his series of nickel-sensitive patients, and Stoddart (1960) reported the case of a patient with delayed contact sensitivity to nickel who developed anaphylaxis after transfusion through a nickel-plated cannula. Shelley and Resnik (1965) studied seven patients with poison ivy dermatitis, and, in addition to showing skin sensitivity to poison ivy oleoresin ether extract, the patients showed the morphological change of basophil degranulation when challenged with poison ivy extract orally. Basophil degranulation in vivo and in vitro occurs during immediate type hypersensitivity (Shelley and Caro, 1962).

We are unable to date the onset of this patient's cutaneous sensitivity to nickel. She had noted no eruption under metal clips, buckles, suspenders, etc. We have concluded that delayed and immediate type antibodies existed, and that the latter reacted with nickel absorbed from the Vitallium nail. Her immediate freedom from urticaria after removal of the nail was dramatic, but the continuation of dermatographism has been a disappointment.

We are indebted to Mr. A. W. Laxen, of the London Splint Company Ltd., for the composition of the alloy whose trade name is Vitallium (chromium 27-30%, molybdenum 5-7%, iron 0.75%, carbon 0.5%, nickel 1%, silicon 1%, manganese 1%, cobalt balance).

A. W. MCKENZIE, M.B., M.R.C.P.,
C. V. E. AITKEN, M.B., B.S.,
Skin Department, Norfolk and Norwich Hospital.
R. RIDSDILL-SMITH, M.B., B.CHIR.,
General Practitioner, Norwich.

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Human Abortion Associated with Infection by Ovine Abortion Agent

Brit. med. J., 1967, 4, 37

Stamp *et al.* (1950) showed that abortion in sheep was caused by a virus-like agent, enzootic abortion of ewes or ovine abortion virus. In affected flocks, abortion, premature lambing, and the birth of decomposed lambs are striking clinical signs of the disease. These generally take place late in pregnancy, but a number of dead or weakly lambs may be born at the proper lambing time. The ewe is generally little affected in health, and the main clinical manifestations of the disease do not give a true incidence of infection. Healthy lambs may be born from apparently healthy ewes, yet the foetal membranes may show lesions and be infected. When these lambs, and surviving weakly lambs, mature and become pregnant they may abort. The infection remains latent until they develop placental tissue in which the virus multiplies selectively. This disease is endemic in sheep in South-east Scotland, and from here it has often spread to other parts. Several outbreaks occur in Ayrshire each year. The agent belongs to the Bedsonia group of organisms, common parasites of warm-blooded animals, some causing human infections such as ornithosis, trachoma, inclusion conjunctivitis, and lymphogranuloma venereum. The possible susceptibility of man to infection with other members of this group is obviously of interest. The following case is of human abortion attributable to the enzootic abortion of ewes virus.

CASE REPORT

A woman aged 22 was admitted to Ayrshire Central Hospital on 4 December 1965 complaining of headache, pain in the back, shivering and sweating, heartburn, and frequent vomiting. These symptoms had begun four days before admission. She had also been febrile during this time and had been given injections of penicillin and streptomycin without effect. She was just over six months pregnant.

On examination she was acutely ill, temperature 102.4° F. (39.1° C.). She was mentally rather confused and had some meningismus. No other abnormal clinical signs were present except for those expected in a febrile dehydrated patient. No obstetrical abnormality was found. Examination of peripheral blood showed anaemia and leucopenia, the haemoglobin being 8.8 g./100 ml., P.C.V. 27%, M.C.H.C. 32%, and W.B.C. 2,100/cu. mm., with white cells in normal proportions. Her blood urea level was 42 mg./100 ml.; serum sodium, potassium, and chloride levels were all low. Four blood cultures were sterile. Chest x-ray examination was negative. Bacteriological examination of sputum, urine, and faeces revealed no pathogens. Lumbar puncture showed clear fluid-cell count 1/cu. mm., protein 12 mg./100 ml. Liver-function tests were within normal limits, except for a slight increase in thymol turbidity. Widal, Paul-Bunnell, and *Brucella abortus* agglutination tests were negative. She had a swinging temperature for four days, during which time she was treated symptomatically, and then was given tetracycline 500 mg. six-hourly for eight days. Her symptoms soon abated; the temperature settled in 48 hours and thereafter remained normal, and she made a good recovery. Four days after tetracycline was stopped she aborted precipitately and with very little warning. The placenta appeared unhealthy, being covered with a dirty greyish exudate. Histological examination showed infarcted placental tissue. There was little upset from this event, and she was dismissed home a few days later.

Antibody Titres of Patient's Serum

Test	Date of Serum		
	6/12/65	17/12/65	12/1/66
Complement fixation: Bedsonia group	16	512	512
Microagglutination: B.A.E. (Q18 strain)	<20 (±)	20	640
Psittacosis	<20	<20	<20
Rickettsiae*	<20	<20	<20

* *R. prowazeki*, *R. mooseri*, *R. burnetii*; trace reaction with *R. conorii*.

Virological Investigations.—Serological tests gave no evidence of infection with influenza A, B, or C, adenovirus, or Q fever. As shown in the Table, diagnostic rising antibody titres were found by complement-fixation tests with Bedsonia-group antigen and by micro-agglutination tests with enzootic abortion of ewes virus but not with psittacosis or rickettsial antigens. Attempts to show enzootic abortion of ewes virus in placenta by microscopical examination of stained smears or attempted isolation in mice were unsuccessful, as only a small specimen was available, and this had decomposed through delay in transit to the laboratory.

Epidemiological Investigations.—There was no history of recent illness of the husband or other human contacts. No history of direct contact with animals or birds was obtained except for occasional visits to a house with a budgerigar and from a friend with a dog. The patient's home bordered on agricultural land on which sheep were kept.

COMMENT

Human infection with enzootic abortion of ewes virus has rarely been recognized. Because of its relatively low pathogenicity for man, enzootic abortion of ewes virus is often used in preference to the dangerous psittacosis agent for laboratory purposes—for example, preparation of group-specific complement-fixing antigen for routine diagnostic tests. Barwell (1955) described an accidental laboratory infection with enzootic abortion of ewes virus which took the form of extensive nonfatal pneumonia.

In the present case the rising titres of complement-fixing antibody leave no doubt that the illness was associated with infection with an agent of the Bedsonia group, and the micro-agglutination tests incriminate enzootic abortion of ewes virus as the member of the group concerned. Human infections with organisms of the Bedsonia group are not uncommon, though the frequent failure to identify avian sources of infection (Grist and McLean, 1964) suggests that some may be acquired from animals—for example, sheep which were in the vicinity of our patient's home.

Experimental infections with enzootic abortion of ewes virus can cause abortions in pregnant cattle, rabbits, and rats (Giroud and Dumas, 1959; Payne and Belyavin, 1960). The relative resistance of non-pregnant animals and the localization of lesions and infections in placenta suggest that the presence of placental tissue facilitates establishment of the infection. Selective multiplication in placental tissue has also been shown with other organisms of the Bedsonia group (Parker and Younger, 1963; Pierce *et al.*, 1963).

Lefebvre (1962) and Giroud (1966) have reported an association between human abortion and infection with various organisms of the rickettsia and Bedsonia groups. Our case provides evidence of this in Britain, and it seems possible that investigations of pregnant women with fever or abortion might show that this condition is more common than is generally recognized.

We thank members of the Maternity Unit, Ayrshire Central Hospital, Irvine, for their help in the management of this patient.

W. ROBERTS, M.R.C.P. GLASG.,

Consultant Physician, Infectious Diseases Unit, Ayrshire Central Hospital, Irvine.

N. R. GRIST, M.B., CH.B., B.S.C., F.R.C.P. ED., M.C.PATH.,

Professor of Infectious Diseases, University of Glasgow.

P. GIROUD, M.D., M.A.N.M., M.C.S.H.P.F.,

Chef du Service des Rickettsioses, Institut Pasteur, Paris.

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Treatment and Survival after Massive Overdose of Adrenaline

Brit. med. J., 1967, 4, 38

Infiltration of solutions of adrenaline is often used to produce a degree of haemostasis, and though dilutions vary considerably the normal maximum dose is restricted to about 0.5 to 1 mg., while reported maximum tolerated doses with survival are in the order of 7 to 8 mg. (Freedman, 1955). This paper reports the inadvertent subcutaneous injection of 16 ml. of the undiluted 1:1,000 solution (16 mg.). The patient survived with no residual disability, and consideration of the treatment used may be of benefit to anyone faced with a similar situation.

CASE REPORT

An otherwise healthy woman aged 23 was admitted to hospital for tympanoplasty under general anaesthesia. Six months previously she had had a left mastoidectomy and a right cortical mastoidectomy and on each occasion anaesthesia with thiopentone, suxamethonium, nitrous oxide, oxygen, and halothane was entirely uneventful. As it was planned to use a local injection of adrenaline, anaesthesia was induced with thiopentone, and endotracheal intubation under suxamethonium was followed by intermittent positive ventilation with nitrous oxide and oxygen, relaxation being maintained by tubocurarine.

After induction, an intravenous infusion of 5% dextrose was set up while the preliminary surgical procedures were taking place. After infiltration of adrenaline, which was thought to be 1:200,000 dilution, the patient's pulse rate became uncountable and her blood pressure rose to unrecordable figures. It was realized that a 1:1,000 dilution of adrenaline had been used and the patient had then received 16 mg. of adrenaline.

Trimetaphan camsylate (Arfonad) 500 mg. was immediately added to the infusion and run in rapidly while 5 mg. of phentolamine (Rogitine) was given into another vein. Within two minutes the pulse rate fell slightly, though it was still too fast to count, and the blood pressure fell to 190 mm. Hg systolic from its previous value of over 300 mm. Hg. Diastolic pressure was difficult to record, but the venous pressure was obviously grossly raised, as shown by the difficulty in maintaining any intravenous infusion during the next three hours. This difficulty persisted in spite of a large catheter inserted into the saphenous vein, and on occasions a pressure pump was required to maintain the infusion.

When about 250 mg. of trimetaphan had been given quickly, over 20 minutes, the pulse rate settled to approximately 150 a minute, the blood pressure falling to about 200 mm. Hg systolic and remaining at this level during the next one and a half hours. When a further 100 mg. had been given more slowly (over the next half-hour) the systolic blood pressure fell to 50 mm. Hg and the ganglion-blocking drug was discontinued. The pressure remained between 70 and 90 mm. Hg for the next 36 hours despite the intravenous administration of 200 mg. of hydrocortisone. Methylamphetamine (Methedrine) 2.5 mg., given during this period of hypotension when the systolic pressure was 80 mm. Hg, produced a transient rise to 140 mm. Hg. Two days after the incident the pressure began to rise spontaneously and reached 120/70 by the

fourth postoperative day. The pulse rate also took a long time to settle and was not under 100 until the fourth postoperative day.

It is interesting to note that when the error was first realized the appearance of the patient was normal, but within five minutes this had changed to a state reminiscent of acute peripheral circulatory failure with cold white skin. This latter persisted for several days and was the most striking feature of this case.

The patient was discharged home on the eighth day with no residual disability, and subsequent progress has been entirely satisfactory.

COMMENT

The choice of anaesthetic in this case was fortunate, because had nitrous oxide, oxygen, and halothane been used (as on the previous occasions) it is very likely that the patient would have developed ventricular extrasystoles or even ventricular fibrillation (Millar, Gilbert, and Brindle, 1958; Rosen and Roe, 1963). The use of controlled ventilation was also favourable in that it maintained a low PCO_2 and prevented a rise in endogenous catecholamine secretion.

After realizing the error in the dose of adrenaline it was decided to continue with the proposed operation, because it was felt that the minor surgical procedure would not materially affect the patient and that continued sedation and intermittent positive-negative ventilation would probably be required for treatment. Marked central stimulation was expected with the massive dose of adrenaline, and if the patient had been allowed to wake the probable restless agitated state with raised venous pressure and inadequate tissue perfusion would have been undesirable. Adequate pulmonary ventilation with an oxygen-rich mixture seemed essential and this could easily be provided with the anaesthetic technique in use.

It is not proposed to discuss the possible effects of very large doses of adrenaline, as much of this would be pure speculation. Hypertension, tachycardia, and vasoconstriction were the presenting symptoms in this case, and treatment with a ganglion-blocking drug (trimetaphan) was aimed at rapidly reducing the systolic blood pressure.

It is difficult to explain the prolonged period of hypotension that occurred. In view of the expected duration of trimetaphan it is not likely to be a factor. One might argue that its use was continued longer than necessary, but in view of the persisting skin vasoconstriction this also seems unlikely. Our knowledge of the relative duration of action of the alpha and beta effects of the catecholamine is not such as to throw any light on the subject, but the answer may well lie therein.

MICHAEL A. LEWIS, M.B., F.F.A.R.C.S.I.,

Department of Anaesthetics, the Queen's University of Belfast, Northern Ireland.

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Current Practice

Road Safety Act, 1967

[BY A SPECIAL CORRESPONDENT]

The purpose of this article is to review changes in procedure which may be necessary when doctors are called to the police station to examine or to take specimens of blood from drivers detained by the police. In 1965 the British Medical Association published a report, "The Drinking Driver,"¹ which sets out a recommended procedure; and reference to this publication, which is widely used by doctors called to advise the police, will be given in this article.

Changes in the Law

The main change is that new offences have been created² of driving, attempting to drive, or being in charge of a motor vehicle while the proportion of alcohol in the blood is in excess of 80 mg./100 ml. The existing offences relating to driving under the influence of alcohol which are found in the Road Traffic Acts, 1960 and 1962, are retained, and the advice contained in *The Drinking Driver* will continue to apply to procedures under those Acts. The older legislation will generally apply where the driver is under the influence of drugs other than alcohol, though it will remain possible for a driver to be convicted under these Acts where it can be proved that his ability to drive properly for the time being is impaired by alcohol even though the blood alcohol concentration (B.A.C.) is below 80 mg./100 ml. It seems likely that in practice the police will have decided the Act under which they propose to proceed by the time the doctor is called to take the statutory specimen of blood. Even in cases where the driver agrees to plead guilty under the Road Traffic Acts, 1960 and 1962, the police cannot be certain that the driver will not afterwards change his mind. Much will depend, therefore, on the procedure adopted by each local police authority.

It is early to give an opinion on the changes in procedure which will follow the introduction of the new Act. Under previous Acts a body of case law grew up on various aspects of procedure and it may be some months before more positive guidance can be given on some of the points covered in this article.

Clinical Medical Examination

B.M.A. reports have always emphasized the need for a comprehensive medical examination of drivers suspected of being unfit to drive as a result of having taken alcohol. The main purpose of such examination has always been the exclusion of illness or injury. These recommendations were based on the assumption that drivers would continue to be detained by the police on a selective basis—that is, only those drivers who showed evidence of intoxication or had been involved in an accident would be arrested by the police. The Government White Paper³ points out that even after 1962 (when the stronger criterion of impairment of driving ability was introduced) the police have rarely proceeded in cases where the B.A.C. is less than 150 mg./100 ml.

The new Act introduces an element of random selection in that a driver who exhibits no symptoms of alcoholic intoxication, and who has not been involved in an accident, may be detained by the police and be required to give a blood sample—for example, where he has committed an infringement of the traffic regulations and he gives a positive breath test upon being stopped by the police. In these circumstances a comprehensive medical examination will not be necessary

unless the doctor called in by the police to obtain the blood specimen has reason to believe that it is desirable to exclude the presence of illness or injury in the circumstances of the particular case. If the police have not requested an examination, but the doctor feels that it is necessary, he should tell the officer in charge of the case so that facilities for an examination to take place may be provided.

The paragraphs in *The Drinking Driver* relating to consent continue to apply, with the exception that the purpose of the examination (which must be explained to the driver) is limited to excluding illness or injury and to enabling the doctor to advise the police whether the driver is fit to be detained. The rule that the driver must be informed that he is entitled to request an examination by a doctor of his own choice was formulated to enable the driver to call his own medical evidence on the issue of fitness to drive. The position has now changed. Under the new Act evidence of fitness to drive based on clinical medical examination is no longer relevant. However, if the driver claims he is suffering from illness or injury and asks for his own doctor every attempt must be made to make the necessary arrangements. Furthermore, the doctor called by the police should bear in mind that in some cases it may be desirable to contact the driver's own doctor (with the consent of the driver) in order to assist in arriving at a diagnosis. This is particularly important where there is reason to believe that the driver may have been under recent active medical treatment.

The Act authorizes the police to carry out a breath test on drivers under certain conditions and provides penalties for drivers who refuse. Though the breath index tubes are relatively crude instruments, they may nevertheless provide useful diagnostic information—as, for example, where the symptoms of intoxication are quite inconsistent with the concentration of alcohol indicated by the tube. In such cases the possibility of the driver suffering from unsuspected illness, injury, or the effects of other drugs must be considered very carefully. Breath tests for alcohol have been available for 30 years or more and it is surprising that they have not been introduced into casualty departments of hospitals. It is not unknown for a suspected "drunk" to be turned away from a casualty department only to die later from an unsuspected head injury.

The driver who refuses unreasonably to take a breath test in circumstances where the police are entitled under the Act to require one is subject to penalties. It follows that medical evidence may be called by the defence when the driver claims on medical grounds to be unable to take the test. It has been found that patients with fairly severe degrees of cardiorespiratory failure are able to take the test without ill consequences. The Government White Paper³ suggested that asthmatics might be unable to take the test, but it should be borne in mind that asthmatics are used to breathing out against resistance and can reasonably be expected to take the test if they are fit enough to drive a car.

Urine Samples

The Drinking Driver recommended that as part of the examination a specimen of urine should be obtained for the purpose of testing for albumin, sugar, etc., but that the police should be consulted before such a specimen is taken in order not to compromise the procedure for taking statutory specimens under the Road Traffic Acts. In practice the statutory specimen under the 1962 Act has nearly always been of urine, and it could be used also for determining the presence of drugs other than alcohol. Under the new Act it is expected that the statutory specimen will nearly always be of capillary blood. Analytical techniques are not sufficiently advanced to determine the presence or quantities of drugs other than alcohol from such small specimens. A urine specimen should be obtained if it is suspected that the driver is under the influence of drugs other than alcohol.

It was the custom in most areas under the 1962 Act for doctors to provide the police with a certificate of opinion at the end of the medical examination. A draft certificate is set out in *The Drinking Driver*, but some of the information which it contains will be inappropriate under the new Act. The certificate should be limited to stating the name of the driver, the date, time, and place of examination, and whether or not the driver is fit to be detained by the police. If no certificate is requested by the police a note of these items should be made by the doctor at the time and retained by him. This certificate is quite distinct from the certificate that blood has been taken. There has been some doubt about the powers of the police to detain drivers under the 1960 Act in circumstances where the driver appears to be unfit to drive home. On occasion drivers have been released from the police station only to be involved in an accident shortly afterwards. The new Act authorizes the police to detain a driver until such time as his B.A.C., as determined by a breath test, is below 80 mg./100 ml. This power is discretionary and is unlikely to be exercised where arrangements can be made for the driver to be driven home.

Sampling Methods

The Road Traffic Act, 1962, permits blood, breath, or urine to be used in support of a prosecution for impaired driving ability. No regulation was ever introduced authorizing the use of breath under that Act, and the new Act withdraws the Minister's power to issue such a regulation. The "screening" breath tests authorized under the new Act are only crude indications of the B.A.C. and they cannot be used in court as evidence of the B.A.C. being in excess of 80 mg./100 ml. Their only function is to assist the police and to determine whether or not the driver can be required to give a specimen of blood.

The Drinking Driver recommended in favour of blood in connexion with a statutory blood alcohol concentration, but the new Act permits the driver to give a specimen of urine if he refuses to allow a specimen of blood to be taken. The driver who refuses to allow blood to be taken must give two specimens of urine within an hour, and if he is unable to do this the obligation to allow a specimen of blood to be taken returns. The first specimen of urine is discarded and analysis is carried out on the second specimen alone. No doubt anticipating the use which would be made by the defence of the detailed objections set out in *The Drinking Driver*, the Act states that a urine alcohol concentration of 107 mg./100 ml. shall be deemed to be equivalent to a B.A.C. of 80 mg./100 ml., thereby preventing any argument in court on the conversion factor which ought to be used in the particular case. As the factor is based on a mean figure, the driver who opts for urine has an even chance of benefiting, thereby providing yet another example of what has been termed the sporting theory of English justice. Under the 1962 Act the analyst is required to state on his certificate the equivalent figure for blood in the case of urine

specimens. Under the new Act no corresponding figure for blood will be given on the certificate. It is expected that police will obtain the urine specimens in cases where the driver refuses to allow blood to be taken.

Upon arrival at the police station the driver must be offered a further breath test by the police, and if this test proves to be negative the police cannot require him to allow a specimen of blood to be taken under the new Act. The consequences of failure, without reasonable excuse, to allow a specimen of blood or urine to be taken are severe under the new Act. Such refusal constitutes a separate offence, the penalties of which are the same as those for the substantive offence. The effect of refusal where the police are proceeding under the previous Acts remains the same—namely, that the fact of refusal will be given in evidence by the prosecution.

Haemorrhagic Disorders

Medical evidence may be called by the defence where the driver refuses on medical grounds to give a sample of blood, but there are very few medical conditions in which it might be dangerous for the driver to allow a sample of capillary blood to be taken. Notwithstanding any consent obtained by the police, the doctor must satisfy himself that the driver consents to a specimen being taken and that the driver understands what is involved. If it is thought to be in the interests of the driver that his arm or head should be steadied while the specimen is taken the reason must be explained to the driver and his consent obtained. There must be no suspicion of the specimen being taken under forcible physical restraint. It is expected that capillary blood will be the specimen of choice under the new Act, and during the past few months police authorities throughout the country have been conducting courses for doctors on the correct technique. Sealed packs containing lancets, plastic labelled cups with airtight lids, and dressings are being supplied to police stations by the forensic science laboratories. Doctors should use the packs supplied and should follow any recommendations contained in them. Three of the cups must be half filled with the blood specimen and the lids firmly replaced, and the cups shaken to ensure admixture with the preservative and anti-coagulant which are contained in the cups. The doctor must then label the cups and complete a statutory certificate stating that he took the specimen with the consent of the driver. It is important that a non-alcoholic solution is used to clean the skin. The police will be responsible for the disposal of the specimens and for offering part of the specimen to the driver.

Evidence in Court

The Act is so drafted that the opportunities given to the defence to discredit the evidence produced by the prosecution are reduced considerably as compared with previous Acts. The wording of the Act rules out any argument based on individual variations in the metabolism of alcohol. It seems that the question will arise under the new Act only in cases where the driver is prosecuted for being "in charge" and the defence seeks to raise the defence (and therefore has to prove) that there was no likelihood of his driving so long as he remained unfit to drive or so long as there was any probability of his B.A.C. being above 80 mg./100 ml. Under the previous Acts he was also required to prove that he had not driven since he became unfit to drive, but the new Act has repealed this and provides that the driving prior to stopping can be ignored for purposes of the "in charge" offence. This should have the desirable effect of encouraging drivers to stop driving if they feel they are affected by alcohol instead of taking a chance on getting home. It is expected that in future the main oppor-

tunity available to the defence will be to question the sampling methods, the identification, transportation, and preservation of the specimens and the analytical method. Accordingly, it will be of paramount importance for doctors to follow explicitly the instructions which are provided by the police for obtaining specimens under the new Act. Clinical medical evidence of unfitness to drive is not an issue under the new Act. The new Act allows the doctor's evidence relating to the taking of the specimen to be given by certificate, which must be served on the defence at least seven days before the hearing. The doctor will not normally be required to attend unless the defence gives notice.

Hospital Cases

The Ministry of Health has sent out a circular which explains the procedure to be adopted when drivers attend a hospital.⁴ It is important to note that the doctor in charge of the case may object not only to the specimen being taken but also to the requirement to provide a specimen being indicated by the police to the patient. The police must arrange for their own doctor to take the necessary specimen of blood and he must take his own equipment with him. Apart from providing facilities of reasonable privacy for the sample to be taken the hospital authorities play no part in the procedure.

Conclusion

The Drinking Driver drew attention to the need for police authorities to appoint doctors on a retaining basis in order that expert medical advice and assistance would be speedily available to the police. The reluctance of many police authorities to do this and the tendency to rely on any doctor who happens to be available has long been a source of irritation and has certainly not been in the interests of justice. It will be impossible to administer the provisions of the new Act unless doctors are freely available to take specimens of blood and to advise the police. Fortunately, the Home Office has already issued two circulars to police authorities drawing their attention to the pressing need to make the necessary arrangements before the Act comes into force, and agreements are being reached between local B.M.A. representatives and local police authorities (who are autonomous in these matters) on the fees and allowances which will be paid to doctors called by the police.

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Fallacies in Four Fevers

R. S. ILLINGWORTH,* M.D., F.R.C.P., D.C.H., D.P.H.

Among other fallacies habitually copied from one textbook to another or lingering in the minds of practitioners as a relic of treatment of the past, because their validity has never been questioned, are those concerning the common infectious diseases of childhood. This paper concerns four common infections—measles, German measles, chicken-pox, and mumps. The fallacies to be discussed concern confinement to bed, quarantine, isolation, undue absence from school, dietary restrictions, and the use of medicines.

Confinement to Bed

When considering the value of any line of treatment, including the administration of any drug, one should always think of three questions: What good may it do? What harm may it do? What harm may be done by not giving this treatment?

It is the practice of many doctors to confine children to bed for any of a wide variety of conditions such as abdominal discomfort, headache, a sore throat, a slight rise of temperature, a cold, or diarrhoea without any apparent reason. The fallacy of such treatment has been discussed by me several times,¹⁻⁴ and subsequently by Jolly.⁵ If a child feels well enough to be up—even merely sitting in a chair by the fireside—and wants to be up, even if his temperature is raised, it is very difficult to think of any reason for confining him to bed. There are possible exceptions: infectious hepatitis, the preparalytic stage of poliomyelitis, and the first few days of rheumatic fever. I can certainly see no reason why it should be thought likely that a child with a sore throat would recover more quickly if he sits up in bed than if he sits up in a chair reading a book in front of the fire. I am unable to think of any physiological mechanism which would make it likely that he would recover more

quickly if he sat on a bed than if he sat on a chair. In hospitals which I have visited in many countries of the world, including Russia, all children are kept in bed. In one hospital I saw a ward full of children with behavioural problems, and in another a ward full of children with epilepsy, and in both cases all children were kept in bed throughout their stay in hospital.

So children with measles, rubella, chicken-pox, or mumps should not be kept in bed if they want to get up. A child in the febrile stage of measles before the rash appears may well prefer to stay in bed. I can see no reason otherwise why children with these conditions would be harmed by being out of bed. There is no physiological or pathological basis for a belief that complications, such as orchitis in mumps, would be more likely if the child were out of bed.

I can see many reasons why confinement to bed may be harmful. It bores children. They sleep less well if they have been confined to bed. The adverse physiological and pathological consequences of bed rest have been well described in the excellent book by Browne,⁶ who aptly wrote that "the bed is often a sign of our therapeutic inadequacy, rather than a therapeutic measure deserving of praise. The bed is the non-specific treatment of our time, the great placebo."

Quarantine

Thanks largely to the work of Smith at Rugby⁷ it is now widely recognized that children should not be quarantined for the common infectious diseases. Quarantine was not successful in the prevention of infectious disease in the past. Ninety per cent. of children acquired measles by the age of 14, 70% acquired chicken-pox, and 50% acquired rubella and mumps. If healthy contacts are prevented from going to school they will assuredly mix with their school fellows after school hours. In

* Professor of Child Health, the University of Sheffield.

the past children were placed in quarantine even if they had had the infection in the past. There is no truth in the idea that contacts can carry the infections of measles, German measles, chicken-pox, or mumps to school without themselves suffering from them. It was quite irrational to isolate contacts throughout the incubation period of infectious diseases. For instance, the usual incubation period of mumps and rubella is about 16 to 18 days. Contacts who are going to acquire the disease cannot be infectious for at least the first 12 days after exposure.

Smith wrote that after 16 years' experience of 75 outbreaks of infectious disease at Rugby School there was no instance in which the originator knew how he had acquired the infection. In the same period 203 boys who had been exposed to infection were allowed back to school, and only one acquired the expected disease at school. There were no secondary cases. If strict quarantine had been enforced 4,224 days would have been lost.

Quarantine for these infections is outmoded.^{8 9} This does not mean that there should not be sensible surveillance—that a careful eye should not be kept on a contact after a suitable point in the incubation period.

Isolation

It is usually futile to attempt to isolate an infected child from others in the family. By the time the diagnosis has been made the other children have already been exposed to him at the most infectious stage of the illness. In any case, there is much to be said for children acquiring the infection in childhood rather than later. Mumps is rarely complicated by orchitis before puberty, so it is better for boys to acquire mumps before then, so that they do not acquire mumps with the risk of orchitis later. It is desirable for girls to acquire rubella before pregnancy. I believe (rightly or wrongly) that adults are liable to be more ill with the common infectious diseases than children are.

It is most regrettable that there are still infectious disease hospitals which do not allow parents to visit their children with these infections, or which, worse still, allow them to see their children through a glass partition—an infuriating and thwarting experience for a small child. The rationale of such isolation measures escapes me. The harm done by them is obvious.

Keeping the Child Off School

At any one time about 10% of schoolchildren in England and Wales are absent from school. Only a small proportion of these are absent for any good medical reason.^{10 11} In the case of the four common infectious diseases many children are kept away from school for much too long a period. The duration of infectivity of these four infections is shown in the Table.

Duration of Infectivity of the Common Infectious Diseases

Measles		Five to six days before the rash until six days after the appearance of the rash if the child is afebrile
Rubella		One day before the rash until two days after the appearance of the rash
Mumps		Two days before the swelling of the parotid gland until the swelling has subsided
Chicken-pox		One day before the rash until six days after the appearance of the rash

It would be interesting to see figures for the mean duration of absence from school for these conditions—and the differences between children from one area of a city or town and those from another.

Obviously no child should go back to school until he is fit, but prolonged absence of a well child from school is altogether wrong.

Dietary Restrictions

There are still some doctors who, without thinking, prescribe a "light diet" for children with infections. Provided that their appetite is unimpaired I cannot see any reason for such a diet.

Medicines

For chicken-pox and rubella there is no indication for any medicine. There is no need to prescribe a lotion for the rash of chicken-pox. For an occasional case of mumps with severe pain a sedative may be indicated, but no medicine should be given otherwise. For measles, unless there is a complication such as otitis media or pneumonia, both of which demand the use of antibiotics, there is no indication for medicine. Investigation¹² has shown that the prophylactic use of an antibiotic in measles does nothing to reduce the incidence of complications. There is no point in giving the child cough medicine. It will achieve nothing. How much money is spent in England and Wales each year on the totally unjustifiable prescription of medicines for children with these four fevers?

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Antibiotics in Measles

Q.—The reasons given by some doctors for the administration of antibiotics as a routine in all measles cases are: (1) It cannot do any harm; (2) it satisfies the child's parents, who expect it; (3) other doctors do so. What are the arguments against this?

A.—Apart from the general undesirability of treating conditions with agents known to be ineffective, there are four reasons why antibiotics should not be given:

(1) It is certainly not true that they are harmless.¹⁻³ The philosophy that antibiotics can do no harm and might do some good underlay the fatal "grey syndrome" in children given prophylactic chloramphenicol.⁴

(2) The prevalence of antibiotic-resistant organisms is proportional to the amount of antibiotic used.⁵ Widespread prescribing of antibiotics for virus infections which cannot respond to them can only increase the chances that initially sensitive bacterial infections will become inaccessible to treatment.

(3) There is a temptation when giving drugs for inadequate reasons to avoid side-effects so far as possible by giving inadequate doses. In the case of antibiotics, apart from facilitating the emergence of resistance, this may suppress any bacterial superinfection just enough to make the diagnosis, and hence the treatment, exceedingly difficult.

(4) Antibiotics are not cheap, and there are more useful ways of adding to the drug bill.

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B.C.G. and Tuberculin-positive Subjects

Q.—What, if any, is the danger in giving B.C.G. to a subject who is tuberculin-positive after a healed primary infection?

A.—There are so far as I know no reports of systematic studies concerning this subject in man, but serious general or focal reactions are improbable. There might occasionally be a mild transient fever, as when a large dose of tuberculin is given subcutaneously to a sensitive subject, and theoretically there might be a focal reaction at the site of the old primary complex. The likelihood of reactivation or dissemination of tuberculosis seems extremely small, though the possibility is difficult to exclude.

The most constant complication of giving B.C.G. to a tuberculin-positive subject, especially anyone sensitive to a small dose of tuberculin, is the occurrence of a severe accelerated local reaction—the classical Koch phenomenon. Ulceration, probably, substantially larger than that occurring after vaccination of an uninfected individual, could be expected within a few days and might prove slow to heal, leaving a larger area of scarring than occurs after the usual B.C.G. vaccination.

The situation in respect of the use of B.C.G. without preliminary tuberculin testing has been summarized by the W.H.O. Expert Committee on Tuberculosis in its eighth report¹ thus: "These studies have not demonstrated local, regional, focal, or general complications detrimental to the health of the tuberculin reactors among the vaccinated individuals. . . ."

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Staphylococcus and Erythema Nodosum

Q.—Is it possible to get erythema nodosum with a *Staphylococcus pyogenes* infection?

A.—So far as I am aware attention has not been particularly drawn to staphylococcal infection as a cause of erythema nodosum. On the other hand, while some causes (streptococcal infection, sarcoidosis, and, formerly, tuberculosis) are much more common than others, it seems that erythema nodosum may develop in suitably sensitive subjects in response to a wide variety of stimuli. Among those identified have been viral, bacterial, and fungal infections, drug sensitivities, neoplastic diseases, sarcoidosis, ulcerative colitis, appendicitis, bronchiectasis, and other assorted states.¹⁻³ It would be surprising in the circumstances if *Staphylococcus pyogenes* did not sometimes excite a similar response.

It is an interesting feature of erythema nodosum that even when it has followed epidemics of viral⁴ or fungal infections, which attack both sexes equally,⁵ it has still appeared almost exclusively in the female.

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Sudden Loss of Vision

Q.—What might be the condition causing sudden loss of vision in one eye when there are arteriosclerotic changes in the fundus and a picture of venous thrombosis of all the branches of the central vein (swollen, dark, tortuous vessels) but no haemorrhages such as are usually found in typical thrombosis?

A.—It is difficult to give an opinion without further details. Sudden complete loss of vision strongly suggests an occlusion of the central retinal artery. The central vein lies very close to the artery in the optic nerve and might be affected by an inflammatory reaction. If the central artery remains occluded the retinal arteries will be narrowed and there will be retinal oedema with a cherry-red spot at the macula.

If the retinal arteries are reasonably normal a condition such as giant-cell arteritis (tem-

poral arteritis) should be considered. Carotid artery disease is another possibility, but preliminary attacks of amaurosis rather than sudden loss of vision are usual.

Medical Equipment for Explorers

Q.—What medical equipment and drugs should four laymen take on a voyage by sailing-boat which might last three months? Are there any books on the treatment of simple illnesses and accidents suitable for travellers?

A.—The following equipment and drugs should meet the case:

Medical Equipment.—Scissors, 5 in. (12.7 cm.) straight pointed, 1 pair. Dressing forceps, 5 in., 2 pairs. Safety pins, assorted, 12. Crepe bandages, 3 yds. long by 3 in. wide (2.7 m. by 7.6 cm.), 2; 3 yds. long by 4 in. wide (2.7 m. by 10.2 cm.), 2. Elastoplast, 3 in. (7.6 cm.) wide, two-way stretch, 2 rolls; 3 in. wide (one-way stretch), 2 rolls. Zinc oxide adhesive plaster 10 yds. long by 1 in. wide (9.1 m. by 2.5 cm.), 4 rolls. Dumb-bell butterfly closures, 1 tin of 100. Gauze swabs, 2 sq. in. (12.9 sq. cm.), 100. Cotton-wool, 1 lb. (0.454 kg.). Sofra tulle, 2 tins. Glacier cream, greasy (Savory and Moore), 4 tubes.

Drugs.—Acriflavine lotion B.P.C. 1/250 dilution for use in 1/1,000 dilution. Cetrimide and chlorhexidine solution 250 ml. for use in 1/100 dilution. Ampicillin capsules B.P. 250 mg., 100. Aspirin soluble tablets B.P. 600 mg., 200. Chlortetracycline eye ointment B.P., 2 tubes. Codeine phosphate tablets B.P. 60 mg., 50. Dimenhydrinate tablets B.P. 50 mg., 200. Hydrocortisone lotion B.P.C. 1%, 250 ml. Omnipon tubonic ampoule syringes 20 mg. (1 ml.), 6. Pentobarbitone tablets B.P. 100 mg., 50.

The proceedings of the symposium on exploration medicine, held on 25-26 October 1962 by the Royal Geographical Society,¹ should prove useful.

REFERENCE

- 1 *Exploration Medicine*, 1965, edited by O. G. Edholm and A. L. Bacharach. Bristol.

Notes and Comments

Ranges of Forced Expiratory Volume.—Dr. J. J. SEGALL (Chest Clinic, Whittington Hospital, London N.19) writes: "With reference to the answer to this question ('Any Questions?' 9 September, p. 668), your expert is surely mistaken in giving the 95% confidence limits as one instead of two standard deviations on either side of the mean. In practice two standard deviations below the mean F.E.V.₁ for sex, age, and height results in too low a limit of normal. For this reason it is preferable in clinical work to regard the lower limit of normal as 85% of the predicted (i.e., average) value, as recommended by the American Committee on Rating of Mental and Physical Impairment."

OUR EXPERT replies: Dr. Segall is quite correct that the 95% confidence limits are two standard deviations: One standard deviation includes only approximately 60% of the community.

Book Reviews

Postgraduate Medical Federation: Early Years

The British Postgraduate Medical Federation. The First Fifteen Years. By Sir Francis Fraser, M.A., M.D., F.R.C.P., LL.D. (Pp. 69+vii. 15s.) London: Athlone. 1967.

Recent developments of medical education in this country lend particular interest to this short monograph on the early years of the Postgraduate Medical Federation by the distinguished physician who was appointed its first director in April 1946. Francis Fraser was well equipped for the responsibility; he had been professor of medicine at the Hammersmith School and Hospital since its foundation in 1934 and had contributed much to the high reputation it so quickly won. His ability and integrity were everywhere acknowledged and in December 1947 the University of London granted to the new Federation the status of a "School of the University" in respect of its facilities at Hammersmith. Within a few years several Institutes representing special subjects were included in the fold and their academic standards were high—by 1960 there were no fewer than 30 professors, of whom five had

been elected Fellows of the Royal Society.

To-day medical institutes are springing up all over the country to provide graduate instruction and facilities for research, and they have the cordial support of the universities, the regional hospital boards, and local industry; together they constitute one of the most promising and valuable developments in the National Health Service and they owe a great deal to the experience gained by the Federation Fraser did so much to shape. How rapid progress has been is revealed by a most interesting account of what had been attempted before the establishment of the Hammersmith Hospital School.

Jonathan Hutchinson was the pioneer. In the closing years of the nineteenth century "he devoted each Wednesday afternoon to a widely attended clinic held at his house for doctors from any part of the world who happened to be in London." William Osler

followed with a Medical Graduates College which became the Fellowship of Medicine. The London undergraduate schools had a Postgraduate Association which dissolved in 1913, and a few non-teaching hospitals provided sporadic courses. Otherwise there was little postgraduate teaching in England. In 1925 Neville Chamberlain while Minister of Health appointed a committee (with himself as chairman) to draw up "a practical scheme for postgraduate medical education centred in London." That committee reported in 1930 and, taking advantage of the Local Government Act of 1929, recommended the establishment of the centre at Hammersmith.

Fraser gave the last years of his life to this book and died two weeks after completing the script. It is a simple record of difficult work well done which has already had wide and enduring influence. In one respect it is incomplete; there is hardly a word about the significant part played by the author. Those who knew Francis Fraser will understand the omission; he never sought a public image—the work itself was sufficient and the only thing that mattered.

ARTHUR THOMSON.

Radiation and Chromosomes

Human Radiation Cytogenetics. Proceedings of an International Symposium held in Edinburgh, 1966. Edited by H. J. Evans, W. M. Court Brown, and A. S. McLean. (Pp. 218. 70s.) Amsterdam: North-Holland. 1967.

This is a valuable collection of papers dealing with a circumscribed subject, so that any reader interested in one will be interested in all. In J. Visfeldt's words, "the principal object of these studies has been the classical desire to establish the dose-effect relationship. If this could be attained by determining chromosome aberration yields from humans irradiated in vivo the basis of human biological dosimetry would be obtained."

There are several papers about techniques, particularly the culture of lymphocytes from blood, and two contributions on the automation of chromosome analysis. There follow a few papers on the lymphocyte lifespan; if a lymphocyte can carry an "unstable" chromosome lesion dating back to irradiation many years before, this may be a vital clue to the mechanism of "immunological memory" (P. H. Fitzgerald and P. C. Nowell). Finally, there is a whole series of papers covering the chromosomal abnormalities found in persons exposed to ionizing radiations from occupational, therapeutic, accidental, and military causes. Not unexpectedly, the Edinburgh group are strongly represented in this section, and there is a noteworthy contribution from Ishihara and Kumatori on the fishermen irradiated by fall-

out from Bikini. In their series there is even a suggestion of formation of persistent abnormal clones, and the discovery of cells from several cases with a Ph¹-like deleted chromosome is of great interest in connexion with the origin of chronic myeloid leukaemia.

The "classical desire" has not been entirely fulfilled, and variations in technique and interpretation have resulted in large differences—for instance, the incidence of rings, dicentric, and fragments in normal controls is 0.01% according to A. B. Bloom and his collaborators in Japan, but 0.8% according to K. E. Buckton and her colleagues in Edinburgh. Some of the differences can be resolved by the uniform use of a 50-hour incubation period, so that all cells are in their first division.

The possibility of using chromosomal defects as a "biological dosimeter" depends on the scoring of very large numbers of cells in order to show statistically significant differences. The editors optimistically say that "developments will be all the more rapid when facilities for the automatic analysis of cells by computer become available—a prospect which may well be realized in the near future." The automatic analysis of a selected perfectly spread metaphase is already well within sight, as D. Rutovitz's contribution beautifully shows; but it could be a far cry from this to the analysis of hundreds of cells in average material.

The editors and publishers are to be congratulated on the rapid publication of this volume, which includes much material not obtainable elsewhere.

A. I. SPRIGGS.

Surgery of the Hand

Hand Surgery. By J. Edward Flynn, M.D. (Pp. 1095+xvi; illustrated. £15 8s.) Edinburgh: E. & S. Livingstone. 1966.

This is a reference book, weighing more than 4½ lb. (2 kg.), which is a sizable volume even for hand surgery. As Sumner Koch notes in a detailed and informative preface, the method of presentation, "popular in the United States, results from the collaboration of a number of men who are specialists in their fields. The editor presents their contributions, usually with comment and change." It is a style which is apt to lead to overlapping of subject material and repetition of detail, but there is a 20-page index which helps to make up for this defect.

The editor has chosen 57 specialists to help him in his presentation of hand surgery; six of them are from Europe. The work is therefore comprehensive of current opinion and teaching. Some of the chapters are outstanding monographs, but others stray unnecessarily far up the arm—to the shoulder joint, or deal surprisingly fully with general medicine—such as tetanus. The omission of a chapter on leprosy and the inclusion of one on disability assessment and compensation in the United States gives the book a parochial stamp out of place in a treatise which must surely have been intended for world circulation.

Having overcome these personal objections to style and choice of material, there is a great deal of interesting and instructive information and experience presented here. In the first chapter H. C. Marble presents

a history of hand surgery, and this is followed by a comprehensive account of the anatomy and kinesiology of the hand by E. P. Kaplan. Hand trauma is covered in about 30 chapters, which include an original contribution on primary and secondary repair of flexor and extensor tendon injuries by Claude Verdan, of Switzerland, and a thoughtful and imaginative discussion of tendon transfers in the forearm by Paul Brand.

Vascular disorders, infections, contractures, and tumours each have several interesting chapters devoted to them. It is surprising, however, that such an important practical subject as rehabilitation of the injured hand gets only sketchy treatment in a few columns in a book of this size.

D. MACG. JACKSON.

Health Services in the U.S.A.

Health is a Community Affair. Report of the National Commission on Community Health Services. (Pp. 252+xiv. 40s.) London: Oxford University Press. 1967.

The American Public Health Association and the National Health Council—the sponsors of this book—created in 1962 the national commission to study, recommend, and report to the people of America on the present and future requirements of the health services.

A long list of members of the commission contains the names of doctors, lawyers, and others who together provide a body of high authority and wide experience. This work ranges over the whole of the health field and provides detailed information of the deficiencies and what are thought to be the needs in America. There is also a mass of stimulating opinion and much guidance for future “programs”—some remedial and some drastic. The United States and this country obviously have problems in common in relation to the health services but in many ways the approach to their solution differs—arising, no doubt, from the differences between their political and economic backgrounds.

Some of the statements in the book are challengeable—for example, “We do not know how to purify air for all the people just before we breathe it. People are in the same relative position with regard to air pollution as are fish with regard to water pollution.” This is not really the case. In both Britain and America we know perfectly well how to deal with air pollution—the trouble is that we fail to do it—and in this respect we are like the poor fish. We know how but we have inadequate drive and vigilance in matters of clean air.

The following statement will clearly find a responsive reaction here: “In addition, each community must be able to enter the recruitment competition with the knowledge that financial reimbursement for all kinds of health personnel will be competitive with that received by people performing comparable jobs in the community.” America, it appears, suffers as we do.

A possible future reorganization is envisaged. “Local community leaders should be encouraged to begin thinking in terms of clusters of cities, towns, and related rural areas which make natural, or at least organizationally feasible and defensible,

regions for improving the health of the area.” This is the same concept apparently as the proposal supported by the majority of the medical profession here—larger administrative regional units. The recommendations on health services and jurisdictional areas will provide food for thought for those who are interested in the work of the Royal Commission on Local Government.

Another recommendation is that every individual should have a personal physician who “will have knowledge of and access to all the health resources of the community—social, preventive, diagnostic, therapeutic, and rehabilitative—and will mobilize them for the patient.” This is a completely acceptable statement, but it may be a surprise to some people that this position has not been reached already in the United States.

The dust cover states that the book is written in a non-technical and readable fashion. Non-technical certainly, and heavy going sometimes, but it should nevertheless be read.

C. METCALFE BROWN

Indulging and Abstaining

Clinical Dietetics and Nutrition. With Special Reference to Tropical Foods. By F. P. Antia, M.D.(Bom.), M.R.C.P.(Lond.), M.S.(Ill.). (Pp. 563+ix. 42s.) London: Oxford University Press. 1967.

The aim of this book is to provide students and practitioners with the knowledge of clinical nutrition and dietetics needed for general and hospital practice. The slant is towards practice in India and the Far East, but the book has been written with the needs in mind of practitioners in any part of the world, tropical or temperate.

There are four parts to the book. The first is composed of sections dealing with substances needed for nutrition such as proteins, vitamins, and minerals. The amounts needed for health and levels in body fluids and tissues are given together with basic facts concerning the role of each in physiology and pathology. The effects of deficiency are described together with the way to supplement a diet with the substance, and where appropriate the way to prepare a diet containing little of it. The well-written section on sodium is an example of the latter. In the second part various foods are described in some detail, not only as regards their constituents and the preparations made from them, but also the diseases they may benefit, cause, or transmit. All this is very well done. The third part consists of descriptions of the dietetic management of many diseases, including peptic ulcer, hepatic cirrhosis, kwashiorkor, cardiac failure, and hypertension. The fourth section is composed of tables of food values, recommended allowances, heights, and weights.

The work is remarkably comprehensive, the information accurate and very practical. It will without doubt provide an invaluable source of information enabling better management and understanding of disease. Physicians tend to be vague when advising patients about diet; partly because detailed instruction in this field is not often given in medical schools, partly because in few books is the necessary information drawn together

conveniently, and partly because knowledge in many parts of the field has advanced rapidly and it is difficult to keep up to date. Use of this book will take care of all these aspects of the problem. It deserves high praise and success.

A. W. WOODRUFF.

Havelock Ellis's Life

My Life. New edition. By Havelock Ellis. (Pp. 614+xli; illustrated. 45s.) London: Neville Spearman. 1967.

Havelock Ellis (1859–1939) is widely known as the author of *Studies in the Psychology of Sex* and other books on kindred subjects. His writings were his life-work, and yet they are hardly mentioned in this detailed, intimate, and often obscure narrative.

At the age of 4 he was first touched by the mystery of woman. Their nurse was wheeling the baby in the perambulator and he was alongside. Unexpectedly she stood still and he heard a sound like a stream of water descending. His mother behaved in exactly the same way several times when walking with him in the park. From the fact that seeing a woman urinating aroused him sexually, he detected in himself a slight abnormality, the germ of a perversion.

He was not robust, and at 16 his father, a sea captain, took him to Australia. He taught in private schools near Sydney for four years and then, quite suddenly, he decided to become a doctor. Returning to London he entered St. Thomas's Hospital, and after a halting career qualified as L.S.A. He held one or two posts as an assistant and then abandoned medical work in 1884. But he remained a member of the B.M.A. all his life.

A remarkable feature of this autobiography is the omissions. Thus Freud's name is not mentioned, though he and Ellis corresponded for 35 years. Eventually misunderstandings appeared and they parted. In his twenties Ellis and Olive Schreiner became close friends. Her letters to him run into thousands, all preserved in numbered bundles. He refused her request to return them, as he read and reread them. She would not have wanted them to be published; nevertheless after her death he made a selection of them available when her life was being written. He held that one who was dead, whose sensitiveness could no longer be hurt, is not the fit arbiter of what should or should not be published.

Marriage brought Ellis and Edith, his wife, joy and happiness. It succeeded, he believes, because they were often apart: she preferred Cornwall and he London. Edith had a succession of lesbian friends and he accepted this situation without reservation. He himself had intimate friendships with several women friends. This hurt Edith grievously and she attempted suicide twice. After one crisis she obtained a legal separation. But “separation” is perhaps a misnomer, for their way of life was not altered and their mutual devotion remained constant till her death in 1916.

Alan Hull Walton's admirable introduction shows Ellis as a pioneer. The rumours that he was impotent and a homosexual are denied. These may have spread because

Ellis had written a book on homosexuality, and had "inadvertently married a lesbian." In the foreword Françoise Delisle writes: "His autobiography stops at his wife's death, leaving twenty-three years untold." Ellis speaks of "my beloved Françoise—whose devotion and sympathy enfold me in radiance, so that sometimes I am almost disposed to begin the narrative of a second and later life."

E. A. BENNET.

"Carleton"

Carleton's Histological Technique. 4th edition. Revised and rewritten by R. A. B. Drury, M.A., D.M.(Oxon), F.C.Path., and E. A. Wallington, F.I.M.L.T. (Pp. 432 + ix; illustrated, 60s.) London: Oxford University Press, 1967.

This new edition of an old friend will be a welcome addition to the laboratory bookshelf, or more probably to the bench. Dr. Drury, who collaborated with the late H. M. Carleton in the 1957 edition, has now revised and extensively rewritten the fourth edition with the help of Mr. Wallington.

The basic pattern remains unaltered but two changes are welcome; much more space is devoted to the theory of technology and the methods are now grouped according to the component to be demonstrated instead of to the organ or tissue. The former change is in keeping with our better understanding of technology, and the latter change makes reference easier. "Carleton" has always been a reliable guide to practical and useful methods, and this present edition should prove as reliable as its predecessors.

Although nominally devoted to histology the text includes methods for enzyme histochemistry, exfoliative cytology, autoradiography, and for the demonstration of bacteria, fungi, protozoa, and worms. There are innumerable practical tips that will assist

the less experienced. A welcome innovation is a list of references with each chapter.

The illustrations have been usefully increased and the print is easier to read. The size of the page is a little larger and the number has increased from 318 to 400. I expect this edition to be even more useful than its predecessors, and I recommend it to anyone engaged in histopathology.

C. V. HARRISON.

Vaccines Against Viruses

First International Conference on Vaccines Against Viral and Rickettsial Diseases of Man. Pan American Health Organization Scientific Publication No. 147. (Pp. 695 + xxviii; illustrated, \$7.00.) Washington: Pan American Health Organization, 1967.

The programme of this congress was arranged under the headings of: the control of respiratory virus infections; exanthemata and mumps; smallpox, rabies, and hepatitis; enteroviruses; and rickettsiae and bedsoniae. One session was held on the problems of vaccination against these diseases. (See *Brit. med. J.*, 1966, 2, 1590.)

The information given in its long report is valuable to all those who practise control of infectious diseases, but the journalness of scientific communications makes many of the papers irksome reading. The value of the commentaries which follow each topic is greatly reduced by "discussants" not discussing, only adding more information, sometimes whole papers, to the load which the reader has already borne. However, the report does reveal new demands and policies which will affect immunization in the future.

Readers will know, or discover, that protection against killing and crippling diseases is not enough, and that immunization against minor infections is now under review. This

congress seems to favour a policy of no action against enteroviruses—poliovirus apart—but to view respiratory infections, though not common colds, in a more serious manner. Measles and rubella vaccines are considered at some length, and the papers make useful reading at a time when the virtual abolition of smallpox and poliomyelitis from certain countries has created environments in which only vaccines free of risk and of discomfort become acceptable.

Chemical treatment of viruses is being used in three ways—to fractionate pure virus antigens, so increasing relative effectiveness and lowering dosage; to disintegrate virions in the hope of broadening the specificity of antibodies induced; to conjugate haptens to antigenic proteins, so creating new antigens. The first of these methods is feasible, the last two controversial, especially in work with influenza and mycoplasma (which was included in the section on respiratory viruses).

The use of adjuvants, particularly a new oil emulsion, has strong advocates and some detractors. The discussion is useful here.

New phenomena continue to appear. It may be that the prophylaxis of virus infections of mucous membranes depends on the quality of antibody produced. There is a suggestion that protection against respiratory syncytial virus may fail because enough IgA antibody is not produced.

Tumour-forming viruses receive much attention, probably too much. Recent discoveries of "hybrid viruses" which have acquired tumour-forming capacity from contaminating viruses in tissue-culture systems will strengthen the desire of many to avoid all active virus vaccines. Certainly, if adenovirus vaccines are ever used, the use of chemically purified antigen, as suggested by one speaker, should obviate risks of injecting foreign nucleic acid during immunization.

These are all large fields to survey. The concluding speaker is right in saying that he would gladly have seen more time for discussion.

K. B. FRASER.

Books Received

Review is not precluded by notice here of books recently received.

Field Guide to Disease. A Handbook for World Travellers. By Berton Roueché. (Pp. 146, 21s.) London: Victor Gollancz, 1967.

Surgery for Acquired Mitral Valve Disease. By F. Henry Ellis, Jr., M.D., Ph.D.(Surgery), F.A.C.S. (Pp. 299 + xiv; illustrated, £5 19s.) London: W. B. Saunders, 1967.

Baby Gymnastics. By Detleff Neumann-Neurode. Revised by Wendula Kaiser. Photography by Hinde Baum. Translated from the German by Agnes Wenham. (Pp. 39 + xii; illustrated, 15s.) Oxford: Pergamon, 1967.

Cancer of the Breast. Major Problems in Clinical Surgery. Vol. 5. By John S. Spratt, Jr., M.D., and William L. Donegan, M.D. (Pp. 322 + xv; illustrated, £3 15s. 3d.) London: W. B. Saunders, 1967.

Symposium on Tumors of the Alimentary Tract in Africans. Held at Geneva, 1965. National Cancer Institute Monograph, 25. Edited by J. F. Murray. (Pp. 315 + xxiii, \$3.25.) Bethesda, Maryland: National Cancer Institute, 1967.

Gaseous Digestive Conditions. By Joseph H. Pollock, M.D., F.I.C.S. (Pp. 163 + xv; illustrated, \$7.00.) Springfield, Illinois: Charles C. Thomas, 1967.

Diagnosis and Treatment of Menstrual Disorders and Sterility. 5th edition. By S. Leon Israel, M.D. (Pp. 638 + xii; illustrated, £9.) New York: Harper & Row, 1967.

The Erotic Minorities. A Swedish View. By Lars Ullerstam, M.D. Introduction by Antony Grey. Translated by Anselm Hollo. (Pp. 146 + x, 30s.) London: Calder & Boyars, 1967.

Wirbelsäulen-Fibel. By Professor Hans Rettig and Dr. Kurt Kollmann. (Pp. 105 + vii; illustrated, DM. 16.80.) Stuttgart: Georg Thieme, 1967.

Peripheral Nerve Regeneration Using Nerve Grafts. By Leonard Marmor, M.D. (Pp. 107 + xi; \$6.75.) Springfield, Illinois: Charles C. Thomas, 1967.

Praxis der Selbsthypnose des Autogenen Trainings. By Dr. Klaus Thomas. (Pp. 90 + vii, DM. 9.80.) Stuttgart: Georg Thieme, 1967.

History Taking for Medical Students. By S. D. Bhandarkar, M.D., M.R.C.P., F.R.F.P.S. (Pp. 80, 3.50 rupees.) Bombay: Popular Prakashan, 1967.

Nutrition and Physical Activity. Symposia of the Swedish Nutrition Foundation, 5. Edited by Gunnar Blix, M.D. (Pp. 143; illustrated, 40 Swedish kroner.) Stockholm: Almqvist & Wiksell, 1967.

Speaking and Writing in Medicine. The Art of Communication. By Clifford F. Hawkins, M.D.Lond., F.R.C.P. (Pp. 159 + xviii; illustrated, \$8.50.) Springfield, Illinois: Charles C. Thomas, 1967.

The Haemolytic Anaemias. Congenital and Acquired. Part 4. 2nd edition. By J. V. Dacie, M.D., Hon.M.D.(Uppsala), F.R.C.P., F.R.S. (Pp. 993-1352 + vii; illustrated, 65s.) London: J. & A. Churchill, 1967.

Symposium on Tetanus in Great Britain. Held at Leeds on 7-8 April 1967. Edited by M. Ellis, F.R.C.S. (144 cyclostyled pages. Available on request for token payment.) Leeds: The Tetanus Unit of the General Infirmary, 1967.

New Concepts in Pain and its Clinical Management. Edited by E. Leong Way, Ph.D. (Pp. 224 + xiv; illustrated, 64s.) Oxford: Blackwell, 1967.

Infant Nutrition. By Samuel J. Fomon, M.D. (Pp. 299 + x, £3 13s. 6d.) London: W. B. Saunders, 1967.

Middle Articles

MEDICAL HISTORY

“Guérir quelquefois, Soulager souvent, Consoler toujours”

L. M. PAYNE*

Brit. med. J., 1967, 4, 47-48

The number of people who have sought for the origin of this quotation must be legion and those who have guessed at its source no less. These words have been used to summarize the vocation of both doctor and nurse. They have been attributed to people as widely separated in time as Hippocrates and Florence Nightingale, Paré and Edward Livingston Trudeau. In a recent paper¹ they were attributed to Oliver Wendell Holmes. The author had taken it from the *Practice of Dynamic Psychiatry* by J. H. Masserman, p. 359 (Philadelphia, 1955). It is significant that of all the quotations found at the beginning of each chapter this one alone lacked the precise reference, the author's name only being given. The fact that these words are found in Latin, French, and English does not make it any easier to document their earliest use. They are found in a window in the New York Academy of Medicine. They are part of the nurses' window in Guildford Cathedral. In a stained-glass window on the history of medicine in the Mayo Clinic they form part of the Lister window, in the description of which the saying is attributed to Trudeau.²

This may be because W. B. James, at a memorial meeting

* Librarian, Royal College of Physicians of London.



FIG. 1.—Bronze statue of Dr. E. L. Trudeau by Gutson Borghum. Formerly at Trudeau Sanatorium grounds, now at Trudeau Institute grounds on Lower Saranac Lake, New York. By courtesy of the Trudeau Institute.

to Dr. E. L. Trudeau in January 1916, told how he had first heard from him a quotation which, they used to agree, briefly and comprehensively described the ideal aim of a physician—“Guérir quelquefois, soulager souvent, consoler toujours”³; or it may be because at Saranac Lake these words are found on the memorial statue of Trudeau in the grounds of the Trudeau Institute (Fig. 1) and beneath an oil painting in the library (Fig. 2).

Since the dedication of the statue in August 1918, if not before, the librarian of the local public library, in common with many other librarians the world over, has sought in vain, far and wide, for the origin of this quotation.

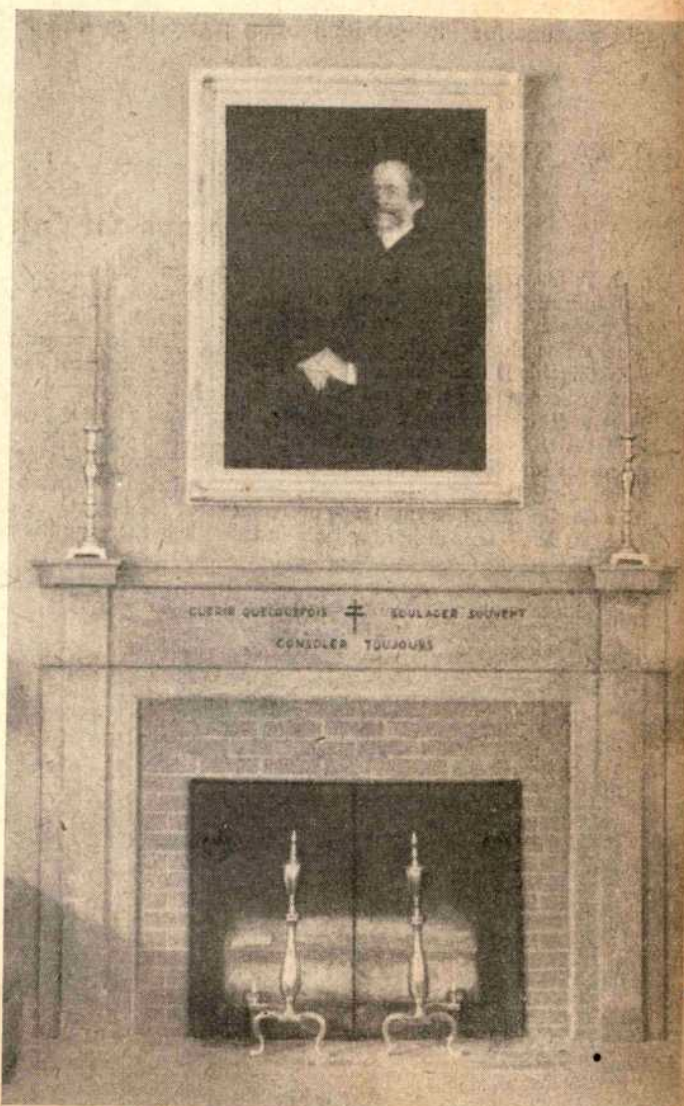


FIG. 2.—Picture of Dr. E. L. Trudeau in library of Trudeau Institute at Saranac Lake, New York. By courtesy of the Trudeau Institute.

When Sir Theodore Fox in his Harveian Oration⁴ used this quotation as "the classical summary of the doctor's vocation" he avoided attributing it to any author. A. L. Donaldson⁵ said that Dr. Trudeau exemplified to the full the maxim of a great French physician which he was very fond of quoting. This may refer to Armand Trousseau; but a search of his works by one librarian⁶ has produced nothing nearer than "... une infirmité sans gravité, qu'on ne peut guère espérer guérir, mais qu'on peut toujours soulager" (*Clinique médicale de l'Hôtel de Dieu de Paris*, 2nd ed., vol. 3, p. 781, Paris, 1865). A similar saying is found in Paré⁷ in *Canons et règles chirurgicales de l'auteur*: "L'office du bon médecin est de guérir la maladie que s'il ne vient à cette fin, au moins faut-il qu'il la pallie." Witkowski, either alone or in co-operation with Cabanès, has written a number of works comprising medical anecdotes and quotations. In one of these he reproduces words attributed to Asclepiades⁸: "the duty of a physician is to cure diseases safely, quickly and happily." It was not until 1909 that Witkowski and Cabanès published a book⁹ with a chapter headed "Proverbes et dictons sur les médecins" which had original quotations in italic and comments in roman type. Beneath the quotation "La présence d'un Médecin profite beaucoup," which is preceded by the words "Au XV^e siècle, on disait," there is this sentence in roman: "Son rôle est de guérir quelquefois, soulager souvent, et consoler toujours."

In the light of this it may or may not be naive to suggest that in this form the quotation is no older than 1909, or the date when Witkowski and Cabanès collected the material for their book; it is clear, however, that a misreading of this book would account for the quotation being regarded as fifteenth

century or earlier. Perhaps it is one of those sayings which have, so to speak, evolved with the passage of time. Professor Ackerknecht,¹⁰ who provided the reference to Paré, thinks it is proverbial. In the Latin and English versions of Paré's *Canons* there has been some rearrangement as compared with the original French, with the result that there are two now fairly close together which embody the sentiments of cure, relief, and comfort:

6. It is the part of a good Physition to heale the disease, or certainly to bring it to a better passe, as nature shall give leave.

10. You shall comfort the Patient with hope of recoverie, even when as there is danger of death.¹¹

By recording known published references earlier than Witkowski⁹ some light may be thrown on its origin, even if the actual source cannot be found.

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- ⁷ Paré, A., *Les Oeuvres*, 11th ed., p. 767. Lyons, 1652.
- ⁸ Celsus, *De medicina*, lib. iii, 4. (cf. Green, R. M., *Asclepiades: His Life and Writings*, p. 128. New Haven, Connecticut, 1955.)
- ⁹ Witkowski, G. J. A., and Cabanès, A., *Gayetez d'Esculape*, p. 283. Paris, 1909.
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NEW APPLIANCES

Cardiff Laryngoscope for Infants

Dr. O. P. GRAY and Dr. M. ROSEN, Cardiff Royal Infirmary, write: The unreliability of laryngoscopes at present available is well known. The electric contacts, both between the folding blade and the handle and with the bulb, become worn in time and the light fails at a critical moment. In addition, the cost makes the widespread provision of extra instruments for occasional or standby use expensive.

The Cardiff infant laryngoscope overcomes these obstacles. It is a more reliable instru-

ment, and its low cost may make it financially possible to have infant laryngoscopes more readily available.

The instrument consists of a standard pen-torch adapted to receive a screw-fitting laryngoscope blade (Figs. 1 and 2). The blade shape is based upon that of the Seward infant laryngoscope, and is made of Perspex, polished except at the tip. The light transmission is excellent and provides a clear view of the larynx. A pen-torch was chosen since it is cheap and is possibly used by clinicians.

It seemed probable that a light used often for other purposes would be in good order when required as an emergency laryngoscope. The blade can be sterilized by immersion in aqueous antiseptic solution.

The laryngoscope is not only satisfactory in use, but is also of value for inspecting the pharynx of neonates, a difficult task without a laryngoscope.

We wish to acknowledge the assistance of Mr. J. Thomas, lately instrument maker at the United Cardiff Hospitals, for making prototype blades. We thank our numerous colleagues for trying the instrument, and the Department of Medical Illustration, United Cardiff Hospitals. We would also like to thank Vickers Medical (Oxygenaire Ltd.), from whom the laryngoscope is available, for their helpful co-operation.

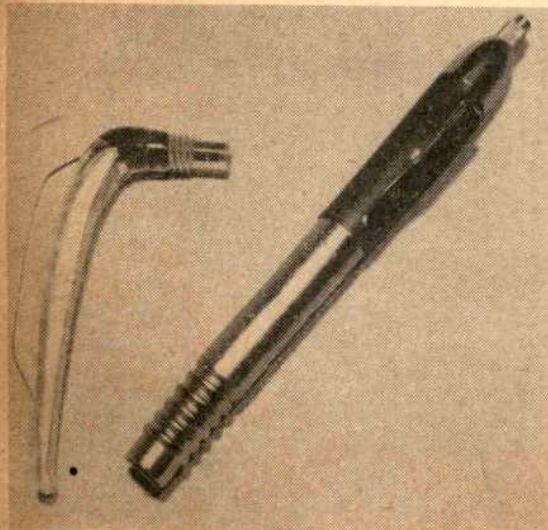


FIG. 1.—Pen-torch and blade.

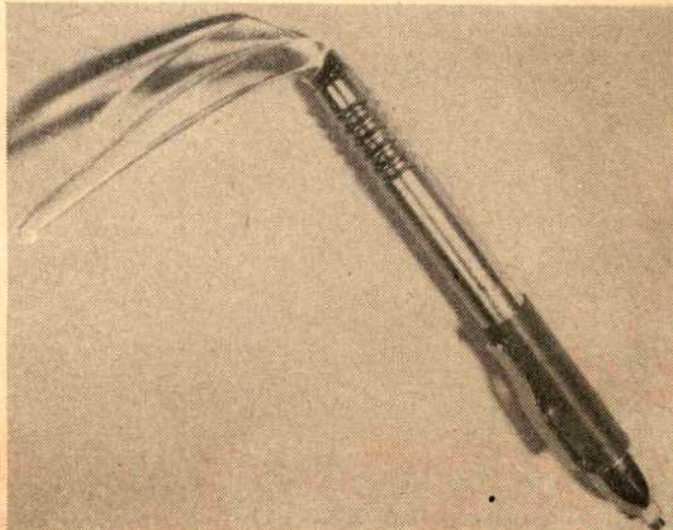


FIG. 2.—The instrument complete.

Correspondence

Letters to the Editor should not exceed 500 words.

Advantages of Health Centres

SIR,—From our 15 years' experience in the William Budd Health Centre we should like to make some comments on Dr. C. H. Warrick's article comparing practice in a health centre with group practice (9 September, p. 672). In Bristol it has been found that a pattern has evolved which might well be regarded as a basis for future development throughout the country. The provision by the local authority of nursing and secretarial staff has enabled general practitioners not only to use their time to the greatest advantage to run their own antenatal and infant welfare clinics in the closest possible co-operation with the obstetricians and local authority, but also to perform a variety of screening procedures, clinical investigations, and minor surgical procedures which normally occupy much of the time and resources of casualty and other departments of hospitals, and for which the "cottage industry" doctor has neither the facilities nor assistance.

Some people have suggested that "casualty units," complete with x-ray equipment, etc., should be set up in health centres and staffed by general practitioners on a sessional basis. This would undoubtedly ease the work load on the undermanned hospitals, and, by a simple extension of this idea, health centres could become local diagnostic units at which consultants could hold their "outpatients" sessions, thus saving further pressure on the hospitals and much waiting and travelling time for patients. Arrangements such as these would also serve to bring about a mutual understanding of their various problems by the consultants and general practitioners, as well as eliminating patients' fears, which seem to be engendered by the hospital environment. Furthermore, the newly qualified doctor, when entering general practice, would not find himself suddenly deprived of the scientific and paramedical assistance to which, as a student and houseman, he has become accustomed, and would not feel that he was entering a cottage industry and an inferior part of medicine. Special skills acquired in hospital could be usefully employed and would not undergo disuse atrophy. A feeling of satisfaction could replace frustration, and the service given to patients could be improved.

It may be said that any group of general practitioners can get together to provide their own purpose-built centre, and this is obviously true. The trouble is that with the present-day high price of land and building the initial financial burden on the doctors would be prohibitive, and with high maintenance costs there is no doubt that doctors embarking on such a scheme under the present system of payment would be subsidizing the Government health services out of their own income. Although the obstacles might be formidable, even privately owned health centres might be possible to maintain if general practitioners were paid on an item-of-service basis for

all the additional services provided. In privately owned health centres it would often be difficult to obtain the same high degree of co-operation between general practitioners and local authority services—a co-operation which has proved valuable to both parties and the patient as well. While it is often thought that doctors working in health centres derive some benefit for themselves, it cannot be too much emphasized that the real benefits are bestowed on the patient, in so far as the doctors, relieved of work which can be quite properly delegated to ancillary workers, are able to devote more of their time and energy to providing a better service to the community. This was in very large measure the object of the planning of this health centre, and we are confident that this has been achieved. There can be little doubt that the quality of service provided is the yardstick by which the value of health centres should be judged. It is believed that economy of costs can be effected if general practitioners and local authority utilize the same premises. The great advantage of privately owned health centres is of course that the security of tenure is absolute, and this factor poses one of the greatest problems faced in regard to those provided by local authorities.

The time has now come when there should be a conference of general practitioners who actually work in health centres to pool their views and iron out problems. The practical doctor must have many ideas for future development, and these should be communicated to the Ministry and the profession. For too long have we been advised by the armchair theorists who have no working knowledge of health centres, but who spend their time telling other people how to do good general practice; and it is these same armchair theorists who seem to have the ear of the Ministry and the profession at the present time.

At the cross-roads at which the National Health Service now stands, any means which can be found to ease the increasing burden of the general practitioner and at the same time give him a real sense of fulfilment in following his vocation should be grasped, and it would seem that the provision of health centres falls into this category.—We are, etc.,

EDWARD LACE.
H. I. HOWARD.

William Budd Health Centre,
Bristol 4.

Melanoma, Halothane, and Liver Necrosis

SIR,—While the similarity may be coincidental, the following two deaths have common features that seem to be worth recording.

Miss A., aged 39, had a melanoma removed from her leg under local anaesthesia. As histological examination showed malignancy with lymphatic invasion, the femoral artery was can-

nulated for infusion of the cytotoxic agent S.P.I. (podophyllic acid hydrazide). On the fourth day the cannula became displaced and was reinserted. On the eighteenth day the scar was widely excised and a skin graft applied. These three procedures were carried out under general anaesthesia with thiopentone, nitrous oxide, and halothane. On the twenty-first day she was drowsy, disorientated, and jaundiced. She died on the twenty-third day. Necropsy showed necrosis of the liver. There was no recurrence of the melanoma.

Mr. B, aged 75, had a melanoma of the back. He had an unexplained thrombocytopenia but no other abnormality. The melanoma was removed, and, as it was found to be malignant, 11 days later it was widely excised and a skin graft applied. He received two pints of fresh and two of stored blood. On the fourteenth day the dressing was changed. The three procedures were carried out under thiopentone, nitrous oxide, and halothane. On the fifteenth day he became jaundiced and he died on the seventeenth day. Acute hepatic necrosis was found. There was no recurrence of the melanoma.

Halothane was theoretically considered as a possible cause of liver damage, but the incidence of jaundice after its use is no higher than that in the general population.¹ There is, however, said to be an increased incidence of hepatic necrosis in patients who have been repeatedly anaesthetized, and halothane sensitization has been postulated.² S.P.I. is not thought to be specially hepatotoxic. It has never been suggested that melanomata produce any internal toxins. Whether the thrombocytopenia in the case of Mr. B was significant was not decided. The connexion between these two deaths remains purely speculative.

The patients were under the care of Mr. W. H. W. Jayne and Mr. G. Westbury.

—We are, etc.,

GEOFFREY ORGANE.

Westminster Hospital,
London S.W.1.

GAVIN THURSTON.

Westminster Coroner's Court,
London S.W.1.

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Prescribing and Withholding Psychotropic Drugs

SIR,—Should we not give more consideration to the criteria for withholding the so-called psychotropic drugs?

Major psychiatric and psychological derangements warrant risks commensurate with their severity, but it is for minor neurosis that the bulk of these drugs is consumed. It is becoming disturbingly common for patients, not past middle life, to regard their medication as a permanent regimen and to attend for prescriptions with a regularity suggestive of dependence.

It is difficult to assess the long-term effects of tranquillizers and antidepressants on the course of the various neuroses, while the safety of permanent regimens of a wide multi-

plicity of new drugs can hardly be taken for granted. Should there be any parallel with the effects of alcohol, for example, in a few years' time there could be a crop of iatrogenic delirium tremens and liver cirrhosis which would hardly bear contemplation.

We should not forget that the present stupendous amphetamine consumption, legitimate and otherwise, was initiated by ourselves, just as the overconsumption of barbiturates is a legacy of the sedative era.

Past experience gives a clear warning. Our collective therapeutic machine is very sensitive to the accelerator and we are driving without brakes.—I am, etc.,

Sheffield.

C. H. FOGGITT.

Treatment of Poisoning by Antidepressants

SIR,—Recent progress in elucidating the metabolism of imipramine and amitriptyline lends strong support to the plan of treatment proposed by Dr. C. M. Steel and others (9 September, p. 663). The important points are:

(a) These drugs and their metabolites are very rapidly excreted, predominantly in the urine. Christiansen *et al.*¹ gave radioactive imipramine to 21 patients and found an average of 40% of the radioactivity in the ensuing 24-hour urine. In our laboratory here we have confirmed and extended this.

(b) Imipramine circulates in the blood, about 90% bound to plasma proteins and therefore undialysable.²

(c) The binding of the drugs to protein, whether in blood or tissues, is not firm, as Dr. Steel and his colleagues state, but labile and reversible.³

(d) Destructive metabolism, principally hydroxylation and glucuronide formation, is rapid and takes place in the liver.⁴

(e) Bile contains a good deal of drug metabolites, which pass into the intestine and are then largely reabsorbed into the circulation.⁵

The protein-binding of the drugs helps to explain why peritoneal and extracorporeal dialysis are ineffective treatment for an overdose. The rapid metabolism of the drugs explains why methods which measure only the drugs themselves and not their various metabolites fail to account for much of the overdose in the urine. (The heptane method mentioned by Dr. Steel and his colleagues does not extract the metabolites.) Other methods, however, will demonstrate rapid excretion. This explains why, provided blood pressure remains adequate for kidney function, the overdose can be rapidly cleared from the body without any special intervention. The literature in fact contains quite a number of reports of severe poisoning, with coma and convulsions, in which with prompt control of the fits patients recovered smoothly in two days or so and were none the worse for the experience (as in Dr. Steel's Case 31). This is what one would expect with a high excretion rate, and makes the tricyclic antidepressant drugs safer than their alarming symptoms would suggest. Circulatory collapse is the great danger, but seems uncommon in these cases. Perhaps, then, it might still be possible to draw off the drug and its metabolites through the bile (duodenal intubation?).

Dr. Steel and his colleagues do not discuss prevention of poisoning with these drugs. There are two relevant points here. They do not mention the sex of their child cases,

but in the literature the vast majority were boys, particularly from 18 months to 5 years old. This, then, is the population at risk. The majority of people bringing the drugs into the home are depressed women, in some cases mothers of boys. Now people with depressive illnesses are apt while ill to be forgetful, careless, and even fatalistically ready to run unnecessary risks—all as part of their sickness, and different from their normal personalities in health. This suggests, therefore, that when we prescribe tricyclic antidepressant drugs for treatment at home we should always inquire whether there are young children, especially boys, in the house and arrange that the tablets are in the care of a responsible relative (for example, husband) for daily issue, rather than in the care of the patient herself.—I am, etc.,

St. John's Hospital,
Stone, Aylesbury, Bucks.

J. L. CRAMMER.

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SIR,—In the article by Dr. C. M. Steel and others (9 September, p. 663) the authors recommend using paraldehyde instead of barbiturates in the treatment of convulsions caused by overdose of antidepressive drugs such as amitriptyline.

However, paraldehyde is potentiated by other central nervous system depressants (and vice versa); and in large doses, which may be necessary to control fits, is known to depress respiration and circulation.¹ Also paraldehyde has been proved to reduce the contractions of mammalian heart-lung preparations.²

In their article the patient cited had a low minute volume before paraldehyde administration, but no second reading was given afterwards, only the bland statement that no ventilation was considered necessary. As respiration and circulation are already depressed in overdose with antidepressives, I consider that neither barbiturates nor paraldehyde should be used, but that tubocurarine or a related drug should be given for convulsions and the patient's ventilation controlled. This would not prove awkward, as any unit treating such cases should have facilities to use artificial ventilation; and the harmful effects of antidepressive drugs have disappeared by 24–36 hours following ingestion; provided no other depressive drugs are administered.—I am, etc.,

Royal Brisbane Hospital,
Brisbane, Australia.

A. B. BAKER.

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- Wollenberger, A., and Krayner, O., *J. Pharmac. exp. Ther.*, 1948, 94, 439.

SIR,—I was interested to read the excellent report on treatment of imipramine and amitriptyline poisoning by Dr. C. M. Steel and others (9 September, p. 663) and would like to make the following comments.

The writers rightly stress the possibility that any factor increasing the cardiac work load in these cases may precipitate the cardio-toxic effects of the drugs,¹ and it is clearly important, therefore, to prevent convulsions. However, the use of the enforced diuresis method of treatment in poisoning is unlikely to increase significantly this risk when infusing fluid into a young, healthy subject with normal renal function and at a rate commensurate with the diuresis. In the situation previously described² there was a progressive fall in the amount of metabolites excreted in the urine during diuresis, which was paralleled by the clinical improvement. It is true that the renal excretion of the free drug is low, but, as pointed out by Dr. Steel and his colleagues, we do not know the pharmacological activity of all the metabolites excreted in the urine; they may be responsible for some of the effects of poisoning by this group of drugs.

It would seem unwise in our present state of ignorance to deny the patient any treatment that may increase renal excretion of the drug or its metabolites, especially as the patient may be continuing to absorb the drug present in the gastrointestinal tract beyond reach of the gastric lavage, and whose blood stream may contain amounts of the drug or its metabolites as yet unbound to the tissues. Likewise, it may also be unwise to imply that peritoneal or extracorporeal dialysis is of no use in such cases of poisoning because of previously reported failures,³ for these cases may have been irreversibly affected by the cerebral and cardiovascular effects of the drug before dialysis was started.—I am, etc.,

Radcliffe Infirmary,
Oxford.

BRIAN J. PROUT.

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- Cairncross, K. D., and Gershon, S., *Med. J. Aust.*, 1962, 2, 372.
- Prout, B. J., Young, J., and Goddard, P., *Brit. med. J.*, 1965, 1, 972.
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Kwashiorkor in Children

SIR,—The detailed haematological survey of children with kwashiorkor by Professor E. B. Adams and his colleagues (19 August, p. 451) is of considerable value, particularly as there are no complications such as malaria and hookworms in Durban. Recent experience in Kampala is pertinent to two points which they raise: firstly the aetiology of the anaemia, and secondly the need for blood transfusion.

One hundred and twenty-two children with kwashiorkor have been admitted since January 1966; 35% had hookworm infestation, 22% malaria, and 13% sickled (three children were homozygous SS on haemoglobin electrophoresis).

Fifty-three of the 122 children had none of these complications. In 25 of these the haemoglobin level was less than 10 g./100 ml. and this "anaemic" group has been compared with the other 28 "non-anaemic" group. Both groups had a mortality of 10%, and similar sex distribution and anthropometric measurements. Clinical signs were also similar, except that the "anaemic" group tended to have more florid hair changes, although the subjective nature of

this sign makes assessment difficult. There was, however, a distinct difference between the mean concentrations of plasma protein in the two groups. Fourteen (55%) of the "anaemic" children had plasma protein levels of below 4 g./100 ml., whereas only 5 (18%) of the "not anaemic" ones had such low levels ($P < 0.01$). This provides some circumstantial support for the association between protein deficiency and anaemia found in Durban.

Blood transfusion for children whose haemoglobin level is less than 6 g./100 ml. is recommended by Adams *et al.*, and this was also the policy here at one time.¹ It is high compared with the 4 g./100 ml. recommended in Jamaica,² and since the introduction here of a low sodium diet providing 1 mEq/kg./day of sodium instead of the 6 mEq/kg./day formerly used it has been possible to manage successfully children with haemoglobin levels of less than 3 g./100 ml. without transfusion.³ The mean change in haemoglobin at the end of the first week in 29 children receiving a low sodium diet was -0.15 g./100 ml., compared with -0.95 g./100 ml. in 30 children on a high sodium diet ($P < 0.001$). It would be of value to know the sodium intake of the Durban children. There seems some virtue in avoiding a transfusion whenever possible in these children, not only because of the cost and possibility of reactions, but also because of the reduction in cardiac output and inulin clearance following intravenous plasma in malnourished children.⁴

Since the introduction of the low sodium diet a rapidly falling haemoglobin has now become very suggestive of an infection, particularly a Gram-negative bacteraemia. We have no rule of thumb for blood transfusion now, but a rapidly falling haemoglobin in the presence of a proved or suspected septicaemia seems a reasonable indication in Kampala, although not necessarily elsewhere. In our experience the "Dean" diet⁵ has continued to give satisfactory results in most children, although, for the reasons just given, we now recommend a reduction in the percentage of sodium.³⁻⁶

To summarize, therefore, our experience in Kampala suggests there is an "anaemia of protein deficiency," but that the use of a low sodium diet enables children with kwashiorkor to be treated without blood transfusions unless there is a complicating septicaemia.—I am, etc.,

BRIAN A. WHARTON.

Medical Research Council,
Infantile Malnutrition Research Unit,
Kampala, Uganda.

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Carcinogenic Properties of Ortho-dianisidine

SIR,—Further to Dr. H. Lehmann's letter (19 August, p. 494) I should like to use

your columns to ask the manufacturers of the widely used reagent tablets "Occultest" and "Hematest" (the Ames Company) whether the tablets contain ortho-tolidine or a related compound, and in what quantity? If one or more of these substances is present in these tablets, do they intend to state this on the label in future?—I am, etc.,

E. D. ACHESON.

Record Linkage Study and
Unit of Clinical Epidemiology,
Nuffield Department of Clinical Medicine,
University of Oxford.

Nephrotic Syndrome in Patient Taking the "Pill"

SIR,—The contraceptive pill has been incriminated as the cause of a variety of conditions. So far, a possible nephrotoxic property has not been demonstrated. Recorded here is a case where a nephropathy occurred during the use of oral contraception.

A 23-year-old nulliparous woman developed extensive oedema of the lower limbs eight days after commencing Ortho-Novin (norethisterone, 2 mg. and mestranol 0.1 mg.). The oedema persisted during three months of pill-taking, and she was found to have gross proteinuria with resultant hypoproteinaemia. The serum cholesterol was elevated and there was an increase in plasma alpha-two globulins and absent gamma-globulin. She had therefore developed the nephrotic syndrome and this has persisted for three months since the withdrawal of the contraceptive pills.

Excretion pycelography displayed a right hydronephrosis for which no cause was apparent. There was no evidence of renal vein thrombosis or other cause for the nephrotic syndrome. Apart from one attack of cystitis a year previously, there had been no renal symptoms prior to this present episode, and the patient had been in excellent health.

Does this case demonstrate a nephrotoxic property of the "pill"—or was it a coincidence that the nephrotic syndrome occurred so quickly during the use of oral contraception?—I am, etc.,

North Devon Infirmary, ALAN J. RILEY.
Barnstaple.

Aversion Therapy in Management of Homosexuals

SIR,—May we reply to the comments made on our paper (3 June, p. 594) by Drs. I. Bieber (5 August, p. 372) and B. Kalcev (12 August, p. 436)? Dr. Bieber takes issue with our claim for a near 60% success rate, considering that only 13 of our cases (30%) shifted to exclusive heterosexual behaviour, another seven cases (16%) becoming heterosexual though not exclusively so. He compares these percentages with his own figures—27% became exclusively heterosexual and an additional 15% became "actively heterosexual though not exclusively so."¹

Our Table VII states clearly: (1) 20 patients (46%) displayed no homosexual practice or fantasy post-treatment, while another five (12%) used weak (i.e., occasional) homosexual fantasy. (2) 13 patients were actively practising heterosexual intercourse (the 13 accepted by Bieber as being exclusively heterosexual), seven were also displaying heterosexual behaviour, though as yet

falling short of sexual intercourse—a not unusual phenomenon—and another five were either "dating" females or using strong heterosexual fantasy. All these data are summarized in our Table VIII in which 23 patients received a post-treatment Kinsey rating of 0 or 1 and two patients a Kinsey rating of 2. That is, none of the 25 patients described as improved were displaying homosexual practices, although six of them still showed occasional interest in directly observed males, and another five used occasional and weak homosexual fantasy. Twenty of the 25 were displaying overt heterosexual behaviour. Where overt sexual behaviour was displayed it was heterosexual in every case; where it was not the weight of interest and fantasy was much towards the heterosexual side of the continuum. The confusion arises because Dr. Bieber uses sexual intercourse as the synonym for sexual behaviour and interest. His 16 cases (see above) who were displaying "heterosexual behaviour though not exclusively so" were therefore bisexual—that is, practising both heterosexual and homosexual intercourse. Overt behaviour is not the only indicator of sexual orientation. It seems sensible to use, in addition, fantasy and desired behaviour, particularly in the absence of overt behaviour. As we pointed out in our paper, the five patients who were having sexual intercourse with their wives prior to treatment had to use homosexual fantasy in order to do so. If we look at sexual behaviour as a balance between heterosexual and homosexual components it seems reasonable to state that nearly 60% of our series were towards the heterosexual end of the continuum post-treatment.

Even if the outcome of treatment was similar in the two series aversion therapy would be the treatment of choice. Our patients received an average of 18 to 20 sessions, each lasting 20 to 25 minutes. Of Dr. Bieber's patients 78 (75%) had 150 sessions (hours) of treatment or more, and of these 38 (36%) had 350 sessions or more. With two exceptions improvement was confined to those receiving 150 sessions or more.

Of the 24 cases in our series who had been practising homosexuality for 10 years or more six became Kinsey 0 after treatment and four Kinsey 1. None of these 10 cases displayed overt homosexual behaviour post-treatment, six of them were having heterosexual intercourse, and two displayed overt heterosexual behaviour short of intercourse.

The term abnormal psychogenic development was used by Schneider² to describe personality aberrations which were not dependent on the patient's sexual status and which when present indicated a severely damaged personality, usually of the self-insecure or attention-seeking types. Non-psychoanalytic workers such as ourselves cannot hope to explore our patients' personalities in very great detail, although we are aware that it is possible to detect abnormal psychogenic developments in relation to relatively insignificant events. We must concede that the personality classification is crude. However, it has the merits of working at a clinical level, and of being used by the World Health Organization.

In reply to Dr. Kalcev, 10 out of the 18 of our series of cases who presented in connexion with a court appearance showed an improvement after treatment. Hence, referral by court is not necessarily a contraindication for success. However, irrespective of success we agree that there is indeed a moral issue here. It is certainly wrong to impose treatment on anyone, and a choice of being sent to prison or receiving treatment is hardly an adequate test of free will.

The term personality disorder is used to describe a serious problem of personal function-

ing other than homosexuality. A high proportion of those who presented for treatment displayed personality disorders because such individuals are more likely to seek help from psychiatrists than those with more normal personalities, particularly as homosexuality has been widely thought of as being beyond help. Dr. Kalcev excludes the seven cases who were sexually attracted to those under the age of 16 from the group which he describes as "subject to a treatment because of society," yet paederasty is the most heavily punished offence.

The argument that it is society that is wrong is very misguided. Which seems more unethical: to treat someone in distress, or to suggest to him that he waits until his practice is as socially acceptable as heterosexuality? The vast majority of our patients have been sad and unhappy individuals seeking help for a problem they see as central in their lives, and pleased with the results when these have been successful. When asked for their motives for wanting to change most patients stated a desire to marry and have a family; surely a long way from 1984, unless we consider such motives as evidence of a dark conspiracy towards social conformity.

Finally, may we make a plea for a less pejorative approach to discussion in this field? We consider our own research efforts as little more than a first approximation, and the problems remaining as greater than those so far attempted—for instance, the relative aetiological importance of genetic, intra-uterine, and early experience factors, the investigation of heterosexual behaviour as a form of social skill, and the importance of single-trial learning at critical periods in establishing and perpetuating specific forms of sexual behaviour.—We are, etc.,

M. J. MACCULLOCH.
M. P. FELDMAN.

Department of Psychology,
University of Birmingham.

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- 1 Bieber, I., et al., *Homosexuality*, 1962. New York.
- 2 Schneider, K., *Psychopathic Personalities*, 1958. London.

Screening by Cervical Cytology

SIR,—The known facts on the incidence of cancer of the cervix prove the Ministry to be wrong in refusing the screening service to women below the age of 35 years.

My records for 200 consecutive cases of carcinoma-in-situ of the cervix and 200 of invasive carcinoma of the cervix show an age incidence as follows:

	20-29	30-39	40-49	50-59	60-69	70-79	80-89	Average
Cervix in situ ..	29	70	67	26	6	2	0	39
Cervix invasive	3	25	45	70	38	16	3	54

During the year 1966 our screening service found 144 women with positive smears. Their ages and the source of the smears are:

	16-20	21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	81-85	Total
Local authority clinics ..	2	3	3	8	19	15	3	4	—	—	—	—	—	—	57
Hospital cases ..	3	6	2	7	5	9	4	6	6	5	2	1	2	1	59
Antenatal clinic and postnatal clinic..	1	2	4	1	—	1	—	—	—	—	—	—	—	—	9
General practitioner	3	—	3	1	7	2	3	—	—	—	—	—	—	—	19
															144

The highest-risk type for cancer of the cervix is the woman who marries early, usually has many children, and is house-bound because of her many cares and low social status. Any national screening programme which leaves out, almost entirely, the highest-risk cases is sure to prove a costly disappointment, worse than this it is likely to lead to quite false conclusions. The Ministry should not only pay general practitioners for taking smears regardless of age but also encourage this before the age of 35 rather than after it. The highest risk cases can be reached only by those who attend them in their many pregnancies and by the home nurses on the staff of the medical officer of health.¹ Dr. Leyshon has found that by the time a woman dies with cancer of the cervix she uses up nine months of a home nurse's time. This home nurse is available for the screening service only when not required for sick cases. Medical officers of health should have a number of home nurses for this work only.—I am, etc.,

G. R. OSBORN.

Pathology Department,
Derbyshire Royal Infirmary,
Derby.

REFERENCE

- 1 Osborn, G. R., and Leyshon, V. N., *Lancet*, 1966, 1, 256.

Drugs and Driving

SIR,—I fully appreciate the layman's dilemma expressed by Mr. John Allan (16 September, p. 739). Nevertheless, Dr. D. V. Foster's remark about "rapport existing between doctor and patient" (24 June, p. 836), endorsed by myself (8 July, p. 109), was not intended to be considered out of its original context, but by so doing Mr. Allan has not surprisingly slanted the emphasis.

At present it would appear that very little is known about the possible effects of the powerful psychotropic and psychosedative drugs we are prescribing on our patients' driving performance. A recent pilot survey on my own psychiatric outpatients showed that approximately one in five are regular drivers while receiving psychiatric drugs singly or in combination. When viewed nationally this represents a not inconsiderable proportion of motorists. The majority believed that their reactions were not impaired and were sometimes even improved by medication, but this situation is merely comparable to the subjective effects produced by alcohol on the mildly intoxicated driver. A number of learner-drivers have come to my notice who take quite large doses of tranquilizers before undergoing driving tests, which would appear to be a surprisingly dangerous practice. The problem is, however, not peculiar to motorists. Some years ago the driver of an express plying between Shrewsbury and Paddington was receiving chlorthalidose

(Librium) 90 mg. daily to reduce anxiety, fortunately without untoward incident, but had an accident occurred one can imagine the Court's reaction to the divulgence of this information.

Applicants for motor-vehicle licences must now disclose whether they "suffer from any form of mental disease or defect," and if so give particulars. This might be taken to include reference to drug treatment, although such information is not specifically requested. Insurance companies do not yet seem to be alive to the problems of drugs and driving, as evidenced by their proposal application forms, despite the fact that the drug alcohol is recognized as a major cause of road accidents. If we are to attempt to halt the increase in accidents then perhaps stiffer medical examinations should be instituted before an individual is permitted to drive a vehicle.

As doctors we must know the effects of the drugs we prescribe on our patients' ability to drive. Only then will we be in a position to offer sound advice.—I am, etc.,

Shelton Hospital,
Shrewsbury, Shropshire.

J. C. BARKER.

Taking Blood Samples

SIR,—A programme was shown on B.B.C. Television ("Twenty-four Hours," 19 September) featuring experiments on the lines of the new breathalyser tests, in which a volunteer was shown about to have a blood sample taken from the tip of the right thumb.

Excluding possibly the eye, I can think of no area where accidental infection of a needle puncture wound could produce such grave and permanent disability as in the pulp space of a digit, especially that of the thumb of the dominant hand. In addition, the highly sensitive skin of the finger tips makes the site inappropriate.

I hope we can rest assured that no member of the public will be asked to agree to blood sampling by this technique for police tests.—I am, etc.,

Cumberland Hospital, W. JOAN FERRABY.
Mitcham, Surrey.

Doctors for Industry

SIR,—Having read the leading article "Doctors for Industry" (16 September, p. 692), I cannot let this pass without comment, and hope that you will find space to publish my letter.

Firstly, I would point out that I represented the Association of Certifying Factory Surgeons on the subcommittee of the Industrial Health Advisory Committee of the Ministry of Labour, and as such find it difficult to comment on a document to which I am a party.

Secondly, I would say that in the main we support the Ministry of Labour report¹ but do not necessarily agree with all the recommendations therein. We are not happy with the format of the suggested certificate. Nor are we happy with the idea that the certificate should be handed to the employer, for this would undoubtedly lead to discrimination.

As regards the suggestion that there should be 100 full-time "A" doctors, my feeling is that there has been misunderstanding here. At the outset it was indicated that if full-time doctors were to run the new service this could be done by between 80 and 100 doctors, but I am not of the view that it was ever intended that the new service should be run by full-time doctors, but by part-time, as at present, and that the number required would be about 400 instead of the present 1,600 to 2,000. It is a known fact that at present 80% of all appointed factory doctors' work is carried out by 20% of the appointed factory doctors—namely, about 400.

Far from accepting our demise with equanimity, we view the new service as a challenge, and a worth-while job for us to carry out with skill and experience.—I am, etc.,

G. A. LAWRENSON,
Honorary Secretary,
Association of Certifying Factory Surgeons,
Manchester.

REFERENCE

¹ *The Appointed Factory Doctor Service*, Report by a Subcommittee of the Industrial Health Advisory Committee, 1966. H.M.S.O.

SIR,—Care of young people except in cases of gross disability is apparently to be abandoned by the factory medical inspectorate. Apparently the *B.M.J.* concurs (16 September, p. 692), and we may soon expect to see the School Medical Service thumbing their textbooks to adjudicate on flaws before fixing red labels for types of defect. What I find disturbing is specious support for official views on a narrow department line. The wider issues and inconvenient aspects which conflict with official policy are ignored.

What are the problems of young people leaving school for work in the metamorphosis of adolescence? What is the meaning of medical care in terms of "whole-man" medicine and particular adolescent stresses? What is the aim of health and educational services in regard to young people? In what way should services be co-ordinated? What information do we need? Is the Ministry of Labour the right place for the care of young people to be centred? Is there need for a service to be developed, rather than to be abandoned, by the A.F.D. as a member of a team, particularly with a reorganized Youth Employment Service and the School Medical Service? Why has survey and experiment before legislation been barred?^{1,2} Is not better care of the less able and socially handicapped young person a field of major economic and social importance? Is it a field where a red card system for the grossly handicapped and virtual abandonment of the rest is medically or socially or educationally acceptable?

There are many other points—and opportunities—to be considered, and it is sad to see your journal preoccupied with physical aspects of health at a time when so much new thinking is pointing the way to changes in the concept of medical care of the young.—I am, etc.,

M. E. M. HERFORD,
Appointed Factory Doctor,
Farnham Royal, Bucks
Windsor and Slough District.

REFERENCES

¹ *Parliamentary Debates (Hansard)*, 1965, 705, 1395.
² *Ibid.*, 1966, 723, 71.

Restrictions on Doctor in South Africa

SIR,—You have already published a letter from very distinguished members of the scientific and medical professions expressing the strongest disapproval of the banning in South Africa of Dr. Raymond Hoffenberg, a most distinguished worker in medical research (26 August, p. 556) and have supported their opinions with an excellent leading article (same issue, p. 512). The effect of the ban is to sterilize his future work. He is still young and it is impossible to estimate the loss to human knowledge and medical science.

We, his former associates at New End Hospital in Hampstead, wish to associate ourselves with these protests. In addition, we wish to point out that the Ministry of Health has now an excellent opportunity of reversing the scientific "brain drain" which has been causing so much anxiety. Dr. Hoffenberg, if he leaves South Africa, will never be allowed to return. Here in Britain he has no source of income. We suggest that a professorial or senior consultant post should be created for him at once. Such a move would be of the greatest advantage to medical research in Britain.—We are, etc.,

GEOFFREY KEYNES.
J. E. PIERCY.
RAYMOND GREENE.
A. STUART MASON.
HELEN E. A. FARRAN.
M. J. LANGE.
A. W. G. GOOLDEN.

New End Hospital,
London N.W.3.

Emergency Admissions for the Elderly

SIR,—The following circular from our hospital group has been received.

"Geriatric Admissions"

"Elderly patients with an acute medical illness requiring admission to hospital are admitted to the geriatric wards at the Kingston Hospital and Hull Royal Infirmary parallel with the rota for acute medical admissions. When geriatric wards are full, and on admission days for Sutton, geriatric medical emergencies are admitted to acute medical wards, but this facility is liable to interfere with the true function of the acute medical wards unless all general practitioners co-operate in restricting as far as possible the number of elderly patients admitted in this way.

"Long-term illness and social problems in the elderly should be referred to the geriatric out-patients or geriatric physician where appropriate.

(Signed)"

What is the true function of acute medical wards but to treat acute medical emergencies? The implication of the above is surely that two standards of medicine are being employed and that elderly patients are regardlessly being shunted into a "chronic" ward.

All doctors experience difficulty over the elderly patients. Some people at 70 are spry and active mentally and physically, yet an acute illness would result in their admission to a chronic ward in the hospital; others at 60 are prematurely old and senile, yet presumably would be admitted into an acute medical ward by reason of their age. Why should an arbitrary decision be made to deny someone the benefit of modern treatment by reason of their age alone—surely *all* should be admitted to acute medical wards and only after initial treatment should they be trans-

ferred to wards for the chronic, the senile, the dying, and the hopeless cases.

General practitioners are now experiencing difficulty in getting elderly, but mentally and physically active, patients to return a second time to a geriatric ward. One experience has been enough, and the general practitioner is faced with the plea from the patient, "Don't send me back to *that* ward, doctor." Surely the general practitioner who has seen the patient at home is the one to decide whether the patient should be admitted in an emergency to a general ward or a geriatric one.

There is an impression that patients over 65 are going to get different treatment, which the hospitals will surely deny, but then why is it necessary to differentiate admissions by age?

Examples of doctors over 70 now active and fit can be quoted. Will they go to the chronic geriatric wards if they become acutely ill? Is no thought to be given to the mental state of an active elderly person in a bed between two senile dying "chronics"?

Long-term illnesses and social problems to, a special department—yes. But differentiate by age alone—*no*.

The hospitals could reply quite legitimately that there are times when they are asked to admit as acute medical emergencies patients who are not so.

This is the basis of the reluctance to admit patients over 65 to the acute wards—it is felt that a bed will be blocked by a patient for whom nothing can be done, and this may deprive a patient for whom something can be done of a bed. Could the answer be that the hospital authorities try trusting the general practitioner to give an honest assessment of the patient's need?

But the answer can never be the arbitrary refusal to admit an emergency into an acute medical ward on the grounds that the patient is over 65.

The public cannot be held blameless, for all too often they put pressure on the medical services to absolve them of the responsibility of looking after their own. The general practitioner must accept his share of responsibility for succumbing too easily to this pressure, but surely the solution, as put forward by the hospital, cannot be correct.—I am, etc.,

Hull.

D. F. C. DEACON.

Resuscitation of the Elderly

SIR,—The report on the B.B.C. television programme "Tomorrow's World" that the doctors at Neasden Hospital had instructions from their medical superintendent not to resuscitate patients over the age of 65 years makes it necessary to restate some of the basic tenets upon which modern care of the elderly is based.

The pessimistic, if not nihilistic, attitude towards therapy of the elderly in the past was based on the misconception that the elderly responded poorly to treatment and that even if they did respond they were in some way "chronic." Analysis of the terms "acute" and "chronic" and their more restricted usage would do much for the cause of modern practice of medicine in the elderly (and, more widely, the practice of geriatrics).

If one analyses the disease processes pre-

capitating direct admission of patients to general medical and geriatric assessment wards one finds that the majority of patients admitted to both types of ward are suffering from chronic diseases, but have been admitted for an acute episode occurring in the course of the disease. In the mediatic or general medical group of patients aged 15-60 or 65 years examples of common chronic diseases that necessitate admission because of an acute clinical episode are: diabetes mellitus (ketosis, infection), hypertension (left ventricular failure), atheroma of coronary arteries (cardiac infarction), chronic nephritis (renal failure), peptic ulcer (haematemesis). Similarly, the geriatric group of patients are also usually admitted for an acute episode occurring in the course of a chronic disease.

It is helpful to analyse further the tempo of disease at different ages to show that the indiscriminate use of the word "chronic" has given rise to the false concept that the elderly and their diseases are in every way slow or "chronic." Acute disease and acute episodes based on chronic disease arise equally abruptly in the elderly as in the middle-aged. The onset in the elderly, however, may be frequently less dramatic and more easily missed. The duration of the acute disease or acute episode in the elderly is usually comparable in length to that in the middle-aged. It is the recovery phase of the acute illness, however, that is often prolonged in the elderly compared with the middle-aged. The prolonged recovery phase of the elderly is often due to the disease being complicated by a physical or mental disability. It is important, therefore, to recognize that acute episodes in the elderly arise as abruptly and are as short-lived as at other ages. It is also important to be clear that the slow recovery phase does not mean that all phases are "chronic."

The difficulties of recognition of the acute episode combined with the slow recovery phase in the elderly have in the past helped to perpetuate the myth that age and chronicity go hand-in-hand. Many elderly people, however, suffer an acute episode from which they recover completely. At any age an acute episode such as ventricular arrest may occur (often precipitated by an anatomically small area of cardiac infarction) and if rapidly rectified may lead to continuance of life of an unaltered quality. There is no medical argument to support the exclusion of a group of patients, defined empirically on age alone, from standard methods of resuscitation.—I am, etc.,

St. Margaret's Hospital,
Nr. Swindon, Wilts.

BRIAN LODGE.

Neasden Memorandum

SIR,—I was delighted to read the letter from so many members of the staff of the Central Middlesex Hospital (30 September, p. 861) supporting "the undoubted integrity of Dr. McMath." Not only was it the B.M.A. who failed to point out the difficulties to the public, but so did the Minister of Health himself and the regional hospital board concerned.

It is true that there was some "small print" stuff commending Dr. McMath on his conscientious approach to this very difficult problem, but the overwhelming impression was that he was being condemned by the Minister and regional hospital board alike (30 September, p. 858).

It really has come to a sad pass when such a person as Dr. McMath can no longer rely on the support of his senior officers, who could so easily have smoothed the whole matter over with some simple explanations to the public instead of turning him into a scapegoat as your correspondents so rightly point out.—I am, etc.,

Hitchin, Herts.

O. H. E. BAYLES.

Remission in Acute Leukaemia

SIR,—We have read with interest your leading article on rubidomycin (3 June, p. 587). Much emphasis has been given recently to this new antitumour antibiotic isolated in France by Dubost *et al.*¹ and active mostly in acute leukaemia.

We should like to report our experience in acute childhood leukaemia using daunomycin, an antibiotic of the antracycline group, a substance identical with rubidomycin. Daunomycin was obtained independently by Di Marco *et al.*²⁻⁴ in the research laboratories of Farmitalia from cultures of *Streptomyces peucetius* sp. nova. The initial clinical trials were done at the National Cancer Institute in Milan⁵ in 1964 and at the Memorial and James Ewing Hospital⁶⁻⁷ from July 1964.

Our experience is summarized in the following Table:

Case No.	Disease	Courses	Disease Progressed	No Change	Remissions	
					Complete	Partial
1	Acute lymphoblastic leukaemia	2				x
2	" "	2		x	x	
3	" "	1				x
4	" "	2				x
5	" "	1	x			x
6	" "	1	x			x
7	" "	1		x	x	
8	" "	1			x	x
9	" "	1		x		
10	" "	3				x
11	" "	1		x	x	
12	" "	3			x	
13	" "	2				x
14	" "	2				x
15	" "	1			x	
16	Acute myeloblastic leukaemia	1		x		
17	" "	2				x
18	" "	1				x

A total of 18 children, 15 affected by acute lymphoblastic leukaemia and 3 by acute myeloblastic leukaemia, received the drug intravenously in a daily dose of 1 mg./kg. Each course of treatment was of five days, followed, if the response was not satisfactory, by a second and eventually a third course after a five-day rest period. Two children were at the onset of the disease, 16 were in relapse; six have been treated twice at intervals of several months for successive relapses. All the children in relapse had become resistant to the drugs previously used, such as 6-MP, vincristine, and methotrexate. Daunomycin was well tolerated but induced in several cases a bone-marrow aplasia, which needed to be treated with prednisone and testosterone. Alopecia occurred frequently. Laboratory studies, including liver-function

tests, blood urea nitrogen, serum uric acid, serum electrophoresis, radiographic studies, and E.C.G.s, did not show other toxic manifestations.

Out of a total of 24 patients treated the therapeutic responses were as follows: 2, disease progressed; 5, no change; 11, good partial remission; 6, complete haematologic and clinical remission.—We are, etc.,

L. MASSIMO.

A. FOSSATI.

E. FORTUNA.

Department of Paediatrics "G. Gaslini,"
University of Genoa,
Italy.

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Menace of Smoking

SIR,—Your leading article "Menace of Smoking" (23 September, p. 753) is indeed an indictment of the greatest hazard to health of our day, and one which is self-inflicted by indulgence in a noxious habit and one permitted by a succession of indulgent Governments and Ministers of Health.

You table some of the consequences: 30,000 deaths a year in the United Kingdom from cancer of the lung; a large measure of responsibility for the ravages of chronic bronchitis and emphysema; some responsibility for cancer of the mouth, larynx, oesophagus, and possibly pancreas and bladder; increasing evidence of inducing a liability to coronary artery disease and cerebrovascular disease. In other words, smoking bears a measure of responsibility for a majority of the present-day captains of the men of death and disability, and you rightly conclude that the smoking of cigarettes especially is surely the greatest menace to the public health of our time, causing death and disability on a scale reminiscent of the epidemic diseases of earlier centuries.

I have seen no mention of this in the national daily press. It should have been emblazoned across the front pages and immediate Government action demanded to put an end to it. Surely no greater indictment was ever made of the consequences of indulging in "hard" drugs, and yet very stringent laws govern their sale and possession, and even the hours during which alcohol may be consumed on public premises is restricted. Motor accidents account for some mere 7,000 deaths per annum, and yet the use of a motor car is governed quite rightly by an increasing number of restrictions.

You state that if the chances of a smoker contracting cancer "were the same as now, but the interval before death was only some months, it is scarcely conceivable that cigarettes would be marketed at all, or, if they were, that legislation would be long delayed to prohibit them altogether." The time before death is hardly a valid consideration

when death frequently strikes down a man during his working life, and not only from cancer but also from cor pulmonale secondary to chronic bronchitis and emphysema, and from coronary thrombosis. This takes no account of the 30 million working-days lost each year due to chronic bronchitis, much of which is due to smoking, and all of which is greatly aggravated by it. To talk of banning cigarette advertising and educational campaigns is a counsel of despair, as very little reduction of cigarette smoking would result.

I submit that it is the immediate duty of the Minister of Health to induce the Government to take effective steps without delay. The findings of the Royal College of Physicians have been known for some time, and the independent investigation of the tobacco industry has merely served to endorse them this year. I suspect that pressure from the department of Inland Revenue and vested interests, and watering-down of resolve by the many smokers in their midst, has diverted the administration from taking what it well knows to be the right course. In the event, much of the loss of revenue would be made up by the improvement in health and saving of life among the working population, and the economy would also benefit externally, as it would no longer be necessary to purchase tobacco, all of which comes from abroad.

The Minister has recently suggested that managers of places of entertainment should prohibit smoking in the public interest, but this amounted to nothing less than asking those who are public-spirited to hand over their profits to those who are not and who continue to permit smoking. His first step should be to ban smoking in all places of public assembly and on public transport, etc. Already this is done in many large stores in our cities. Neither their staff nor their customers have become nervous wrecks, nor have their sales suffered. This should be followed by the prohibition of smoking in public at all. Another measure which should be adopted is the annual raising by one year of the age below which it is illegal to purchase tobacco.

Such steps would provide only a moderate reduction in consumption, but would be of considerable assistance to a large proportion of smokers who desire to cease the practice, and would greatly increase their numbers. Most important of all, however, it would prepare the public for the only fully effective remedy—the complete ban on the sale of tobacco.—I am, etc.,

J. HAMILTON GIFFORD.
Waterloo Chest Clinic,
Liverpool 22.

Sodium Uptake in Peritoneal Dialysis

SIR,—Dr. M. V. Moriarty (23 September, p. 798) is quite correct in his observation that the removal of large volumes of fluid by hypertonic peritoneal dialysis is an efficient means of depleting the body of sodium. This is well shown in Fig. 4 of my paper (5 August, p. 345) and is indeed emphasized in the text.

However, the urea concentration of the fluid removed by hypertonic dialysis is higher than can be explained on a simple concentration gradient basis.¹ It has been suggested that this is attributable to "solvent drag"

by the large volume of fluid passing through the peritoneal membrane. The purpose of the table to which Dr. Moriarty refers is to indicate that sodium does not behave as urea under these circumstances. The net sodium movement is, as both my paper and Dr. Moriarty's letter suggest, dependent upon the serum sodium concentration and the volume of fluid removed.—I am, etc.,

Westminster Hospital,
London S.W.1.

J. D. SWALES.

REFERENCE

- ¹ Henderson, L. W., *J. clin. Invest.*, 1966, 45, 950.

Place of the Mentally Retarded

SIR,—The single authority responsible for all services for the mentally subnormal advocated by Dr. M. E. York-Moore (23 September, p. 798) would have much to commend it, but one serious, we believe decisive, disadvantage: it would perpetuate the separation of the hospital care of the subnormal from that of all other classes of patients. It is surely indisputable that isolated institutions cannot provide an acceptable standard of medical and nursing care, and cannot offer research on the scale the field of subnormality requires.

As Dr. York-Moore recognizes, there can be no rapid transfer of half the hospital population to local authority accommodation which does not exist. But, if the sensible recommendations of H.M. (65) 104¹ are to be implemented, it is essential to make a beginning by inclusion of approximately 80 subnormal beds per 100,000 population in district general hospitals, and by provision of small hostels which in time would replace the large isolated institutions. We readily concede that there is need for careful consideration of the balance of advantages of an education or a health administration for children under local authorities.—We are, etc.,

THOMAS MCKEOWN.

Medical School,
Edgbaston, Birmingham 15.

IAN LECK.

University College Hospital
Medical School,
London W.C.1.

REFERENCE

- ¹ *Improving the Effectiveness of the Hospital Service for the Mentally Subnormal*, H.M. (65) 104.

Streptomycin, I.N.H., and Thiacetazone

SIR,—A combination of isonicotinic acid hydrazide (I.N.H.), streptomycin, and thiacetazone is frequently employed in India for the treatment of bone and joint tuberculosis. Recently we came across three cases of serious adverse reactions to such therapy.

A 24-year-old female with advanced caries of the spine was treated with a combination of streptomycin (1 g. daily) and Unithiben (I.N.H. 75 mg. and thiacetazone 37.5 mg. per tablet, six tablets daily). The patient developed a generalized erythematous skin rash with marked itching after three weeks on this therapy. The skin eruption subsided after stopping all the drugs. However, a second attempt to administer Unithiben alone led to recurrence of itching and characteristic skin lesions. Routine laboratory investigations at this stage revealed nothing abnormal.

Severe vomiting developed in a 15-year-old female with caries of the spine 12 days after treatment with streptomycin and Unithiben (dosage schedule as above). On withdrawal of Unithiben alone vomiting stopped. In this case there was mild leucocytosis, 10,200/cu. mm., with 6% eosinophils.

A 55-year-old female with caries of the spine, under treatment with streptomycin and Unithiben (dosage schedule as above), developed a generalized macular erythematous skin rash with marked pruritus, jaundice, and mental disorientation. These symptoms appeared approximately five weeks after combined therapy. The skin rash progressed to an exfoliative dermatitis. The patient developed coma and deep jaundice and died a few days later.

In the first two cases the combination of I.N.H. and thiacetazone seems to be implicated. In the last case also the combination might have been responsible for the adverse reactions. Hypersensitivity reactions to I.N.H. are considered to be rare effects.¹ Hepatotoxicity and skin reactions have been reported after thiacetazone.

The concurrent use of I.N.H. and thiacetazone has been reported to be of great promise in the treatment of advanced pulmonary tuberculosis,² but the use of such drug combination may be hazardous in some cases.—We are, etc.,

S. N. DUTTA.

R. K. SANYAL.

S. B. KOHLI.

Department of Pharmacology,
Associated Irwin and G.B.Pant
Hospitals,
New Delhi, India.

REFERENCES

- ¹ Honycutt, W. M., and Huldin, D. H., *Arch. Derm.*, 1963, 88, 190.
² Hinshaw, H. C., and McDermott, W., *Amer. Rev. Tuberc.*, 1950, 61, 145.
³ *Lancet*, 1963, 2, 817.

Dangers of Humidification

SIR,—Dr. W. M. Edgar (26 August, p. 557) rightly draws attention to the risk of contamination of water in Woulfe bottles used for humidification of oxygen. Every variety of container for water used for this purpose is liable to contamination. The risk is not confined to the Woulfe bottle. Plastic containers obscure the turbidity which would otherwise draw attention to grossly contaminated water.

I would therefore, expand Dr. Edgar's important advice regarding the frequent washing and sterilization of Woulfe bottles to include all types of containers used for that purpose, as well as the tubing leading from the container to the mask, catheter, etc.—I am, etc.,

BERNARD J. FREEDMAN.

Dulwich Hospital,
London S.E.22.

Diabetes Mellitus Complicating Alkaptonuria

SIR,—We are interested in the letter on diabetes mellitus complicating alkaptonuria, by T. W. Wikramanayake (29 April, p. 312). We have come across a case, a male 45 years old, complaining of backache and stiffness of both knee joints and the small joints of both upper limbs of about one year's duration. Biochemical investiga-

tions revealed that he is an alkaptonuric with moderate diabetes mellitus.

The presence in his urine of homogentisic acid is confirmed by extraction¹ and chromatographic identification,² and of glucose by osazone and Selivanoff's tests. Curiously enough, Clinistix failed to detect glucose in this urine. Further investigation has brought to light that this failure of Clinistix was due to the inhibition of peroxidase reaction by homogentisic acid.³

This case seems to be the second to be reported from India since that of Bose *et al.*⁴ where diabetes mellitus and alkaptonuria are coexistent.—We are, etc.,

B. NAGANNA.
G. ETHIRAJULU.

Departments of Orthopaedics
and Biochemistry,
Guntur Medical College,
Guntur, India.

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- ³ Naganna, B., Rajamma, M., and Vasudeva Rao, K., *Clin. chim. Acta*, 1967, 17, 219.
- ⁴ Bose, J. P., and Ghosh, S., *Ind. med. Gaz.*, 1929, 64, 61.

Psychological Factors and Ulcerative Colitis

SIR,—I have just seen your leading article (1 July, p. 1), the associated paper by Feldman *et al.* (p. 14), and the resulting correspondence. The whole makes clear that in receiving new it is important not to forget old testimony. Which way does the accumulated evidence point?

You refer to the fine pioneer paper of C. D. Murray¹ on the emotional associations of ulcerative colitis, to the delineations of characters of subsequent writers, and to the summary of G. L. Engels.^{2,3} More recently progress in understanding and treating ulcerative colitis has been largely somatic. But the somatic information includes the importance of steroid chemistry and specific sensitivity studies. These in themselves leave the disease wide open psychologically, at the same time bringing it further into line with asthma as a sensitivity disease. A great deal of the observed psychological abnormality of ulcerative colitis can be regarded as emotional hypersensitivity; and the full understanding of the relationship between such states and body chemistry must still be far ahead.

In the meantime I would prefer Halliday's⁴ definition to yours. A psychosomatic disease is, strictly, not one in which the organic lesions are the consequence of emotional disturbances, but one in which the disease as a whole cannot be fully understood until psychological factors are considered. Also, in the hands of some, psychotherapy can (still) improve medical treatment.⁵ Open and inquiring minds must continue to be exercised in this assessment.—I am, etc.,

Shelton Hospital,
Shrewsbury.

RANYARD WEST.

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- ² Engels, G. L., *Psychosomat. Med.*, 1954, 16, 496.
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- ⁴ Halliday, J. L., *Lancet*, 1946, 2, 185.
- ⁵ Zetzel, L., *New Engl. J. Med.*, 1964, 271, 891.

SIR,—A recent leading article (1 July, p. 1) reviews the controversy concerning the role of psychological factors in ulcerative colitis and warmly endorses a paper by Dr. F. Feldman and others (1 July, p. 14). Careful reading of that paper, however, reveals two disquieting facts: (1) The authors do not draw the conclusions ascribed to them by the leading article. (2) The paper is based on methods to which the reader has no access.

The leading article describes this paper as "one of the few psychiatric studies to discount the importance of psychological factors in the aetiology of ulcerative colitis." The authors, on the other hand, merely "raise the question whether the disease should be regarded as 'psychosomatic.'" This is not only a more cautious conclusion, it is a different conclusion, for they define "true psychosomatic diseases" as those "which must have a psychogenic component as part of the cause, or they cannot exist." By way of comparison they cite "illnesses which appear physical in origin but may be exacerbated, triggered, or hastened by psychogenic factors." These "would be regarded as not 'truly psychogenic' illnesses but ones influenced by psychophysiological factors." This emphasized contrast between "truly psychogenic" and "psychophysiological factors" indicates that they regard psychogenesis, in the strict sense of the word, as a necessary condition before a disease may be regarded as "psychosomatic." This is a spurious issue, for few any longer espouse a pure psychogenic concept of ulcerative colitis. Most hold that ulcerative colitis is a physical process commonly triggered or exacerbated by psychological factors through as yet unidentified physiological processes. Some suggest in addition a degree of specificity about the kinds of background psychological issues most likely to be involved in this chain of events, but this a far cry from invoking pure psychogenesis.¹⁻³

Actually the paper itself is so inexact and inconsistent in terminology as to leave the authors' intent open to many possible interpretations, but this has been true of many papers in the field of psychosomatic medicine. Terms such as "psychosomatic" or "psychogenic" are rarely defined, and many are guilty of using the term "psychosomatic diseases" to designate illnesses in which psychological factors are alleged to play a dominant role. Properly speaking, there can be no such entity as a "psychosomatic disease"; rather there are psychosomatic factors in disease, referring to the interactions, through nervous system activity, between psychological and physiological processes and their resulting influences on somatic systems. The same objection may be raised to the use of such expressions as "genetic disease" or "biochemical disease." For example, the demonstration of a genetic factor underlying deficiency of glucose-6-phosphate dehydrogenase does not justify designating as a "genetic disease" the haemolytic anaemia that sometimes ensues upon interaction with certain drugs. One might equally well call sunburn a "genetic disease" in the light of the role of the genetic factors influencing pigment formation. Genetic factors and psychosomatic factors are probably significantly involved in the pathogenesis of many diseases, and with appreciation of the multifactorial aetiology of disease it is time to put an end to such simplistic either/or concepts as are promulgated in both the paper and the leading article.⁴

The second criticism is a grave one. On the surface the authors appear to have evolved a highly original and sophisticated methodology, but unfortunately they provide no details. Briefly, the primary data consist of two or more

interviews averaging a total of 10–12 hours for each patient, but no mention is made how such data were recorded or handled. One hundred and eight patients, 34 with ulcerative colitis and 74 controls, were studied over a period of 22 months. In that period 65 psychological variables, bearing on seven criteria selected as necessary to prove psychosomatic disease, were judged on a five-point scale for each of the 108 patients. Now this is an exceedingly complex undertaking, even when utilizing tests with established reliability. Yet we are not told what the 65 variables are, how they were selected, how their relative values *vis-à-vis* the seven criteria were established, or what the judging procedure was; indeed, none of the facts required to evaluate the results. The only reference is to an unpublished 200-page handbook. Besides not knowing what was being scored, one may also question whether a task of data analysis involving a total of from 7,000 to 70,000 judgements of personality variables (estimated on 65 judgements for each of 108 patients or for each of 1,200 patient-interview hours) could be accomplished in such a short time without sacrificing the standards required for this type of psychological measurement.

When subjected to the cold glare of critical scrutiny one is forced to say that the leading article drew an unwarranted conclusion from a study which posed the wrong question, applied an unknown method, and obtained a dubious answer.—I am, etc.,

GEORGE L. ENGEL.

University of Rochester
Medical Center,
Rochester, New York, U.S.A.

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- ² Daniels, G. E., O'Connor, J. F., Karush, A., Moses, L., Flood, C. A., and Lepore, M., *Psychosom. Med.*, 1962, 24, 85.
- ³ Engel, G. L., *Gastroenterology*, 1961, 40, 313.
- ⁴ — *J. Psychosom. Res.*, 1967, 11, 3.

Paraproteins and Bence Jones Protein

SIR,—I was intrigued by Dr. J. R. Hobbs's outstanding contribution to the study of paraproteins (16 September, p. 699). However, there was one point which I did not understand, and this seems to me to explain a discrepancy. The statement has been made (Fig. 2) that "patients producing Bence Jones protein only . . . present with lower production rates than the others, suggesting differentiation of their tumours," whereas in the discussion it is stated that "an increase of light chain excretion reflects an inefficient process and probably implies that the synthesizing cells have lost their differentiation." As I understand it,¹ the quantity of Bence Jones protein in the urine cannot be taken as an indication of the rate of production, since catabolism of Bence Jones protein occurs in the kidney, and especially is this so when there is normal renal function.—I am, etc.,

Royal Victoria Infirmary,
Newcastle upon Tyne.

E. N. WARDLE.

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Diabetic Lipaemia

SIR,—I was interested in the letter on diabetic lipaemia (26 August, p. 557). Perhaps this condition is not as rare as was

previously thought in young diabetics. I wish to record a recent case.

A 12-year-old girl, a known diabetic for six months, had been controlled on 42 units of lente insulin daily. On the day of admission she had received her insulin and was complaining of faintness and vomiting.

On examination she was ketotic and dehydrated. Urine sugar was 2% and acetone + + +. Her maximum blood sugar was 253 mg./100 ml., serum sodium 110 mEq/l., the serum potassium 4.6 mEq/l., and serum bicarbonate 3.5 mEq/l. On venepuncture the blood was pink and greasy. The serum was milky in appearance.

She was treated with soluble insulin and intravenous infusion. Her serum cholesterol was 830 mg./100 ml. on the first day, and on the third, seventh, and fourteenth days was 225 mg./100 ml., 272 mg./100 ml., and 172 mg./100 ml., respectively.

This case of diabetic lipaemia occurred in a girl well until 24 hours prior to admission, and cleared after two days. She has remained well since, on only 60 units of lente insulin daily.

I wish to thank Dr. I. Kessel for permission to report this case under his care.

—I am, etc.,

JUDITH TROWELL.
West Herts Hospital,
Hemel Hempstead, Herts.

Sales Promotion

SIR,—A good deal of criticism is being levelled at the pharmaceutical industry on account of the volume of its publicity, and I must confess that I am sometimes irritated by the amount of advertising in its various forms that passes through my hands. However, I am beginning to glimpse a tendency on the part of some firms to provide the general practitioner with material of practical value, and to help stimulate informed use of their product. I regard examples of programmed learning and diagnostic handbooks of real value, and more recently I was offered, and readily accepted, some disposable proctoscopes, for which I shall certainly find real use.

If this is a trend for the future I would welcome it as a method of improving the understanding between doctor and manufacturer, and wonder if my colleagues have any views upon it.—I am, etc.,

BASIL MARSHALL.
Blechingley,
Surrey.

Drug Names

SIR,—While many will agree that the Sainsbury Committee is wise not to recommend the nationalization of the pharmaceutical industry, it seems unfortunate that they are contemplating the abolition of brand names for future drugs.

Surely anything that assists identification in the prescription of drugs outweighs any consideration of commercialization in the industry and helps to avoid misinterpretation by pharmacists of the written prescription.

With many years' experience in the promotion of drugs in this industry, such a proposal appears to me to point to a lack of consideration of all the factors concerned. The British pharmaceutical industry is in fact way ahead of any other country in the world, and this, in my opinion could do nothing but harm to it.—I am, etc.,

MAURICE KEATING.
Morden,
Surrey.

Reprints: Who Should Pay?

SIR,—The problem of dealing with requests for reprints, which has been raised in your correspondence columns (16 September, p. 740), is not a financial one for most of us; the difficulty is to find time to answer requests when already pressed to cope with routine work and one's research activities without secretarial help. The vast majority of inquiries come from the U.S.A., and often seem to be needed merely to add to a library file. The nominal sum now charged for a photostat copy of an article should make routine collection of reprints unnecessary; if everyone ignored requests not accompanied by a personal letter the practice would soon die out.—I am, etc.,

Hornchurch,
Essex.

S. E. BROWNE.

Doctors in the Armed Forces

SIR,—The Association undertook to inform medical officers in the armed Forces of progress in negotiations on their pay structure. There has been little or no news for some time; can we infer that an impasse has been reached and that the black-listing by the Association of the armed Forces medical services has proved ineffectual in the face of the defence cuts?

Service medical officers are in a very difficult position; there must be many like myself who, enjoying the life and believing that it enables them to practise good medicine, nevertheless feel considerable anxiety over their future careers and financial prospects and must soon decide between remaining in the Services and seeking the greater financial rewards and security of civilian life. The Prime Minister has made no secret of his need to foster recruitment to the National Health Service at the expense of the armed Forces (*Supplement*, 18 February, p. 50); but how many of us would willingly transfer from frying-pan to fire? Besides, for the ex-regular officer, re-entry to the N.H.S. would involve in many cases loss of pension rights unless considerable superannuation back payments were made.

We could be materially assisted in these decisions by information from the Association of our future prospects. Can we, for example, expect any consideration in the biennial pay review due next year? Or will we again, by dilatoriness, have no link either with the executive or with doctors in the N.H.S.? If negotiations are to reopen have we any proposals to make? I know of no efforts by the Association to canvass the views of serving officers.—I am, etc.,

Co. Derry.

R. P. DOHERTY.

B.M.A. as a Negotiating Body

SIR,—The time is surely much closer when the British Medical Association must establish fully democratic representative machinery for junior doctors. It was thus very encouraging to read the clearly defined aim of the Junior Hospital Doctors' Association in Dr. J. H. Briggs's letter (16 September, p. 741).

So long as junior doctors, especially those in hospital practice, feel that they have no proper voice within the B.M.A. they will refrain from joining its ranks.

It is to be hoped that a satisfactory conclusion will soon be reached in the talks currently being held between the B.M.A. and the J.H.D.A. Then and only then will it be worth while for the B.M.A. to hold a vigorous membership campaign among colleagues in the field of junior hospital practice.—I am, etc.,

London E.15.

CHRISTOPHER BOLT.

Christmas Gifts Appeal

SIR,—I should be grateful if you would once more allow me to make known in your columns the Christmas gifts appeal that is made annually by the Royal Medical Benevolent Fund. This special gifts fund is distributed to the hundreds of beneficiaries at Christmastide, when the little extra makes such a welcome increase to their happiness. We feel sure that the profession will make a generous response to this appeal.

Contributions marked "Christmas Gifts" should be sent to the Royal Medical Benevolent Fund, 24 King's Road, Wimbledon, London S.W.19.—I am, etc.,

ZACHARY COPE,
President,
Royal Medical Benevolent Fund.
London S.W.19.

Points from Letters

Mercury Perchloride in Surgery of Bowel Cancer

Mr. C. L. HEANLEY (Worthing, Sussex) writes: The use of mercury perchloride to prevent wound contamination by malignant cells has been shown to reduce implants statistically. How does it work? It is interesting when one has cut excess skin, when skin grafting, to soak pieces of excess skin in varied solutions, and reapply to the donor surface with a control piece. After the graft has been in transient contact with spirit, cetrimide, or gum mastiche it is killed, whereas soaking for five minutes in 1:4,000 or 1:1,000 mercury perchloride does not kill the graft. One can also graft over Hibitane (chlorhexidine) powder.

It would appear that mercury perchloride in these strengths will not kill normal epithelial cells; however, this is no proof it will not kill "cancer" cells.

Consultants' Views of General Practitioners

Dr. D. M. MACMANUS (London S.W.1) writes: I have practised as a general practitioner for 53 years, and in that long time I have learned tolerance and to respect the opinions of other doctors, even if I didn't agree with them. The infinite variety of man is shown among doctors as among other professions. I have employed very many consultants and sent very many patients to consultants at their hospitals, and by an enormous majority they have proved exceedingly helpful, and always keep me up to date with the patient's condition. I do not always agree with the consultant's opinion—I like to stand on my own feet—but he is usually, not always, right. I have met some consultants for whom I have had no respect.

Again, the majority of general practitioners are very hard-working, conscientious individuals, and their main consideration is for their patient. They are immensely dependent on the consultant, and he does not often realize his indebtedness to them. This bickering is really stupid. All we doctors wish for is the welfare of our patients. To quarrel among ourselves about who does what is nonsense. It takes all sorts to make a world, and please let us be tolerant and understanding of each other.

Obituary Notices

Sir JAMES LEARMONTH, K.C.V.O., C.B.E., LL.D., M.D., CH.M., F.R.C.S.
F.R.C.S.ED., F.R.A.C.S., F.A.C.S., F.R.F.P.S.GLASG.

Sir James Learmonth, formerly professor of surgery and regius professor of clinical surgery at the University of Edinburgh, died on 27 September. He was 72.

James Rognvald Learmonth was born at Gatehouse, Kirkcudbright, on 23 March 1895, and received his early education at Girthon School and Kilmarnock Academy.



(Walter Stoneman)

His studies were interrupted by the first world war, during which he served with the King's Own Scottish Borderers. On demobilization with the rank of captain he entered Glasgow University, graduating M.B., B.Ch. with honours in 1921, and was awarded the Brunton Memorial Prize

for the most distinguished graduate in medicine for the year. After early house appointments at the Western Infirmary, Glasgow, he worked for a time as assistant to Professor Archibald Young, first at Anderson College of Medicine, Glasgow, and later at Glasgow University. In 1924 he was awarded a Rockefeller medical fellowship, and spent a year at the Mayo Clinic in the United States, returning to Glasgow, where he took the Ch.M. with high commendation in 1927, and in the following year was elected F.R.C.S.ED. He went back to the Mayo Clinic in 1928 as a neurological surgeon on the staff of the clinic and associate professor of neurological surgery in the University of Minnesota. He returned to Scotland in 1932 as regius professor of surgery at Aberdeen. In 1939 he was appointed professor of surgery at the University of Edinburgh, and in 1946 regius professor of clinical surgery. In 1951 he was appointed a member of the Medical Research Council, and in 1954 Sir Arthur Sims Commonwealth Travelling Professor of the Royal College of Surgeons of England.

Many honours and distinctions came his way. He was appointed C.B.E. in 1945 and was made a Chevalier of the Legion of Honour in 1950. In recognition of his distinguished contributions to surgical science he was awarded the Lister medal in 1951. Having been called in November 1948 to attend King George VI in his illness, in 1949 he was appointed a surgeon to the King in Scotland, and the K.C.V.O. was conferred on him in the same year. He was a surgeon to the Queen in Scotland from 1952 to 1960, and was extra surgeon since this time up to his death. His outstanding work was recognized by the award of honorary degrees from the universities of Oslo, Paris, Sydney, and Strasbourg, in addition to those from Glasgow, Edinburgh, and St. Andrews. He was elected an honorary fellow of the Royal

College of Surgeons of England in 1949, and of the American College of Surgeons in 1950. In 1954 he was elected an honorary fellow of both the Royal Australasian College of Surgeons and of the Royal Faculty of Physicians and Surgeons of Glasgow. A member of the British Medical Association, he was vice-president of the Section of Surgery at the Annual Meeting in 1936, and president of the Section in 1939.

On his retirement from Edinburgh University at the end of September 1956 the title of Professor Emeritus was conferred on him.

He married in 1925 Charlotte Newell Bundy, of St. Johnsbury, Vermont, U.S.A., who survives him with a son and a daughter.

D. M. D. writes: To work with James Learmonth was to see the impact of a fine brain and a powerful character on the many problems associated with running a busy university surgical unit. He was an outstanding scholar with an abiding love of books, a quality no doubt derived from his father, who was a schoolmaster in Galloway. He was also a much-loved doctor whose patients spoke of him with warmth and affection. An imaginative administrator, he established during the tenure of his chair in Edinburgh university departments of urology, plastic, thoracic, and paediatric surgery, each of which is now internationally famous. A shy man with an austere manner, he was warm-hearted and infinitely thoughtful to those near to him. Inspiring loyalty in others, his loyalty to his friends was legendary, and many surgeons everywhere have cause to be grateful to him for his help and advice.

He received the highest honours from all over the world, and though he valued them he valued far more the free interchange of ideas which association with colleagues and friends gave him. Nothing delighted him more than to talk over research projects with his staff. His criticisms were outspoken but fair and he recognized that failure was irrelevant; to try was the important thing. A man of the highest integrity, he never shirked an unpopular decision if it was the right one. He ranks with William Mayo, Harvey Cushing, and Geoffrey Jefferson as one of the surgical giants of our time.

A. L. writes: Sir James Learmonth retired from the chair of surgery at Edinburgh in 1956, when he said he had occupied it for as long as any man ought to hold so important a professorial office. Few developments in surgical teaching pleased him more than the formal incorporation in the department of surgery 10 years previously of subdepartments in specialties recently and incompletely separated from general surgery. The staff of these departments had a peculiarly close clinical and academic relation with him. He was severe in his criticism and generous in his appreciation of their work, and no comment ever lost him a fraction of the respect and affection in which he was held. He gave, and received, complete loyalty. As a forum

for surgical discussion he instituted Saturday morning departmental meetings. These began on the first stroke of 9 o'clock. One or other unit acted as host and presented aspects of its work—clinical, experimental, or literary. Many remember from these occasions something of their colleagues' contribution, but far more of Sir James's devotion to the interests of the University, his gentleness and kindness to patients, his deep concern for the welfare of his juniors, his ability to bring common sense to bear on a clinical or administrative problem, and his undeviating honesty.

J. McM. writes: James Learmonth's distinguished career began where he was born, in the tranquil and lovely valley of the Fleet in Kirkcudbrightshire. He was leaving the little local parish school of Girthon about the time I entered. We were both much influenced by his father, who was our strict and comprehensive schoolmaster, passing rich on perhaps £140 a year; his erudition and scholarship seemed all-embracing, and in later years we often talked of his influence in teaching us how to enjoy deep study. Running some years behind, I watched this handsome, brilliant student sweep forward in his medical career. He published papers, while still a student, on blood-group inheritance and on wind-speed measurements in relation to gas warfare in the first world war. Though chastened somewhat by his combatant war experience, he graduated with all honours and moved rapidly into his successful career in surgery. At one time his future seemed to be in America, where he had found a place on the staff of the renowned Mayo Clinic, but finally loyalty to this country prevailed and he returned to Aberdeen as regius professor in surgery, moving later to the larger responsibility of Edinburgh in succession to Sir David Wilkie. His continuing researches on the detailed anatomy of the sympathetic system, and on the innervation of the bladder, made him the ideal academic surgeon of his time. His determination to hold the reins of academic leadership imposed the strains of wide-ranging responsibility, and made exacting demands not only on him but also on his staff and colleagues. His aim was always towards an ideal, and any failures to achieve his objective told heavily upon him. Like his father, he could be an embarrassingly strict disciplinarian, but as a teacher he was superb. When he was off the beat and more relaxed discussion on university responsibility could be fruitful and challenging, and a last visit to him a day or two before his death found him deep in contemplation and lucid exposition of the problems of academic development that lay before us. His influence and example will be long-lasting.

A Glasgow colleague writes: Some years after he had retired James Learmonth was elected an Assessor of the General Council on the Court of the University of Glasgow. Always an honoured and welcome visitor to his Alma Mater, his appointment gave universal pleasure and he himself derived a very

deep and lasting satisfaction in the duties of this office. Those whose privilege it was to come most in touch with him in his new work soon realized that all the fine qualities of earlier days were not only undimmed but indeed enhanced by the measure of detachment he imposed on himself in his judgements and advice. Such restraint was a part of the way of life he set for himself and which found its highest expression in the selfless, disciplined behaviour of his last days.

**LEONARD COLEBROOK, D.Sc., M.B.
B.S., F.R.C.S., F.R.C.O.G., F.R.S.**

Dr. L. Colebrook, formerly director of the Medical Research Council's Burns Unit at the Birmingham Accident Hospital and pioneer of studies of wound infection, of the sulphonamides, and of the modern treatment of burns, died on 29 September. He was 84.

Leonard Colebrook was born in Guildford on 2 March 1883 and was educated at Guild-

ford Grammar School; the High School, Eastbourne; Christ's College, Blackheath; and St. Mary's Hospital, London, graduating M.B., B.S. in 1906. After graduating he continued to work as one of the brilliant team of bacteriologists which included Sir Alm-



roth Wright and Sir Alexander Fleming. He was later to publish a biography of Wright, whom he greatly admired, in 1954. Hearing Colebrook speak of him one would not have suspected by how much the disciple had outstripped his great teacher. During the first world war Colebrook went to France as a member of a research team studying wound infection. They looked for a treatment which would attack the infecting organism without damage to the body's own defences. After a further period of work at St. Mary's Hospital for the Medical Research Council, which he joined in 1920, Colebrook seized upon the possibility that the sulphonamides might fulfil this role, and he was the first to establish their life-saving value in puerperal sepsis. This work was done in collaboration with Dr. M. Kenny at Queen Charlotte's Hospital, where Colebrook was honorary director of research from 1930 to 1939.

At the outbreak of the second world war he was commissioned as colonel, and appointed bacteriological consultant to the Army in France. Serious problems were then being presented by burns, and, seeing this as a further field where wound infection was of the utmost importance, in 1942 Colebrook joined a Medical Research Council team in Glasgow which produced the now classical M.R.C. special report *Studies in Burns and Scalds*. The Accident Hospital in Birmingham was starting at this time, and in 1944 Colebrook accepted an invitation to organize and direct its new burns unit. Already famous for his work on wounds and on puerperal sepsis, he now founded a new

worldwide reputation in the care of burns. He introduced aseptic dressing techniques, full use of modern drugs, and exploitation of the developing techniques of early skin grafting.

Honours came to him, and in 1945 he was made a Fellow of the Royal Society. He was elected to the honorary fellowship of the Royal College of Obstetricians and Gynaecologists in 1944, to that of the Royal College of Surgeons of England in 1950, and in the same year an honorary D.Sc. was conferred on him by Birmingham University. At the 14th British Congress of Obstetrics and Gynaecology, held at Oxford in 1955, Colebrook was presented with the Blair Bell medal for his work on puerperal sepsis, begun at Queen Charlotte's Hospital in 1936. In 1962 the council of the Royal Society of Medicine awarded him the Jenner Medal.

"Coli's" great humanity and unwillingness to remain passive in face of unnecessary suffering fired a continued interest in the prevention of burning accidents. By publications, lectures, and personal approaches he drew attention to the need for action. His stimulus was behind the later legislation for protection, particularly of children, by guarding of fires and the use of safer fabrics. It was a great joy to him in his later years to see that these efforts were beginning to show results.

His colleagues and associates greatly appreciated his penetrating but kindly understanding of their problems, and to a wonderful extent these abilities were retained to the end. In the trials of advancing years he was supported with great understanding by his wife, Vera, to whom, as well as to her beloved husband, tribute is due.—J. P. B.

A. B. PORTEOUS, M.D., D.P.H.

Dr. A. B. Porteous, formerly consulting bacteriologist at St. Mary's Hospital, Paddington, London, died on 21 September after a long illness. He was 80.

Arthur Borland Porteous was born on 22 October 1886, and received his medical education at St. Mary's Hospital, London, graduating M.B., B.S. in 1910. He held

early appointments at St. Mary's Hospital, and was influenced by the strong tradition in pathology there at the time. At the outbreak of the first world war he joined the R.A.M.C. as a general medical officer, later being graded as a bacteriologist, and worked as a member of the team at Boulogne on war wounds and gangrene among the troops. After demobilization with the rank of captain, when Sir Almoth Wright reassembled his group at St. Mary's after the war, Porteous became a diagnostic bacteriologist, and interested himself in public health. He took the D.P.H. in 1920, and proceeded M.D. the following year. He was



[Bassano & Vandyk]

soon one of the small number of clinical pathologists in practice between the wars. He made no academic claims, and published little, but he provided a service to his clinical colleagues, within the limitations of the techniques of the period, that was well above the average. His confidence, his physical stamina, and his technical competence, particularly with needle and syringe, provided the sort of help needed in private house or nursing home.

Porteous had a remarkable flair for briefing himself on problems as they occurred. He was able to tackle not only bacteriology but haematology, transfusion work, and the necessary minimum of chemistry. In a generation when all pathologists appeared to have nicknames, his versatility and ubiquity earned him the modification of his own name to "Proteus." With the opening of chest clinics in the London area he became tuberculosis officer for Paddington, and ran a clinic first in the basement of the Wright-Fleming Institute and later near Westbourne Grove in one specially built there. He was always popular with his patients, and retained many of them as friends. If his equals occasionally found him pugnacious, his juniors, the technicians, and the students found him kind, and he was one of the most useful persons to turn to when faced with a difficult venepuncture or similar problem. He took considerable interest in the student life, particularly in the Yacht Club, and remained a keen sailor on the Thames until recently.

During the second world war his position as bacteriologist to the Boroughs of Paddington and Kensington made him the obvious person to take charge of public health bacteriology for the St. Mary's sector. This he did in company with Dr. M. Y. Young, first at King Edward Memorial Hospital, Ealing, and later back at St. Mary's. After the war he returned to private practice, and continued in it until his retirement due to increasing ill-health only about three years ago.

He is survived by his second wife and by his son, Dr. A. C. Porteous.—W. H. H.

W. WEINER, M.D., F.C.PATH.

Dr. W. Weiner, who directed the Birmingham Regional Blood Transfusion Service until the end of October of last year, died on 31 August after a long illness. He was 68.

Walter Weiner was born in Austria on 14 June 1899. He studied medicine at Prague, graduating M.D. in 1924. He was then appointed a clinical assistant in the university clinic, and he also practised as a physician. During this time he started to develop his interest in haematology, particularly in morphological haematology. Just before the second world war he came to England, where after a period in practice and as a medical officer in a sanatorium he joined the R.A.M.C., with whom he saw service in Africa. After demobilization in 1946 he was appointed deputy director of the Birmingham Regional Blood Transfusion Service, and when the physician in charge of the Service retired Dr. Weiner took over those duties.

Under Dr. Weiner's guidance the Service developed rapidly, although it operated in unsuitable accommodation. It was moved from one very old building to another that

was slightly less inconvenient, but it became apparent that a much more specialized building was required if the Service were to function efficiently. Much of Dr. Weiner's time in his last years as director was spent in designing and supervising the building of the new Blood Transfusion Service building, and the Regional Hospital Board encouraged him to stay in charge until it was running smoothly in its new headquarters. Soon after the new premises were occupied it was obvious that the thought he had put into its design had produced a very practical building.

Apart from the routine provision of blood products, which were always being augmented when the need became apparent for some new application of blood transfusion services, Dr. Weiner built up a very well organized antenatal serological screening service, and from this developed his interest in the protection of the susceptible women with antirhesus antisera. In spite of his preoccupation with the running of his Service he was a very active bench worker, and became particularly interested in the problem of acquired haemolytic anaemia. He will be best remembered for his classification of autoimmune anaemias, and for the technique which he evolved to elute antibodies from sensitized red cells. He became a Fellow of the College of Pathologists in 1964.

Dr. Weiner was a welcome visitor in many hospitals in all parts of the region, where he would go to see patients and specimens if he were asked. He was a man of great integrity who did not accept dogma for the sake of conforming. All those who knew him had hoped that he would be able to continue his research work after retiring. Unfortunately his retirement was marred by the illness which caused his death, regrettably before he had completed writing a book which was to have contained the data he had accumulated on the autoimmune anaemias.

He leaves a widow and a son.—K. B. R.

G. LISSANT COX, C.B.E., M.A., M.D.

Dr. G. Lissant Cox, formerly chief tuberculosis officer to Lancashire County Council, died at his home in Church Stretton, Shropshire, on 27 September. He was 88.

George Lissant Cox, son of George H. Cox, J.P., was born in Birkenhead on 14 September 1879, and was educated at Abbotsholme School, Derbyshire; Christ's College, Cambridge; and Liverpool University, qualifying with the Conjoint diploma in 1906, and graduating M.B., B.Ch. the following year. After early appointments at the Royal Infirmary, Liverpool, he became honorary assistant physician at the Liverpool Consumption



(Lenare)

Hospital, and assistant lecturer in pathology and bacteriology at Liverpool University. He proceeded M.D. in 1910, and some two years later he became central tuberculosis officer to Lancashire County Council.

Lissant Cox was a member of the standing advisory committee on tuberculosis of the Minister of Health, chairman of the Joint Tuberculosis Council of England and Wales, an active member of the National Association for the Prevention of Tuberculosis (now the Chest and Heart Association), and a member of the editorial board of *Tubercle*. He was chairman of the Preston Division of the British Medical Association in 1927-8, and vice-president of the section of tuberculosis at the Annual Meeting in 1929.

His valuable work in the tuberculosis service was recognized in 1944, when he was appointed C.B.E., two years before his retirement in 1946. In 1959, at a dinner held on his 80th birthday, his friends and colleagues of the Tuberculosis Association presented him with a book and the Varrier-Jones memorial medal for his outstanding work in the field of tuberculosis.

In 1919 he married Sarah Marguerite Howarth, and they had a son and two daughters.

A. D. writes: I had known Lissant Cox for over 60 years. He was educated at Abbotsholme School, of which in later life he became a governor; at Christ's College, Cambridge; and, for clinical work, at Liverpool, where his father was well known in commercial and political circles. After resident appointments at the Liverpool Royal Infirmary he was elected to a fellowship in pathology, where he worked with Professor Sir Rupert Boyce and Professor Ernest Glynn. At this time he was assistant pathologist to the Royal Infirmary, which implicated him in the diagnosis, in 1910, of one of the last cases of human plague to occur in Britain.

He was attracted early to the study of chest diseases, and was appointed to the honorary staff of the Consumption Hospital, Liverpool. All seemed set fair for a successful career as a consulting physician in Merseyside. But the Health Insurance Act with its provision for the treatment of the tuberculous insured (extended by later legislation to cover the entire population) was about to come into operation, and changed the direction of his career. Among the profession there was general hostility to this Act, but Cox and his father were strong supporters of Lloyd George's policies, and that no doubt was the reason why he applied for and obtained the post of central tuberculosis officer for the Lancashire County Council. His friends told him that it was professional suicide, but it led eventually to national, and even international, acclaim.

Lancashire's tuberculosis scheme became the model which other large local authorities tried to emulate, but in which they never quite succeeded. He had a better clinical background than most of the other early tuberculosis officers, and a strong and wealthy county council behind him. He believed in decentralization, and gathered around him an extremely able team, who later were snapped up by other local authorities, and they spread the "gospel according to Cox." He co-operated easily with the county boroughs of Lancashire, overcame the jealousies which so often cause disharmony, and arranged many joint appointments and joint use of premises. He was responsible for planning the sanatoria provided for the county.

He was in great demand on the national level, and was an active member of the Council of the National Association for the Prevention of Tuberculosis, which is now the Chest and Heart Association; he was also a member of the Minister of Health's advisory committee on tuberculosis, and chairman of the Joint Tuberculosis Council for England and Wales. An interest which he retained long after his retirement was membership of the editorial board of *Tubercle*. The Ministry of Health always sent foreign visitors seeking information about antituberculosis work to see Cox, and to study the Lancashire scheme. He received the C.B.E. in 1944, and the Varrier-Jones gold medal in 1959.

He was an enthusiastic angler, and went to fish in Loch Maree every year. In 1922 he was involved in a virulent outbreak of botulism at the hotel where he usually stayed, but on this occasion he had not booked early enough and was in a neighbouring one, and was called in to help with the dying guests.

His retirement over 20 years ago was from medical work to fruit farming. His farm was at Church Stretton, Shropshire, where he specialized in apples. As a grower of Cox's Orange Pippins his name was an asset, and it intrigued his friends to see vans being driven along the Shropshire lanes painted on each side, "Lissant Cox, Fruit Grower." But the fruits of his professional work will remain for many a year. Tuberculosis is not now the problem it was, and it needed a man of the stature of Lissant Cox to tackle it when it was at its zenith. He was the last survivor of the original tuberculosis officers, and the greatest of them all.

He had a great sense of humour, and the loudest and most infectious laugh I have ever heard.

He had a happy family life, and great sympathy will be felt for his widow and three children.

S. BOLTON, M.D., F.R.C.S.E.D.

Dr. S. Bolton, formerly general practitioner and consultant surgeon, died on 15 September in the Royal Halifax Infirmary, the hospital in which he had worked as honorary and consultant surgeon for nearly 40 years. He was 78.

Stuart Bolton was born at Enstone on 22 December 1888, the son of an Oxfordshire farmer, and one of nine brothers and sisters, three of whom entered the medical profession. He was educated at Burford Grammar School, and graduated M.B., Ch.B. at Edinburgh University in 1912. His first house appointment was as house-surgeon to Charles Cathcart, and this probably influenced his career, because there followed a period as lecturer and demonstrator in the anatomy department. A study of comparative anatomy ended in a thesis which in 1915 gained for him an M.D. and the Goodsir Memorial Fellowship and prize. Soon after his marriage he went to help his overworked friend and Edinburgh contemporary Charles W. Graham, who was in practice in the Shetlands and attached to the Royal Navy as surgeon and agent. Based on the small Gilbert Bain Hospital in Lerwick, they made an ideal surgical partnership. Daily and often nightly they were in boats of all kinds.

They had no x-ray machine, no ambulance, and no regular anaesthetist. It was a hazardous and always exciting life. In 1923 he returned to Edinburgh and took the F.R.C.S., coming to Halifax the same year as a partner in a general practice. He was appointed honorary surgeon to Halifax Royal Infirmary in 1926, and for the rest of his professional life he filled this dual role of general practitioner and surgeon, this position being confirmed in 1948 with the beginning of the National Health Service.

Although a general surgeon, he developed interest later in obstetrics and gynaecology, and he was responsible for the formation and growth of the midwifery department and school at the infirmary, which was later incorporated—inevitably, and to his disappointment—in the larger unit at the General Hospital. He retired from his appointment in 1955 but retained his interest in the hospital service. He was a member of the management committee for many years, and was particularly concerned in the development of the geriatric and allied social services in the town. He will be remembered also for his love of the humanities and his exceptionally wide range of interests, which stimulated all those with whom he came in contact and made him what he was—a family doctor.

His first wife died in 1959, and after a few lonely years he married a second time. To his widow, and to his son and daughter, we extend our sympathy.—J. H. F.

J. H. PALMER, M.B., CH.B., D.M.R.D.

Dr. J. H. Palmer, consultant radiologist to Aberdeen General and Special Hospitals, died suddenly at his home in Cults on 18 September. He was 38.

James Hugh Palmer was born in Kingussie on 7 February 1929, and was educated at Kingussie School, where he was the MacGruer Dux medallist. He received his medical education at Aberdeen University, graduating M.B., Ch.B. in 1953. After early appointments as house-surgeon at the Royal Northern Infirmary, and house-physician at Raigmore Hospital, Inverness, he was appointed regimental medical officer to the 19th Field Artillery Regiment, Royal Artillery, with whom he saw service in Germany and Hong Kong, and active service in Korea. On demobilization he began a career in diagnostic radiology in Edinburgh, taking the D.M.R.D. in 1958. After a brief spell in Barnet General Hospital he returned to Aberdeen in 1959 as a senior registrar, and four years later was appointed consultant to the Aberdeen General and Special Hospitals.

In his short career Palmer made a wide contribution to radiology in the north-east of Scotland. At the Royal Infirmary he devoted much time to radiology of the urinary tract. He had sole charge of the x-ray department at the City Hospital, did regular sessions at the Royal Aberdeen Hospital for Sick Children, and made many visits to the Orkneys and Shetlands. His humane attitude to patients, his skilful approach to his subject, his modest manner, and his dry sense of humour gained him respect and popularity among his hospital colleagues. Jimmy Palmer was a congenial colleague and companion who had a real zest for life. He loved all

kinds of gadgets from x-ray apparatus to fast cars. He had a ready wit, was a generous host and guest, and loved, above all, his family and friends, to whom he was invariably kind, courteous, and considerate.

In 1954 he married Elaine Yule, a nursing sister, and when a few years later his career was interrupted by a serious abdominal illness her help was a major factor in his recovery to health. His sudden and premature death came as a profound shock to all who knew him, and our deepest sympathy is extended to his devoted wife.—D. A. E. M. and L. E. G.

R. A. J. STANFORD, B.Sc., M.B., B.Ch. B.A.O., L.M.

Dr. R. A. J. Stanford, a general practitioner in Scunthorpe, Lincolnshire, died on 14 July. He was 58.

Russell Aubrey John Stanford was born in India on 12 September 1908. He was educated at Blackrock College, and entered University College, Dublin, where he took the B.Sc. (Pathology) in 1931, and graduated M.B., B.Ch., B.A.O. in 1933, later in the year taking the L.M. at the National Maternity Hospital, Dublin. He held early resident posts at St. Vincent's Hospital, Dublin, and later was honorary assistant physician and pathologist at the Beckett Hospital, Barnsley. He settled in general practice in Scunthorpe, Lincolnshire, where he established a highly successful group practice. His medical interests were widespread. Besides his extensive work in general practice, he was deputy medical officer of health to Scunthorpe Corporation for 12 years, medical officer to Scunthorpe United Football Club for six years, and medical officer to Firth-Brown's steel works. He was also a member of Scunthorpe Hospital Management Committee for some years, and an active member of the Scunthorpe Division of the British Medical Association, serving as chairman in 1949–50.

Outside medicine his interests were equally widespread, and he was well known at all the social activities in Scunthorpe and North Lincolnshire. For many years he was an active member of Rotary, and in 1959 he visited America representing Rotary International for District 102. A Roman Catholic, he was keenly interested in all functions of the Catholic community, particularly education and charitable activities. He was a much liked and respected public figure in the area, and his early and untimely death will leave a gap in the medical and public life in North Lincolnshire.

Russell was a big man, in both physical and mental stature. He had a lively and pleasant personality, and displayed a deep and personal interest in everyone he met. He kept himself abreast of all the various aspects of modern medicine, and could be relied upon to be up-to-date in the latest medical developments in diagnosis and treatment. His enthusiasm and love of life made him a wonderful and lively companion, particularly when he attended the rugby international matches. It was always "open house" at "Donaghadee," his home, and one could be certain of a warm welcome, wonderful hospitality, and entertaining conversation. Towards the end, when facing a major opera-

tion, he showed, as one might have expected, deep and profound resources of courage, cheerfulness, and exemplary fortitude.

We offer our sincere sympathy to his wife and family in their sad loss.—J. R. C.

F. J. BENTLEY, M.D., F.R.C.P., D.P.H.

Z. A. L. writes: Frank Bentley (obituary, 30 September, p. 869) was a man of wide interests, all of which he pursued with inspiration and enthusiasm, and whatever he decided to do he did well. He was a kind, modest, generous, and public-spirited man, giving his advice unostentatiously in the form of a question. Pulmonary tuberculosis was his main interest. His personality led him to work in the public health service in the first part of his career, chiefly as an administrator in the reorganization of the tuberculosis services of the L.C.C. During this time he kept in close touch with clinical medicine. His report to the Medical Research Council on artificial pneumothorax in 1936 summarized and evaluated this most important therapeutic weapon against pulmonary tuberculosis between the two wars. Later he published the first comprehensive paper on mass radiography in this country in the pages of the *B.M.J.* in 1940, which was the outcome of his work with the large number of soldiers who had joined up at the outbreak of war, concealing their tuberculous past, but were invalidated from the Services because of recrudescence of their lesions.

The most creative and fruitful part of his life were the 12 years spent at High Wood Hospital after 1947. Here he had the opportunity to follow the course of tuberculosis in a community of 250 growing children during the difficult postwar years, and to experience the influence of increasing affluence and the newer antibiotics, together with modified therapeutic techniques, on the natural history of tuberculosis in childhood and adolescence. The outstanding success of this period can be summed up by the fact that, at the time of his appointment to High Wood, sanatorium beds had to be hired in Switzerland, and that twelve years later his own hospital had to be closed on account of the greatly reduced incidence of tuberculosis in this country. The High Wood experience was summarized in the book *Tuberculosis in Childhood and Adolescence*, published in 1954, and was further developed and evaluated in the many hundreds of carefully chosen slides which were deposited with commentaries in the Harveian Library of the Royal College of Physicians of London.

An asthmatic childhood and continued ill-health during his professional life imposed a great deal of restriction on him. In spite of this he was gregarious, liked good company, films, theatre, good books, and enjoyed good food. He was an erudite and witty conversationalist. He pursued many hobbies. Earlier on he was a keen gardener. Later, when ill-health kept him out of the country during the winter months, he became a passionate traveller and exquisite colour photographer. After his enforced retirement he became an excellent croquet player—defying his medical advisers—and died at Hurlingham, which he had come to love so much, after a pleasant game.

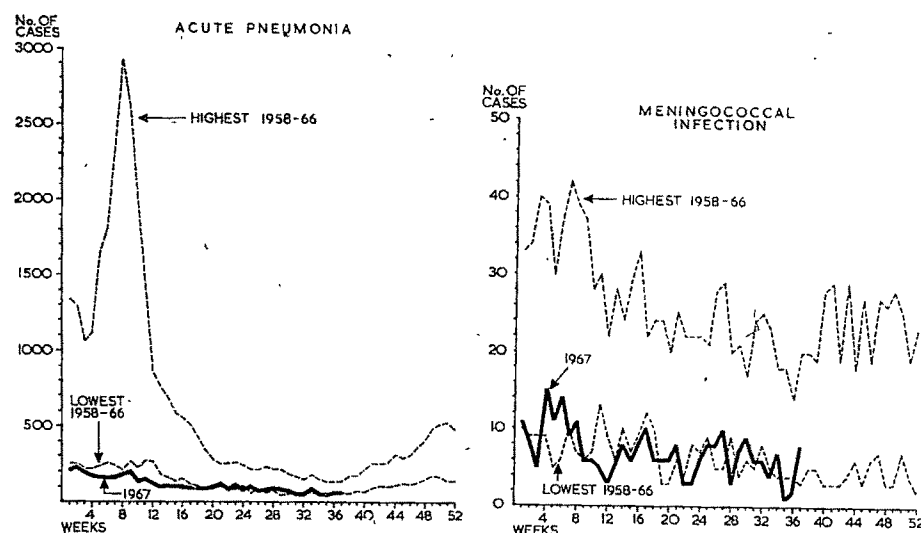
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of acute pneumonia and meningococcal infection in England and

Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending	
	15 Sept.	22 Sept.
Dysentery		
Greater London ...	26	51
Redbridge ...	5	15
Lancashire ...	43	33
Manchester C.B. ...	6	10
Warwickshire ...	20	17
Birmingham C.B. ...	17	11
Yorkshire West Riding ...	54	34
Leeds C.B. ...	19	21
Glasgow ...	46	63
Edinburgh ...	14	15
Food-poisoning		
Greater London ...	29	32
Lancashire ...	13	25
Liverpool C.B. ...	6	12
Sussex ...	9	45
Brighton C.B. ...	2	43

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 16 September (No. 37) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	0	0	
Dysentery ..	248	26	91	3	3	211	42	104	13	4
Encephalitis, acute ..	3	0		0		2	0		0	
Enteric fever: Typhoid ..	4	1	0	0		4	0	0	0	1
Paratyphoid ..	1	0	0	0		5	1	0	0	0
Food-poisoning	127	29	8	2		121	25	6	3	
Infective enteritis or diarrhoea under 2 years										
				32	46				27	35
Measles* ..	807	70	7	9	25	2,673	327	63	30	55
Meningococcal infection ..	8	0	5	0		6	2	3	0	2
Ophthalmia neonatorum	9	0	3	0		11	1	0	0	
Pneumonia† ..	66	8	61	2	1	56	8	49	1	1
Poliomyelitis, acute: Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic ..	1	0	0	0		0	0	1	0	
Puerperal fever‡	110	38	6	0		91	32	1	1	
Scarlet fever ..	110	17	12	5	5	184	28	14	3	10
Tuberculosis: Respiratory ..	196	57	25	6		225	43	22	6	
Non-respiratory ..	36	10	5	2		40	7	4	0	
Whooping-cough	988	117	78	10	72	575	64	49	6	11
DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute ..				0						0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	7	2	0	0	0	3	1	0	1	2
Influenza ..	2	1	0	0	0	4	1	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	554	114	17	10	8	455	83	13	18	5
Poliomyelitis, acute ..	0	0		0	0	1	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	44	7	4	0	3	29	7	3	0	3
Non-respiratory ..				0	0				0	0
Whooping-cough	2	0	0	1	0	1	0	0	0	1
Deaths 0-1 year	232	42	19	8	9	250	49	21	8	7
Deaths (excluding stillbirths)	9,392	1563	489	95	173	8,676	1374	500	99	134
LIVE BIRTHS	15,442	2568	831	266	419	16,251	2786	878	314	400
STILLBIRTHS	210	36	15			243	39	13		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

‡ Includes puerperal pyrexia.

MEDICAL NEWS

M.R.C. Social Medicine Research Unit

The address of the M.R.C. Social Medicine Research Unit under Professor J. N. Morris changed from the London Hospital to the London School of Hygiene and Tropical Medicine on 1 October. On that date Professor Morris took up the Chair of Public Health in the University of London and became Honorary Director of the unit.

The M.R.C. have stated that the unit will be continuing its investigations of the causes and prevention of heart disease, particularly coronary thrombosis, the working of health services, and of social and psychological factors in delinquency. It will also be participating in the school's programmes for the training of community doctors.

European Society for Paediatric Nephrology

The foundation meeting of the European Society for Paediatric Nephrology took place in Glasgow from 17 to 21 September. So far the Society consists of 43 members from 20 European countries. The founders are Dr. GAVIN C. ARNEIL (University of Glasgow) and Dr. HARMAN A. W. M. TIDDENS (Wilhelmina Children's Hospital, Utrecht, Netherlands). During the course of the three-day meeting thirty scientific papers were read and the foundation lecture was given by Professor HENRY L. BARNETT, of the Albert Einstein College of Medicine in New York. It is intended that annual general meetings will be held, and arrangements are in hand for the next meeting in Utrecht in 1968.

Queen Elizabeth Hospital for Children

The hundredth anniversary of the founding of the hospital was commemorated on 18 September by a service at the Parish Church, St. Peter's, Bethnal Green. Other celebrations included a dinner and a garden party, while there was also an exhibition of past and present work of the hospital. A small illustrated brochure to commemorate the centenary is available from the Hospital Secretary (price 5s.).

Vaccination Against Smallpox

A new edition of the Ministry of Health's *Memorandum on Vaccination Against Smallpox* has recently been published (H.M.S.O., price 1s. 6d.). Among the principal changes are the description of the new presentation of vaccine in plastic tubing; the inclusion of pregnancy and leukaemia among the contraindications to routine vaccination; and complete revision of the paragraphs on the inspection and recording of results.

Degree Course for Nurses

Starting in September 1968, St. Bartholomew's Hospital, London, in co-operation with the City University, will select four of its student nurses to combine their nurses' training with a social science degree.

Miss K. M. HALPIN, a governor of the hospital, said at a conference recently that experiments in such integrated courses had already been introduced in a few hospitals in this country, and had proved successful. The course was intended for students whose first intention was to become a nurse, but who also had the desire and academic ability to read for a degree.

Miss W. E. HECTOR, principal sister tutor at St. Bartholomew's Hospital, emphasized that the introduction of this course in no way lessened the value of student nurses taking the ordinary general training leading to enrolment as State-registered nurses. But the future pattern of nursing was changing, and there would be a need in the higher grades for nurses who essentially must know the clinical background of nursing but who must also have the knowledge and experience to take up administration and to interpret and formulate policy and deal with social relations at the highest levels in hospitals, central government, and at international level. It would be a four-year course, the first year of which would be spent in the nursing school, before beginning the honours degree at the City University. It was hoped in time to increase the number of places available for nurses who wished to do the course.

A second scheme, which it is hoped to start at the same time, will link the London Hospital and Queen Mary College, in the University of London. This course will also last four years, but will lead to a degree in economics instead of in social science.

Erwin Stengel Prize

Professor E. STENGEL retired from the chair of psychiatry at the University of Sheffield last month. To mark the contribution he has made to the teaching of psychiatry, his colleagues have inaugurated a prize of £120 in his name. This will be awarded every three years to the doctor who has submitted the best piece of research in any field related to clinical psychiatry and carried out during tenure of an appointment in the Sheffield region. Preference will be given to doctors who have qualified not more than eight years. Any doctor is eligible whether or not he is working in a psychiatric setting. A statement of the prize and list of subscribers was presented to Professor Stengel at a reception at the University Staff Club on 29 September by Dr. H. V. DRICKS, President of the Royal Medico-Psychological Association.

Postgraduate Travelling Fellowships

The Governing Body of the British Postgraduate Medical Federation invites applications from registered medical or dental practitioners for a limited number of postgraduate travelling fellowships. Further details may be found on page xxxv of this week's advertisement columns.

Fulbright Travel Grants, 1968-9

Under the provisions of the Fulbright programme travel grants are available to citizens of the United Kingdom and dependent territories to go to the United States for academic and education purposes, such as study, research, or lecturing. Awards are competitive and are made by the Board of Foreign Scholarships in Washington on the recommendation of the United States Educational Commission in the United Kingdom. Applications should be made as soon as possible and details of the awards can be obtained from the Commission at 71 South Audley Street, London W.1.

Lalor Foundation Research Grants

The Lalor Foundation is offering awards for 1968 for research in the field of reproductive physiology. Awards may be for a

few months or up to one year, and may range from \$1,300 to \$8,500. Preference will be given to younger members of academic staff. Details and forms of application can be obtained from the Lalor Foundation, 4400 Lancaster Pike, Wilmington, Delaware 19805, U.S.A. The closing date is 15 January 1968.

National Council on Alcoholism

At a meeting of the National Council on Alcoholism held on 28 September the following appointments were made: *president*, Dr. LINCOLN WILLIAMS; *vice-president*, LORD EVANS OF HUNGERSHALL; *chairman*, Dr. W. A. R. THOMSON.

People in the News

► Professor I. FRIEDMANN was admitted to membership of the Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum at a recent meeting of the Collegium in Chicago.

News in Brief

Royal Air Force Hospital, Wroughton, Wiltshire, has been renamed Princess Alexandra's Royal Air Force Hospital.

The Speech Therapists' Professional Association will in future be known as the Union of Speech Therapists.

Recent Publications

A Report on Day-Care Centres and Residential Units, by a subcommittee of the Multiple Sclerosis Society of Great Britain and Northern Ireland, includes a summary of a national survey to members of the Society. As a result of the survey the subcommittee has recommended the building of two prototype combined day-care centre and residential units to be undertaken by the Society in the first instance. Copies can be obtained (postage 4d.) on application to the Society, 10 Stratford Road, London W.8.

What to Do When Someone Dies, a booklet describing formalities and procedure in England and Wales. Differences that apply to Scotland are noted. There is an index. Consumers' Association, 14 Buckingham Street, London W.C.2, 10s.

Coming Events

Institution of Electronic and Radio Engineers.—Symposium, "Ultrasonics in Medicine and Biology," 11 October, 2.30 p.m., Middlesex Hospital Medical School, London W.1. Fee 10s. Tickets from the Institution, 8-9 Bedford Square, London W.C.1.

National Society for Clean Air.—Annual conference and exhibition, 17-20 October, Empress Hall, Blackpool.

Abortion Law Reform Association.—Annual public meeting, "Abortion Bill—Will It Work?" 21 October, 7 p.m., Kensington Central Public Library, Phillimore Walk, London W.8. The chairman will be LORD SOPER, and speakers include Professor GLANVILLE WILLIAMS, Mr. P. L. C. DIGGORY, and Dr. ELIOT SLATER. Admission is free.

Research Defence Society.—Stephen Paget memorial lecture, "Animals in Captivity," by Professor A. S. PARKES, F.R.S., 24 October, 5.30 p.m., Physiology Lecture Theatre, University College London, Gower Street, London W.C.1.

Charing Cross Hospital Medical School.—Inaugural address by LORD INMAN, Thursday, 26 October, 5 p.m., at Royal Commonwealth Society, London W.C.2.

Royal College of General Practitioners.—Study day on "Practice Organization," in collaboration with the Postgraduate Board of Medicine, Edinburgh University, 28 October, 9.30 a.m., Western General Hospital (lecture theatre), Edinburgh (note change from Hume Tower). Applications to Dr. CONSTANCE GIBBS, Livingstone House, 39 Cowgate, Edinburgh 1.

Newcastle Regional Hospital Board.—Conference on "Prescribing, Distribution, and Administration of Drugs in Hospital," 28 October, 10 a.m., Physics Auditorium, Newcastle upon Tyne University. Details from the Secretary to the Board, Benfield Road, Walker Gate, Newcastle upon Tyne 6.

B.M.A. Mid-Essex Division and Chelmsford Medical Society.—Symposium, "Disabilities in Middle-age," 28-29 October, Broomfield Hospital, Chelmsford. Details from Secretary, Medical Academic Unit, Chelmsford and Essex Hospital, Chelmsford, Essex.

Societies and Lectures

For attending lectures marked Ⓢ a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Friday, 6 October

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Mr. W. M. Capper: Surgery in the Region of the Ampulla of Vater. (2) 6.30 p.m., Mr. R. H. Franklin: Replacement and Reconstructive Operations of the Oesophagus.

Monday, 9 October

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. H. Baker: Biology of the Epidermis.
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., combined staff consultation clinical meeting.
KINGSTON-UPON-THAMES MEDICAL CENTRE.—(1) 5.15 p.m., slide seminar by Dr. M. E. A. Powell: Lymph Nodes. (2) 6.30 p.m., Dr. G. B. Hill: Basic Statistics.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Professor J. C. Goligher: The Place

of Surgery in the Treatment of Ulcerative Colitis. (2) 6.30 p.m., Sir Clifford Naunton Morgan: Inflammatory Diseases of the Large Intestine.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. S. Shaldon: Intermittent Haemodialysis in the Home.

SOCIETY OF INSTRUMENT TECHNOLOGY.—At Royal Institution, 6 p.m., Thomson lecture by Sir Henry Jones: Sources and Uses of Energy.
WHIPPS CROSS HOSPITAL.—At Medical Education Centre, 8.45 p.m., Leyton Doctor-Clergy Group meeting.

Tuesday, 10 October

B.B.C. 2 TELEVISION.—1.15 p.m., medicine today: Rheumatoid Arthritis. (Sponsored by A.S.M.E.)
HEATHERWOOD HOSPITAL, ASCOT.—At Outpatient Hall, 8.45 p.m., Mr. J. G. Taylor: The Painful Shoulder—Differential Diagnosis.
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Professor C. D. Calnan: Pattern of Cutaneous Disease.
INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 2 p.m., Professor D. V. Fairweather: Perinatal Mortality. (Admission by ticket only, obtainable from Secretary, Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, London S.W.3.)
KENT AND SUSSEX HOSPITAL.—8.30 p.m., Professor W. H. Trethowan: The Couvade Syndrome.
NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., Mr. J. E. Mitchell: Minor Ano-Rectal Conditions.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Mr. D. R. Davies: Surgery of the Parathyroid Glands. (2) 6.30 p.m., Mr. K. Bloor: Principles of Treatment of Peripheral Vascular Occlusion.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Professor R. Shackman: Uraemia.
WHIPPS CROSS HOSPITAL.—At Medical Education Centre, (1) 1.15 p.m., B.B.C. programme, medicine today: Rheumatoid Arthritis; (2) 5 p.m., seminar by Dr. P. Marshall Jones: Renal Function Tests.

Wednesday, 11 October

BRITISH SOCIETY FOR THE HISTORY OF PHARMACY.—At Pharmaceutical Society of Great Britain, London W.C., 7 p.m., Dr. Marie B. Hall: Apothecaries and Chemists in the 17th Century.
CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. Y. M. Clayton: Identification of Pathogenic Fungi.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. R. L. Yeager (New York): A Combined Hospital and Outpatient Programme for the Treatment and Control of Tuberculosis.
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Society of Medicine, 8.30 p.m., symposium: Medical Problems of the Immigrant.
MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University Medical School, 5 p.m., Dr. A. Goldberg: Iron and Anaemia.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—5.30 p.m., postgraduate museum demonstration by Mr. C. J. Mackinlay: Ovarian Tumours.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Mr. D. Ranger: Tracheostomy and Endotracheal Intubation. (2) 6.30 p.m., Dr. A. R. Harrison: Calcium Metabolism and the Kidney in relation to the Formation of Calculi.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. G. P. McNicol: Fibrinolysis.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conference by Dr. C. T. Dollery, Dr. E. D. Williams: Hyperaldosteronism. (2) 2 p.m., Dr. G. A. Rose: Calcium Metabolism in Relation to Metabolic Bone Disease.

STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Mr. R. R. L. Pryer: clinical cases. (2) 6 p.m., Dr. C. S. Pitcher: Megaloblastic Anaemias—II.
WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Dr. M. W. McNicol: Management of Respiratory Failure.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, course for general practitioners, 2 p.m., Dr. N. Galbraith: Immunization and Immunology; 3 p.m., Dr. H. Wyatt: Physical Medicine in Hospital and Community.

Thursday, 12 October

DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Sir Edward Wayne: The Impact of Automation on Clinical Medicine.
LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.15 p.m., presidential address by Mr. M. Klein: Glaucoma.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5 p.m., Gordon-Watson lecture by Brigadier J. M. Matheson: Infection in Missile Wounds. (2) 6.15 p.m., Mr. A. H. Hunt: Management of Portal Hypertension and its Complications.
ROYAL NORTHERN HOSPITAL, London.—5 p.m., Professor F. T. G. Frunty, Dr. J. Jenkins, Dr. C. W. H. Havard: Hirsuties.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. J. A. H. Hancock: Reiter's Syndrome.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Mr. D. J. MacRae: The Acid Base Relationship between the Mother and the Foetus.

Friday, 13 October

BRITISH GERIATRICS SOCIETY.—At Royal College of Physicians of London, 5.30 p.m., Guinness lecture by Professor G. Bull: Myocardial and Cerebral Infarction.
INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 3 p.m., discussion: Endometriosis. Speakers, Mr. D. W. T. Roberts, Mr. W. L. Whitehouse. (Admission by ticket only, obtainable from Secretary, Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, London S.W.3.)
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Mr. J. L. Hayward: An Assessment of Etiological Factors in Breast Cancer in relation to Treatment. (2) 6.30 p.m., Mr. M. A. Falconer: Surgery in Lesions of some of the Cranial Nerves.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Dr. L. M. Franks: Hormonal Control of Normal and Malignant Tissues. (2) 11.30 a.m., Professor R. Shackman: clinicopathological conference (urology). (3) 4 p.m., Dr. J. W. Laws: Radiology of the Small Intestine.
WHIPPS CROSS HOSPITAL.—At Medical Education Centre, (1) 11.30 a.m., child psychiatric case conference by Dr. W. R. Little; (2) 1 p.m., medical films and discussion.

Saturday, 14 October

ROYAL POSTGRADUATE MEDICAL SCHOOL.—9.30 a.m., anaesthetic teaching meeting: Humidification and Intermittent Positive Pressure Ventilation.

Deaths

Cox.—On 27 September 1967, at 2 Oaks Road, Church Stretton, Shropshire, George Lissant Cox, C.B.E., M.D., aged 88.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 14 OCTOBER 1967

Pointers

Penicillinase: Bacterial enzymes that destroy penicillins are discussed by Professor M. R. Pollock, who considers they may have had a common evolutionary origin and may be of importance in nature (p. 71). *Leader*, p. 66.

Hepatic Coma: Drs. J. A. McLean and H. A. Luke, of Melbourne, describe four patients with hepatic coma, with one recovery, who were treated by exchange blood transfusion (p. 78).

Influenza: Dr. Marguerite S. Pereira and colleagues report that an epidemic due to current strains of virus is unlikely (p. 80). Dr. G. C. Schild and Professor C. H. Stuart-Harris discuss the possibility of foretelling influenza outbreaks from information about antibodies in children (p. 82). *Leader*, p. 67.

Blood Loss: Dr. J. M. Holt and colleagues describe a sensitive method of measuring blood loss with radioactive iron (p. 86).

Blood Rouleaux: Some plasma expanders but not others cause rouleaux to form and may interfere with blood grouping, according to Dr. A. J. Salisbury (p. 88).

Paget's Disease: Six cases in three generations are reported by Drs. J. Verrier Jones and Mervyn F. Reed (p. 90).

Autonomic Nerves: In a familial form of autonomic nervous disease the pupil responses are described by Dr. E. Shinebourne and colleagues (p. 91).

Postoperative Gas Gangrene: A leader discusses why thigh amputations for obliterative arterial disease are specially hazardous (p. 68).

C.M.O.'s Report: Sir George Godber is critical of "firm" system in hospitals (p. 69).

Case Reports: Corrosion of stomach simulating carcinoma (p. 93); complications of methyl-dopa (p. 94); Goodpasture's syndrome (p. 95); ichthyosis and breast cancer (p. 96).

Digestive System: In "Current Practice" Dr. N. F. Coghill discusses the diagnostic significance of dyspepsia (p. 97).

"Medicine Today": An article on the management of rheumatoid arthritis complements the television programme on the subject (p. 99).

Human Experimentation: C.I.O.M.S. conference on ethics (p. 105).

Aspirin and Gastric Bleeding: Correspondents question whether paracetamol is the right alternative (p. 107).

Safer Night Driving: Article by Motoring Correspondent (p. 119).

Scottish Hospitals: Meetings of Scottish Committee for Hospital Medical Services and Hospital Junior Staffs Group Council (*Supplement*, pp. 11 and 13).

B.M.A. Planning Unit: Progress report (*Supplement*, p. 14).

Postgraduate Education in Scotland

In September 1965 the Scottish Postgraduate Medical Association, on the invitation of the Scottish Home and Health Department, set up a working party "To inquire into the needs of postgraduate medical education in Scotland so far as the National Health Service is concerned." The report¹ has now appeared, and though approved by the association in principle for wider circulation it is not put out as a statement of agreed policy. The outcome of considerable, though uncoordinated, activity in postgraduate education in Scotland, discussed also at a conference held in Glasgow earlier this year,² the report owes much to the stimulus given to this whole problem by the Nuffield Provincial Hospitals Trust in 1961. What has emerged is that education and training must go hand in hand and that "they must be placed upon a more organized footing than was thought necessary in the past."

The report outlines the role of the universities in providing teachers, libraries, laboratories, and so on and in the supervision of the preregistration year; of the colleges in setting professional standards, offering specialist courses, and holding examinations; of the N.H.S. in providing the training posts, supervision by senior staff, study leave, secondments, and facilities for research; and of the Postgraduate Association in bringing together the various bodies concerned. However, despite certain advantages in Scotland there seems to be a lack of co-ordination, and no central authority can be identified as ultimately responsible for carrying out a policy, properly conceived and financed.

If postgraduate training in an era of intense specialization is to be effective it must be continuous from the undergraduate period until retirement, as was likewise stressed in the report on medical education submitted last year by the British Medical Association to the General Medical Council.³ Consequently the discontinuous career structure in the Health Service should be revised to enable junior staff to undertake planned schedules of training leading to their chosen vocation, thus bringing them into line with senior registrars. The report looks forward to a five-year period of basic medical education followed by two years' preregistration, in the second year of which some specialization might be begun. Thereafter at S.H.O.-registrar level there should be a regionally organized and financed system of in-service specialist training, with rotation through teaching and district hospitals and laboratories. To carry out a scheme of this kind would require a central postgraduate organization with associated regional and area bodies. This organization would bring together representatives of the National Health Service, the universities, and the colleges, but it would be expected that the main financial burden would fall on the National Health Service.

Special concern was expressed for the training of general practitioners. It is recommended that the training should extend over four years, that two years should be spent in hospital and two in teaching health centres. The need to develop comprehensive health centres is strongly argued.

The competing claims of staffing for service needs and for training are considered in some detail, particularly in the appendix on surgery. Since only a fraction of S.H.O.s and registrars in any specialty will eventually become consultants in that specialty, alternative careers must be offered. In the case of surgery, for example, it is suggested that about half the registrar posts should be earmarked for the training of future consultant surgeons in the N.H.S. This would maintain a ratio of registrars to senior registrars of about 5:4. The remaining surgical posts would be filled by Commonwealth trainees and trainees for general practice. This pattern is worthy of serious consideration.

The report is both realistic and practical. It deals largely with existing institutes, facilities, manpower, and staffing structure, and it suggests how we may make the best

use of what we now have. For this reason the role of the teaching hospital is given most prominence and that of community medicine the least. The stimulus it offers to new developments in patterns of patient care is welcome. It expects that, before long, registration of specialists (which would include general practitioners) will be introduced as outlined in the 1967 Recommendations of the G.M.C.⁴ and suggests that active steps should be taken now to bring this about.

¹ *Report of a Working Party on Postgraduate Medical Education within the National Health Service in Scotland, 1967.* Scottish Postgraduate Medical Association.

² *Brit. med. J.*, 1967, 2, 435.

³ *Ibid.*, 1966, 2, 125.

⁴ *Recommendations as to Basic Medical Education, 1967.* General Medical Council.

Origin of Penicillinase

Penicillins are attacked by two enzymes of microbic origin. One is amidase, which simply severs the side-chain leaving the nucleus intact, a reaction which is now the first step in producing the many new semisynthetic penicillins. The second is penicillinase, which opens the β -lactam ring of penicillin and deprives it of all antibacterial activity. It was recognized more than 20 years ago that this enzyme was formed by some strains of staphylococci, and that they owed to this their resistance to the antibiotic. These strains have little "intrinsic" resistance; it is not that they can tolerate penicillin, but that they can destroy it. All resistance to penicillin in staphylococci is of this nature. The formation of this enzyme at a site of infection can prevent the action of penicillin on another fully sensitive organism. Thus in mixed infections by staphylococci and haemolytic streptococci treatment with cloxacillin may be indicated, since it is both resistant to penicillinase and active against the streptococcus.

Soon after the recognition of staphylococcal penicillinase it was found that other bacteria form the same kind of enzyme. These include many Gram-negative bacilli such as species of *Pseudomonas*, *Proteus*, and *Klebsiella*, various *Bacilli* such as *B. cereus* and the anthrax bacillus, and even tubercle bacilli. In some of these organisms resistance to penicillin does not depend entirely or even largely on the enzyme; many of them also possess a high degree of intrinsic resistance. An exception is *B. anthracis*, which is intrinsically so sensitive that anthrax responds readily to treatment with penicillin. The structure of penicillinases—and cephalosporinases, corresponding enzymes attacking the nucleus of the cephalosporin group of antibiotics—is not exactly known, but it is clear that they are a family of enzymes and not a single substance. Many of these enzymes are inducible—that is to say, exposure to a penicillin will immediately cause them to be formed in much larger amount. It has also been established that different penicillins vary in their capacity to act as inducers, and indeed nafcillin is claimed to have a therapeutic advantage in that it is a very weak inducer of penicillinase formation.

Professor M. R. Pollock, who has made extensive studies of penicillinases and the kinetics of their formation and activity, chose this subject for an Almroth Wright lecture

which we print on page 71. His title refers to the origin and function of penicillinase as a "problem in biochemical evolution," and the main question which he asks is how it came about that some bacteria form such an enzyme, which is of no use to the cell forming it except as a means of eliminating an antibiotic from the environment. He reaches the interesting conclusion that formation of the enzyme may have resulted from an evolutionary change related to this very function. Some of his arguments will be appreciated only by those with a considerable knowledge of bacterial chemistry, but others will make a more general appeal. He points out, for instance, that the distribution of numerous moulds now known to form penicillin and of bacteria forming penicillinases is not dissimilar. Their habitats include not only the soil but the skin, where an interesting example is the reported coexistence of a penicillin-forming dermatophyte and a penicillinase-forming staphylococcus on the skin of hedgehogs. Two other pieces of evidence are derived from hitherto unpublished work. It has at last been shown that a *Penicillium* will actually produce penicillin in natural soil in the laboratory. Secondly, Pollock himself has shown in the same environment an antagonism between the growth of a penicillin-forming mould (*P. chrysogenum*) and a penicillinase-forming bacillus (*B. licheniformis*) in the sense that when growing together they attain lower total numbers than either growing alone.

This tentative conclusion has wider implications. Soil has been searched for antibiotic-forming species on a gigantic scale not only because it contains an enormous variety of micro-organisms but because it was originally regarded as a battle-ground of warring species, their weapons being antibiotics. Of late years this belief has lost many adherents, and antibiotics are commonly regarded as having no natural function—at least of any importance. In the words of S. A. Waksman and H. A. Lechevalier,¹ "... we can conclude that the production of antibiotics, as we visualize it in the laboratory, does not occur in nature ... too little solidly grounded information is available to warrant much more than speculation about the ecological significance of antibiotic production." If we are now to grant that penicillinase formation is the result of an evolutionary process of a

¹ Waksman, S. A., and Lechevalier, H. A., *The Actinomycetes*, 1962, vol. iii. London.

defensive nature, it follows that antibiotics themselves have a function in suppressing other species than those forming them and thus securing a more liberal supply of nutrient. "Nature red in tooth and claw," an expression intended to refer only to the animal kingdom, has thus an equivalent even among the lowest plants—a forbidding thought to the believer in peaceful co-existence as a natural way of life.

Spread of Influenza

The prognosis of an individual patient's disease is always difficult even with a straightforward infection like influenza. Likewise to predict the appearance and course of epidemics is chancy. Nevertheless international co-operation, particularly through the World Health Organization's Reference Centres, has given us a fairly complete picture of what is happening to the viruses causing influenza epidemics.

In 1947 and in 1957 completely new serotypes of influenza appeared—types A1 and A2—and these spread across the world, producing large epidemics. More epidemics followed in later years, and comparison shows that the virus strains have changed the antigens on their coats appreciably. This is presumably because new variants have a better chance of survival against the antibody induced by the last variety of influenza. Two distinct new antigenic modifications have occurred since the first A2 (Asian 'flu) viruses appeared, and have usually been associated with new epidemics.¹⁻⁶

However, whether a virus spreads in a country depends not only on the "newness" or otherwise of its antigens but on the antibodies the inhabitants are carrying. Influenza A in Britain tends to recur at about two-year intervals,⁷ but recent years have shown exceptions to this rule (which is not followed in other parts of the world). It has therefore been suggested that if we know the immune status of the population of a country, in particular if we know the number of people carrying antibody against the current strain, then we may be able to predict an epidemic, and perhaps forestall it by vaccinating with the virus for which the population has no antibody. When new strains have appeared such studies have been made, and they are easy to interpret. In the 1957 pandemic only the very old had antibody against the A2 virus strain, and everyone else had no antibody and was susceptible. In the interpandemic period serological surveys are not so easy. Such studies have been made abroad, usually with the haemagglutination-inhibition tests to detect the antibody.⁸ The first of such studies from Great Britain are reported in this issue of the *B.M.J.* (p. 80). Dr. Marguerite Pereira and her colleagues report that sera were collected from October 1965 to May 1966 from routine blood specimens examined in public health laboratories, and were tested by a specific complement-fixation test for antibodies against the surface (V) antigens of recently isolated strains of influenza A2 and B. Only about one-half of the preschool children had antibody against influenza A and a quarter against influenza B, but over half the school-age children and adults had antibody. The peak level of antibody to recent strains was in the age group 15–24, possibly because they had been heavily affected by influenza and also because they had relatively little experience of the antigens of the earlier influenza serotypes which "condition" the immune mechanism to produce antibody against the earlier types rather than against the recent ones. This phenomenon was

called "original antigenic sin,"⁹ and the mechanism has recently been studied by reproducing the phenomenon in rabbits injected successively with different influenza virus vaccines.¹⁰ It is thought to occur when clones of antibody-producing cells proliferate after the first antigenic experience of the virus, and are restimulated when partly cross-reacting antigens are met. But if large amounts of such new antigens are given they may not be adequately dealt with and may stimulate the formation of a new clone.

The second study, by Dr. G. C. Schild and Professor C. H. Stuart-Harris, appears at page 82. They used sera collected from children in South Yorkshire in three periods—namely in 1965, early 1966, and the winter of 1966–7. There was an outbreak of influenza due to both A2 and B viruses in the area in 1966, and the study therefore sheds light on the response of the "antigenically inexperienced" part of the population. In general antibody was less common and of lower titre in the younger children. Though most children had antibody against the 1964 influenza A2 before the epidemic, there was by 1966 a marked increase in the number with high titres, presumably as a result of natural exposure. Fewer children had antibodies against the 1965 influenza B strain, but the proportion of these with medium or low titres increased during the epidemic. The lowest frequency of antibodies was found in each case against the most recently isolated strain of influenza—that is, the 1966 strain—though by tests with sera prepared in the laboratory their antigenic composition did not seem to be particularly different from the viruses isolated one or two years before. The authors suggest, in fact, that tests with children's sera may be the most delicate way of distinguishing between closely related influenza viruses, and certainly differences shown with human sera may well be important in epidemiology. On the other hand, sera from adults would probably distinguish between viruses less sharply than animal sera do.

The results of the survey by Dr. Pereira and her colleagues show that many people have antibody against the current influenza virus strains, and the authors say we are unlikely to have an epidemic due to these or similar strains. This is reassuring, but it leaves another question unanswered. How

¹ Robinson, R. Q., *Progr. med. Virol.*, 1964, 6, 82.

² Isaacs, A., Hart, R. J. C., and Law, V. G., *Bull. Wld Hlth Org.*, 1962, 26, 253.

³ Morris, J. A., Hatano, M., Robinson, R. Q., Aulisio, C. G., and Smadel, J. E., *Proc. Soc. exp. Biol. (N.Y.)*, 1963, 114, 406.

⁴ Weinberger, H. L., Buescher, E. L., McCown, J., and Gauld, J. R., *ibid.*, 1963, 114, 413.

⁵ Pereira, H. G., Pereira, M. S., and Law, V. G., *Bull. Wld Hlth Org.*, 1964, 31, 129.

⁶ Zhdanov, V. M., Zaxstelskaya, L. Y., Nesterenko, M. K., Yakhno, M. A., and Isachenko, V. A., *Amer. J. Epidemiol.*, 1967, 85, 175.

⁷ Stuart-Harris, C. H., *Influenza and Other Virus Infections of the Respiratory Tract*, 2nd ed., 1965. London.

⁸ Pešek, J., and Vobecký, J., *J. Hyg. Epidemiol. (Prague)*, 1964, 8, 21.

⁹ Davenport, F. M., and Hennessy, A. V., *J. exp. Med.*, 1957, 106, 835.

¹⁰ Fazekas de St. Groth, S., and Webster, R. G., *ibid.*, 1966, 124, 331.

¹¹ Magill, T. P., *ibid.*, 1955, 102, 279.

¹² Schäfer, W., *Z. Naturforsch.*, 1955, 10b, 81.

¹³ Pereira, H. G., Tümová, B., and Law, V. G., *Communicable Disease Center, Zoonoses Surveillance Report No. 5*, p. 26, 1965. Atlanta.

¹⁴ Tümová, B., and Fišerová-Sovinová, O., *Bull. Wld Hlth Org.*, 1959, 20, 445.

¹⁵ Waddell, G. H., Teigland, M. B., and Sigel, M. M., *J. Amer. vet. med. Ass.*, 1963, 143, 587.

¹⁶ Kasel, J. A., Alford, R. H., Knight, V., Waddell, G. H., and Sigel, M. M., *Nature (Lond.)*, 1965, 206, 41.

¹⁷ Schild, G. C., and Stuart-Harris, C. H., *J. Hyg. (Lond.)*, 1965, 63, 479.

¹⁸ Minuse, E., McQueen, J. L., Davenport, F. M., and Francis, T., jun., *J. Immunol.*, 1965, 94, 563.

¹⁹ Kloene, W., et al., *Virology*, 1966, 28, 774.

²⁰ Green, I. J., Hung, S. C., Yu, P. S., Lee, G. W., and Pereira, H. G., *Amer. J. Hyg.*, 1964, 79, 107.

²¹ Schulman, J. L., and Kilbourne, E. D., *J. exp. Med.*, 1963, 118, 257.

²² In *Proceedings of the Third International Biometeorological Congress*, ed. S. W. Tromp and W. H. Weike, 1966. Oxford.

²³ Schulman, J. L., *J. exp. Med.*, 1967, 125, 467.

long will it be before the virus changes sufficiently to evade the immune barrier which the human herd has raised against it?

Attempts to produce the "next" variant in laboratory animals have not been successful.¹¹ In recent years it has become clear that influenza A and B viruses can in fact be isolated from cases of respiratory disease between epidemics, in periods when clinical or epidemiological observations such as the frequency of deaths from pneumonia, sickness claims, or outbreaks in institutions or local communities do not show that an epidemic is in progress. Thus, though the virus may seem to have disappeared, it can be found if looked for sufficiently thoroughly. However, so far no new serotype has been caught in the act of antigenic evolution.

An even less predictable event is the appearance of radically new influenza viruses, such as the Asian influenza virus. For many years it was thought that they might come from an animal reservoir. Unfortunately, in the best-studied example, that of influenza in American pigs, it seemed more likely that the virus had gone from man to pig in the 1918 epidemic rather than the reverse. But it does now provide a good example of an influenza virus which maintains itself in animals. Its life cycle, involving earthworms and nematodes, is rather extraordinary, but it is apparently independent of man—except that it is man who keeps the pigs. However, in recent years we have learnt much more about influenza viruses in animals. It was discovered in 1955 that the long-known fowl plague virus is actually an influenza A virus,¹² and since then there are also other antigenically distinct influenza A viruses affecting ducks,¹³ turkeys, terns, and game birds, and two different serotypes have been recovered from horses both in Europe¹⁴ and in North America.¹⁵ Human beings have been infected experimentally with one of the horse viruses, but large doses were used and only one volunteer became sick.¹⁶

Antibody against one of the horse viruses has been found in the sera of old persons.^{17 18} It is difficult to interpret this. But if man was infected in the last century with a virus related to one now infecting horses, that does not prove that it came from horses or from any other animal. Furthermore, there is no well-documented instance of an epidemic beginning in animals and spreading to man, though it might be a rare event and also take place in economically impoverished places where man and animals live close together and opportunities for precise observation are few. There are examples of almost completely new antigenic serotypes of influenza B which produced local outbreaks of disease in man but did not spread across continents as they were expected to do.^{19 20} They apparently lacked something, perhaps the ability to survive in air and so spread rapidly, which would have made them into completely successful epidemic strains. So animal influenza viruses which would ordinarily grow rather poorly in the cells of man would, if the theory were correct, be likely to produce a few cases more often than a distinct epidemic. Any possible examples should be quickly reported and investigated by expert virologists.

Recent experiments on mice^{21 22} have shown that the virus is transmitted as airborne droplets, and that the rate of transmission can be reduced by increasing ventilation and modified by the temperature and humidity of the air. Some viruses are much better "spreaders" than others, though it is still not clear why they are. Further experiments, just described,²³ show that though serious disease can be prevented by vaccinating mice with live or killed vaccine the live vaccine also reduces the ability to transmit infection to other animals

when mice are reinfected, while mice protected with killed vaccine can still act as transmitters.

The epidemiology of influenza is rather like the study of economics: it does not tell us what is going to happen so much as why things happen after they have done so. Consequently a prediction for the coming winter in Britain must be based on a balance of probabilities. Two years ago we had influenza A2 and B, so we might expect influenza A2 to return this year, as it seems to have done in the southern hemisphere during our summer. There is no sign of a radically new antigenic type of virus, and many people carry antibodies against the current types. So if an epidemic comes it is likely to be mild.

Postoperative Gas Gangrene

It has recently been reported in the daily press that two cases of gas gangrene, one of them fatal, have followed amputation through the thigh in a Birmingham hospital, and that an operating-theatre suite has consequently been closed. Some comments on this occurrence¹ refer to the ubiquity of pathogenic bacteria in the hospital environment and the necessity for greater and very expensive precautions in order to reduce the risk so entailed. A further report² concerns three cases of gas gangrene at a London hospital, but gives no information about the circumstances in which they arose.

No lessons can be drawn from these two episodes until a full account of them is available, but there are certain facts about the causation of this infection, and particularly with regard to its source, which apparently deserve to be more widely known. The organism almost invariably causing postoperative gas gangrene is *Clostridium welchii*. It is a normal inhabitant of the bowel of man and animals, and almost always to be found in soil, dirt, and dust. Its spores are capable of prolonged survival. Their exclusion from the hospital environment is impossible. For instance, E. J. L. Lowbury and H. A. Lilly³ found them in every sample of air examined in a hospital, including that of operating-theatres. Moreover, the organism is not uncommonly present in the exudate from traumatic wounds or burns which are the seat of nothing more than transient suppuration. It is thus implanted in many traumatic wounds and probably in a substantial proportion of surgical wounds without giving rise to the acute necrotising myositis with formation of gas which is gas gangrene.

What, then, is the missing factor which ensures these patients' safety? It is simply that the tissues involved have an adequate blood supply and thus an oxygen tension in which clostridia cannot grow. The spores of an anaerobe cannot even germinate in a tissue normally supplied with blood. In traumatic gas gangrene the infection originates in muscle which has been crushed or cut off from its blood supply. Only profuse growth of clostridia in such an area can create conditions in which normal muscle can subsequently be invaded.

For three reasons gas gangrene is more likely to follow thigh amputation for obliterative arterial disease than other

¹ Observer, 1 October 1967.

² The Times, 5 October 1967.

³ Lowbury, E. J. L., and Lilly, H. A., *J. Hyg. (Lond.)*, 1958, 56, 169.

⁴ Williams, R. E. O., Blowers, R., Garrod, L. P., and Shooter, R. A., *Hospital Infection*, 2nd ed., 1966. London.

⁵ Parker, M. J., *Brit. med. J.*, 1967, 2, 698.

⁶ Price, D. J. E., and Shooter, R. A., *ibid.*, 1964, 2, 1176.

operations. Firstly, the incision must be through skin not far distant from the anus, and intestinal bacteria are more widely distributed over this area than is commonly realized; among them the spores of clostridia are resistant to ordinary methods of skin disinfection. Secondly, the operation entails severing large masses of muscle in which bacteria from the region of the incision can be directly implanted. Thirdly, and most important, the disease which has necessitated the operation reduces the blood supply to the area, and may thus reduce the oxygen tension to a level permitting clostridial growth. The degree to which this area is so affected is doubtless one variable factor determining the outcome. Others are the efficacy of skin cleansing and the toxigenicity of the patient's own strain of *Cl. welchii*. This is a property in which different strains vary widely.

This operation carries the imperative indication for penicillin cover in doses allowing for the fact that clostridia are less sensitive to penicillin than, for instance, streptococci. At least 500,000 units should be given at intervals of not more than six hours for seven days.⁴ Other operations with a similar risk meriting penicillin cover were recently referred to in our correspondence columns by M. J. Parker.⁵

Gas gangrene is a rare and terrifying condition, and it is perhaps natural that operating-theatre staffs should regard it as calling for exceptional measures. In fact it is much easier to disinfect a theatre after a case of gas gangrene than after a dirty operation on the lower bowel, because in the former the organisms are all in the vulnerable vegetative form, whereas in faeces they exist largely as resistant spores. That most strains from the normal bowel are as toxigenic as those which have had the opportunity of causing gas gangrene has been shown by D. J. E. Price and R. A. Shooter.⁶ It remains to be seen whether conditions in the operating-theatres concerned in these recent episodes are considered to require improvement. What can be said with some confidence is that when gas gangrene follows thigh amputation there is no need to look any further for the source of infection than the patient's anus.

Standardization in Human Cytogenetics

The explosion in our knowledge of human chromosomes and their abnormalities which has occurred during the past ten years has resulted in many difficulties, particularly of communication and nomenclature. There have now been three conferences to consider these problems. The first of these was in Denver in 1960, the second in London in 1963, while the third and last was convened at the University of Chicago in September 1966. The aim of each of these meetings has been to improve communication and understanding in the field of human cytogenetics. At Denver order was brought into the system of numbering human chromosomes, and the international system agreed at that meeting has remained essentially unaltered since. In London the Denver system was consolidated and the alternative use of letters to classify the different chromosome groups, which had been advocated by some workers since 1961, was agreed internationally to be a useful alternative to the Denver system of nomenclature. At the conference it became clear that little progress had been

made in chromosome identification over the three preceding years.

The report of the Chicago Conference, published recently, is perhaps one of the most important documents published in the field of human cytogenetics. It considers new means for describing the normal chromosomes and deviations from the normal complement, and proposes an entirely new system of notation for the uniform description of the human chromosome set and its abnormalities. This shorthand system is also applicable to the description of the somatic chromosomes of non-human species, so that perhaps from this conference a universal system of notation may eventually develop. The system is most carefully designed so that it should be adaptable to automated data processing and information retrieval systems, which are becoming more and more widely used.

Other topics discussed at the meeting included the recording of data, and recommendations are made in the report on the essential information required if accounts of chromosome abnormalities and variation are to have maximum value. The place of autoradiography in chromosome identification was considered as well as problems related to the automation of chromosome analysis, population cytogenetics—and in particular the types of population suitable for study and the information which might be derived from such studies—and the effects of radiation and mutagenic substances on chromosomes.

The conference needs following up in two important respects. Its recommendation "that in view of the expansion in human cytogenetics during the past six years it is now desirable to explore the feasibility of establishing a central organization for collecting and analysing data on the variability of the human karyotype" should be acted on by the appropriate international and national bodies. Secondly, its report is available. If investigations and journals publishing paper in this and related fields would use the system of notation recommended in the report then the clarity of published work would be considerably improved. In the past there has been confusion, and valuable data have been lost by the publication of inadequate and incomplete case reports. Widespread acceptance of the recommendations of the Chicago conference should make this a thing of the past.

Health Priorities

The Ministry of Health's team visiting the U.S.A. and Canada to persuade British medical emigrants to return is now at work. Can it offer the attraction that conditions are so different from what they were, or what the emigrants thought they were, that some will be tempted to return? The Ministry's views, as expressed by its Chief Medical Officer, Sir George Godber, in his annual report,¹ are robustly hopeful of better times ahead for doctors working in both hospital and general practice. That the department has its views also on what the profession should be doing is apparent from Sir George's observation that, "Given an acceptable and workable opportunity . . . the medical profession has shown its ability to work constructively and successfully with the department."

In his introduction Sir George dwells on the year he is reviewing, 1966, as one that "may well be seen in retrospect

¹ *Chicago Conference: Standardization in Human Cytogenetics*, Birth Defects, Original Article Series, 1966, Vol. 2, No. 2, New York. Copies can be obtained free from the Medical Department, The National Foundation—March of Dimes, 800 Second Avenue, New York, N.Y. 10017.

² *On the State of the Public Health*, The Annual Report of the Chief Medical Officer of the Ministry of Health for the Year 1966. 1966. H.M.S.O.

³ *Management Functions of Hospital Doctors*, Ministry of Health, 1966. H.M.S.O.

is the critical year" for new developments in the Health Service and also as "a turning point." The new arrangements in general practice came into being and do indeed offer a better framework in which to practise medicine. But among the outstanding problems remaining are the closer co-ordination of the different branches of medical practice and improvement in the opportunities for postgraduate and continuing education. The justifiable complaint is still prevalent among registrars that training for a consultant career is overwhelmed by the provision of care of patients. Sir George criticizes the arrangement of hospital staffs in "firms" as tending to preserve "the wasteful, inalienable ownership of hospital beds by individual consultants." He complains that last year's report on management functions of hospital doctors produced by the Advisory Committee on Management Efficiency² seems to have had less attention than it deserved—but this may be because it did not inspire the confidence of some of the readers to whom it was directed. The general pattern that Sir George outlines is of large district hospitals ("we are still struggling with several times as many hospitals as we need") linked with groups of general practitioners, mainly in health centres, working in close partnership with hospital specialists. In an increasingly urban population such arrangements seem likely to be a natural development.

Though Sir George reports that "Broadly the health record of the year was favourable," it is evident from a later section of the report that Britain's health is not all it should be. Despite the risks of drawing conclusions from international comparisons of statistics it is impossible to dismiss as of no consequence Britain's relatively poor showing in this respect. The Ministry has ranked a number of developed countries by standardized death rate, late foetal death rate (stillbirths), infant mortality rate, and maternal mortality rate combined. In this list the United Kingdom comes eighth, bracketed with the U.S.A., despite its very different arrangements for medical care. Countries with better health statistics are, in order of ranking, Sweden, Switzerland, Australia, Netherlands, Canada, Czechoslovakia, and Belgium. Though such facilities as the health services of these countries provide are only part of the explanation for their ranking in the league table, any judgement on the N.H.S. must take account of the U.K.'s relatively low position. Are its priorities right? is a question that has been asked before.

Wandering Oesophagus

Displacement and deformity of the oesophagus as found on barium-swallow examination provides a valuable aid to the diagnosis of many intrathoracic lesions. In most cases the changes are constant and do not vary during a single examination or even during successive examinations, but N. Shahin¹ has recently drawn attention to the fact that in cases of displacement of the lower third of the oesophagus considerable alteration in its position can occur. He describes this finding as "wandering oesophagus," a term which appears

to have been first used by E. Zdansky.² J. F. K. Hutton³ used the same term to describe a changing displacement of the lower third of the oesophagus in a case of mitral stenosis with enlarged left auricle. In his case he found that at one time the displaced oesophagus was pushed backwards and to the right (the usual displacement), while at a later stage in the examination, after a change in the patient's posture, the oesophagus slid over to the left. M. Brombart in his comprehensive monograph on the oesophagus⁴ describes a similar case, and it is of interest that his patient complained of considerable pain when the oesophagus was displaced to the right but was quite free of pain when it lay to the left of the dorsal spine. Shahin found 12 examples of wandering oesophagus during a single year, and he suggests that the condition is more common than is generally realized and would be found more frequently if radiologists looked carefully for it.

The thoracic aorta commonly becomes dilated and tortuous with advancing age, especially in the presence of hypertension. These changes produce a characteristic displacement of the lower third of the oesophagus, which often shows mild compression, as described by P. G. Keates and O. Magidson.⁵ The changes in position do not usually cause pain and only rarely are they associated with obstructive symptoms. The experience of Shahin and Brombart suggests that wandering of the oesophagus may well explain some of the cases of intermittent pain of oesophageal type, usually associated with dilatation and tortuosity of the aorta, but occasionally in association with mitral valve disease. In such circumstances it would be worth while subjecting the patient to the manœuvres described by Shahin to see if the displaced oesophagus changes position and to note if this change is associated with the pain. Shahin found that repeated acts of swallowing while the patient lay prone or while leaning forward were most likely to induce the oesophagus to wander.

International Relations

To foster contact between members of the medical profession throughout the world the Royal Society of Medicine has set up an Office for International Relations in Medicine. Supporting the venture are the Royal Colleges in England and Scotland. The first director of the office is Dr. Hugh Clegg, and perhaps a specially warm welcome for the choice may be allowed in this journal, for which during his 20 years of editorship he did so much to build up an international reputation. Nobody can doubt the need for such an office at present. The world of learning seems to contract the faster it goes, according to some relativity principle yet to be formulated. News by satellite and travel by jet have made neighbours of all mankind. Nowhere is this truer than in medicine.

The basis of the new office is to be a register of relations between British medical schools, medical institutions, and specialist medical societies with similar bodies and medical centres in other countries, particularly in the Commonwealth. Medical centres as well as individuals should find the register useful, and in helping to ease medical communication throughout the world it will be complementing the work of the Commonwealth and International Medical Advisory Bureaux run by the B.M.A., which are able to offer much help and advice to individual visitors. The address of the R.S.M.'s Office for International Relations in Medicine is Chandos House, 2 Queen Anne Street, London W.1.

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Papers and Originals

Origin and Function of Penicillinase: a Problem in Biochemical Evolution*

M. R. POLLOCK,† M.B., F.R.S.

Brit. med. J., 1967, 4, 71-77

The title of this lecture is intentionally provocative. It is well known that there are many varieties of the enzyme that can split the β -lactam bond of penicillins and/or cephalosporins (Fig. 1)—the specific reaction referred to generally as “penicillinase.” And their physiological role in the life history of the bacteria which produce them is still a matter of controversy. But the case I wish to argue will be one in favour both of recognizing the relation between the various “brands” of the enzyme, despite many striking chemical differences, and of considering the possibility of a common or similar evolutionary origin.

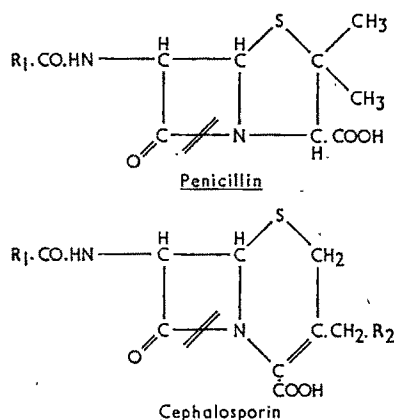


FIG. 1.—Basic structure of penicillins and cephalosporins, showing the position of the main variant side-chains (R_1 , R_2) and the specific β -lactam (CO-N) bond (indicated by the oblique double line) that is split by “penicillinase.”

At our present state of knowledge the history of penicillinase began in 1689. I know there was no enzymology in those days, but I'll explain how a little later on.

The penicillin and cephalosporin β -lactamases are produced by a wide range of Gram-positive and Gram-negative species of bacteria, and differ from each other enormously in the relative rates at which they hydrolyse different substrates. The range of substrates, which differ (in the penicillin class) in the side-chain (R_1) attached to the free NH_2 group of the “nucleus,” 6-amino-penicillanic acid, and (in the cephalosporin class) in that side-chain and also in the side-chain (R_2) attached to C_3 of the cephalosporanic acid nucleus, runs into many thousands. Most types of the enzyme, though predominantly attacking either the cephalosporins or the penicillins, will hydrolyse some members of the other group of compounds at a significant rate. It is the Gram-positive species that produce enzyme

with the highest activity and also in greatest quantity. This, when the relevant gene is maximally active (full “derepressed”), may amount to about 2% of the total bacterial dry weight, or probably over 3% of its protein.

In most of these strains the system is inducible: the penicillinase gene is usually strongly repressed, and production of the enzyme is minimal until a penicillin or cephalosporin is added to the culture, after which it may increase several hundredfold.

In most instances the enzymes are certainly responsible (probably exclusively) for the high degree of resistance to penicillins and/or cephalosporins manifested by the organisms that produce them. (For recent accounts of their biological, chemical, and physicochemical properties see the reviews by Pollock (1965a) and Citri and Pollock (1966).)

“Function”

The penicillinases of Gram-positive bacteria are among some of the most active enzymes known: second only to catalase. Their specific activities, expressed as turnover numbers (molecules of substrate split by one molecule of enzyme per minute at 30° C.), range around 1.5×10^5 (Pollock, 1965b).

Nevertheless, there are certain difficulties in accepting what many believe to be the naive assumption that the main or sole function of penicillinase, in the orbit of the organism that produce it, is to destroy penicillin.

The objections raised can be classified under four main headings. I will deal with them systematically and try to produce the counter arguments as we go along.

1. Substrate Specificity

It has been claimed that the enzyme may have a broader specificity than that provided by the β -lactam bond of penicillins and cephalosporins (Saz and Lowery, 1964; Saz *et al.* 1964). The a priori argument is that the penicillin nucleus is really only a condensation of two amino-acids, L-cysteine and D-valine, with an additional cross-bridge, and that the CO-N bond split is only a modified peptide link (Fig. 2). Penicillinase, then, might be regarded as a sort of modified peptidase: its penicillin-hydrolysing ability could be “incidental.”

Original suggestions (Saz *et al.*, 1964) that certain peptides were in fact hydrolysed by what were claimed to be purified preparations of *Bacillus cereus* penicillinase have not, however, yet been substantiated or successfully repeated.

Rather more impressive were reports from these authors of the specific inducing activity of certain straight chain amino

* Being the substance of the first Almroth Wright Lecture, in the 1967 series, given at the Wright-Fleming Institute of Microbiology, London W.2, on 1 May 1967.

† Professor of Biology, University of Edinburgh.

cyclic oligopeptides, on wild-type inducible penicillinase systems in *Staphylococcus aureus* and *B. cereus*. Their findings have not yet been consistently reproducible in all laboratories where they have been investigated. But the idea behind them is a particularly interesting one, and only a few weeks ago further reports appeared from Saz's laboratory (A. K. Saz, personal communication) claiming that induction of *B. cereus* penicillinase had been demonstrated with extracts from the cell walls of *Staph. aureus* containing muramic acid and peptides. The suggestion here, again, is that penicillinase is really a modified peptidase, perhaps one originally mainly concerned

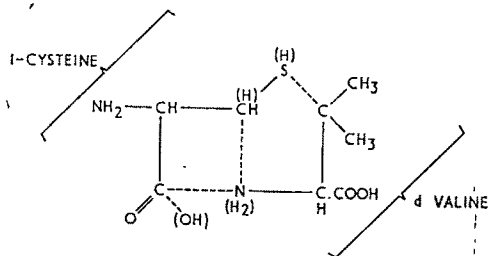


FIG. 2.—Basic structure of penicillin viewed as a cyclic dipeptide: L-cysteinyl-D-valine.

in cell-wall metabolism; but in any case not originally or primarily orientated towards the β -lactam ring of penicillins and cephalosporins.

We shall consider the possible relation of the enzyme to cell walls, from an evolutionary point of view, later on. But at the moment it is essential to point out that:

(a) No isolated and identified substance other than penicillins and cephalosporins has ever been unequivocally shown to act as substrate for purified preparations of β -lactamase—that is, so far as possible uncontaminated with other enzymes. Even if some slight peptidase activity had then been demonstrated it would hardly alter the significance of the overwhelming orientation of purified enzyme towards this particular β -lactam bond.

(b) Strains of *Staph. aureus*, *B. cereus*, and *B. licheniformis* genetically deprived of their β -lactamase activity—be it through a point mutation in the penicillinase gene or a complete deletion by plasmid elimination from the cell—show a profound loss in resistance to the penicillins. As might be expected by reason of its extracellular location and detoxifying action, the enzyme is a collective weapon against the antibiotic and does not often, in these organisms, give much protection to single isolated cells. But if resistance is tested with whole populations the effect of penicillinase can be shown to increase their penicillin-resistance by several orders of magnitude—for example, from 0.01 unit to several hundred units/ml. in *Staph. aureus*, and from 0.01 unit to several thousand units/ml. in *B. cereus* and *B. licheniformis* (M. R. Pollock, unpublished observations).

Significance of Low Penicillinase Activities

Many (fully induced) Gram-positive bacteria produce very high levels of activity—5,000 units per mg. dry weight being not at all unusual. However, among Gram-negatives—in particular the coliforms—activities may be so low (<1 unit per mg. dry weight) that it is difficult, at first sight, to believe that it could be of any value to the cells as an anti-penicillin agent. Moreover, there is often rather little apparent correlation between penicillin and cephalosporin resistance among coliforms and levels of their β -lactamase, as measured in the laboratory.

There are, however, a number of factors operative in this sort of comparison which make an assessment of function extremely difficult:

(a) Strains differ considerably in their “intrinsic” susceptibility to penicillins and cephalosporins. This, possibly, is a question of the sensitivity or accessibility of cell-wall synthesizing enzyme systems to these antibiotics; at all events it has nothing directly

to do with penicillinase. Many penicillinase-producing coliforms have a high intrinsic resistance, and the extra margin of resistance contributed by β -lactamase might be expected to be, for that reason, smaller than for those organisms with low intrinsic resistance.

(b) It may be most misleading to translate enzymic activities, as usually measured in the laboratory, into enzymic function in vivo under natural conditions. There are here three main relevant factors to be taken into consideration, as follows:

(i) The chemical and physical cell relationships and extra-cellular environment may be very greatly and significantly different in nature—for example, in the soil or in animal and plant tissues—from those normally operative in laboratory assays, where enzyme solutions or homogeneous cell suspensions have normally to be used. The degree of cell clumping, the local concentrations, and “feed-in” supply of substrate, etc., may be expected to be particularly important in relation to detoxifying enzymes.

(ii) The location of the enzyme with respect to the cell may be of vital significance. There may be advantages for an intrinsically sensitive cell to produce a penicillinase that is extracellular (like *B. cereus*, *B. licheniformis*, and some strains of *Staph. aureus*) for “clearing a way free of penicillin” in order to prevent the antibiotic actually reaching the susceptible cell itself (Pollock, 1962). But this involves a huge dilution effect, so that large quantities of the enzyme would need to be produced (as indeed appears to be the case with exo-penicillinase-forming organisms).

With different types of cell it may be more effective to have very small amounts of enzyme strategically located next to the cell-wall synthesizing enzyme systems on the surface of the cell—or attached to the membrane, as might indeed be the case with many of the coliforms which have small quantities of enzyme firmly and completely bound to cell structure (Smith, 1963a; Smith and Hamilton-Miller, 1963; Hamilton-Miller, 1963). It would be of great interest to know whether this enzyme is concentrated at “growing points” on the cell surface (in so far as they may be restricted in number and location), where active synthesis of cell-wall material is occurring—see reviews by Salton (1964) and Rogers (1965).

(iii) Enzymic efficiency in vivo can probably only rarely be gauged by measurement of maximal activity (“ V_{max} ”) in enzyme assays. This is because, in the latter, the enzyme is, by definition, always saturated with its substrate, whereas there are good reasons for believing that in the intact cell most metabolites are at very low concentrations, and their enzymes are therefore highly unsaturated. Operational enzyme activity is determined as much by affinity for the substrate as by turnover number. This means that in vivo the rate of the reaction catalysed by one unit of any given enzyme is governed as much by the concentration of its substrate as by its maximum specific activity.

These considerations apply especially to the penicillinases, where the affinity constant or “ K_m ” (defined as the substrate concentration at which the enzyme functions at 50% maximal efficiency), when measured for the common penicillins, is nearly always well above the minimal growth inhibitory concentration of the antibiotic.

A more valid measurement for any particular variety of the enzyme would therefore be one which has been referred to as “physiological efficiency,” being defined as V_{max}/K_m (Pollock, 1965b). This is directly proportional to the rate of substrate hydrolysis under conditions of gross enzyme undersaturation, and allows direct comparison between different penicillinases at any given penicillin concentration. By using this value it has been possible to show that varieties of penicillinase from the same species may differ at least sixfold in V_{max} but not significantly at all in physiological efficiency. The reason for this can be interpreted quite simply in enzymological terms; but the essential point here is that there is no difference between the rate at which they hydrolyse penicillin at the low concentrations normally expected in nature.

These factors still, of course, do not take into account further discrepancies that may arise between enzymic measurements on soluble extracts (which are necessary for controlled enzymological work) and those made in vivo with enzyme that is bound to intact cells. With whole cells, substrate-accessibility barriers (Smith, 1963b; Smith and Hamilton-Miller, 1963; Sabath *et al.*, 1965; Ayliffe, 1965; Hennessey, 1967) and/or factors altering the shape or “conformation” of the enzyme molecule associated with its binding to other

structures may often be operative and affect what might be termed the "cellular efficiency" of an enzyme.

(c) In certain instances normal, penicillin-sensitive wild-type strains of bacteria may be found to produce measurable but exceedingly minute quantities of penicillinase (Ayliffe, 1963, 1965; Smith and Hamilton-Miller, 1963; Eriksson-Grennberg *et al.*, 1965). It would seem at first sight to be an utterly useless activity. However, in some instances cells mutate spontaneously to form greatly increased quantities of the identical type of penicillinase. They thereby acquire greatly increased penicillin-resistance (Pollock, 1957; Eriksson-Grennberg *et al.*, 1965).

The classical case is that of a variety of *B. cereus* studied by Sneath (1955), where overnight culture of the original penicillin-sensitive strain in broth containing 1 unit of benzylpenicillin/ml. permitted its conversion to a new ("mutant") population of cells forming the same enzyme at 5,000 times the previous rate, with 300 times the resistance to the antibiotic—even when tested against single cells. The phenomenon was unequivocally shown to be due to a spontaneous mutation (presumably in some type of regulatory gene), the effect being to cause complete derepression of a pre-existing penicillinase structural gene, followed by selective overgrowth of the mutant by the penicillin present.

Previously, such combined mutation-plus-selection phenomena in bacteria were termed by Stanier (1953) "evolutionary adaptation" to distinguish them from "physiological adaptation," which included enzymic adaptation processes involving all the cells in a population and no change in genotype.

I do not, however, believe that this particular phenomenon has anything at all to do with evolution in the general sense. Rather it would seem to be a mechanism of biological adjustment, itself evolved as a type of populational adaptation to meet the needs of a whole community of individuals in the face of an intermittently intruding situation. Such a situation—the presence of toxic quantities of penicillin—may be supposed to have been previously encountered often enough to have allowed the acquisition of a fully fashioned structural gene for an enzyme which, however, is kept rigidly repressed (for economy of effort), apart from occasional "release" mutants which can be immediately selected by the penicillin if and when it presents itself in the environment.

3. Formation of Penicillins and Cephalosporins in Nature

So far, attempts to demonstrate the formation of these antibiotics in soil under natural conditions have not been successful, and a certain scepticism has developed about whether they are even indeed capable of being produced except as laboratory freaks (see Brian, 1957).

There are, however, several reasons why it might be difficult to isolate them from the soil: they are likely to be present in extremely low concentrations; they may be rapidly destroyed by the chemical environment or adsorbed on soil surfaces; and they may, indeed, be hydrolysed by the penicillinase formed by the large numbers of *B. licheniformis* and *B. cereus* cells undoubtedly present in most types of soil all over the world.

It does not really seem that attempts to demonstrate their formation have been anywhere near exhaustive.

Moreover, recently a strain of *Penicillium chrysogenum* has been coaxed to form penicillin, by growth on the surface of sterilized soil—rather capriciously, admittedly—and will form the antibiotic more regularly, under strictly controlled conditions, in aqueous soil extracts containing only lactose as additional nutrient factor (P. Hill, private communication).

4. Physiological Role of Penicillins and Cephalosporins

It is also sometimes argued that even if these antibiotics are formed under natural conditions they can be nothing other than waste products which are fortuitously toxic to certain bacteria. It is further argued that, in any case, susceptible bacteria must meet the antibiotics only very rarely, and it is

therefore unlikely they would have evolved enzymes specially to deal with them.

There are quite a number of points that must be emphasized here:

(a) Penicillins and/or cephalosporins are not rare oddities in the fungal world, as was once supposed. Table I lists no fewer than nine distinct genera of microfungi—comprising a total of at least 36 species (there are probably in reality many more)—that produce one or both of these two classes of antibiotic. All these genera may inhabit the soil at one time or another, and three out of nine are dermatophytes, normally saprophytic on skin and/or other keratinized body surfaces.

TABLE I.—Microfungal Genera Forming Penicillins and/or Cephalosporins

<i>Aspergillus</i> (7 species) (see Sanders, 1949; Cole, 1966)
<i>Cephalosporium</i> (see Abraham, 1962)
D <i>Emicelopsis</i> (see Kavanagh <i>et al.</i> , 1958; Uri and Valu, 1963)
D <i>Epidermophyton</i> (Uri and Valu, 1963; Cole, 1966)
<i>Maibranchea</i> (see Sanders, 1949)
<i>Paecilomyces</i> (Pisano <i>et al.</i> , 1961)
<i>Penicillium</i> (23 species) (see Sanders, 1949; Cole, 1966)
<i>Streptomyces</i> (Miller <i>et al.</i> , 1962)
D <i>Trichophyton</i> (see Sanders, 1949; Uri and Valu, 1963; Smith and Marples, 1964; Cole, 1966)

D=Dermatophytes.

(b) All the main penicillinase-producing species of bacteria are either natural inhabitants of soil and water in large numbers (*B. cereus* and *B. licheniformis* and *Pseudomonas*) or are found there from time to time (such as *Aerobacter*, *Klebsiella*)—or they are typical skin saprophytes (*Staphylococcus*). In other words the natural environments of penicillin-formers seem to be similar to, if not identical with, those of penicillin-destroyers.

It is probable that strains of *Penicillium* or *Aspergillus* are not infrequently present together with *B. cereus*, *B. licheniformis*, or *Pseudomonas* in the same sample of soil (Holding *et al.*, 1965). And penicillinase-forming *Staph. aureus* has been found coexistent with penicillin-forming *Trichophyton* on the skins of hedgehogs in New Zealand (Smith and Marples, 1964).

There seems no need to puzzle why some strains of *Staph. aureus*, isolated in 1937 well before the therapeutic era of penicillin, were found to produce the same penicillinase in just as potentially large amounts as that formed by "modern" post-penicillin strains. Therapeutic penicillins have, of course, certainly enormously increased the incidence of penicillinase-positive strains of staphylococci—presumably by natural selection (see Ciba Foundation, 1962). But they have not detectably altered the nature of the penicillinase genotype (M. H. Richmond, private communication). It can be argued that the evolutionary stimulus had already been there previously—perhaps for many millions of years.

(c) Finally, it seems a priori probable that most soil organisms are engaged in a perpetual struggle for survival in an environment where supply of nutrients is a constant factor limiting growth and multiplication. Any weapon reducing the growth rate of a competitor might be expected to help survival and further growth of the organism producing it.

It is indeed possible to demonstrate, in the laboratory, that both *P. chrysogenum* and *B. licheniformis* inoculated together (the latter somewhat after the former) into the same soil sample will grow to a final total number which is considerably lower than that attained by either alone, when inoculated into an aliquot sample separately (M. R. Pollock, unpublished experiments).

The stage could therefore be said to be set for a battle between the microfungi and the bacteria, such as to encourage the evolution both of the penicillins and cephalosporins on the one hand and of the enzymes to hydrolyse them on the other.

Moreover, it must be remembered that penicillinase is known only among those organisms with *N*-acetylmuramic acid-containing mucopeptide in their cell walls (the synthesis of which is specifically inhibited by the penicillins) which are sensitive to, and threatened by, penicillin. If penicillin hydrolysis is only an incidental by-reaction of another type of enzyme activity with real physiological significance, why is it not found in organisms that do not have to bother about penicillin?

At least it can be said that the situation, as thus analysed, makes teleological sense.

The evidence is, however, circumstantial, and it must be accepted that this interpretation remains highly questionable. All that can be claimed is that it is not unreasonable.

"Origin"

1. Physiological Adaptation

(a) In general, most wild-type penicillinase-producing strains of bacteria isolated in the absence of penicillins and cephalosporins show very low enzymic activity. However, nearly all Gram-positive strains and a proportion of Gram-negatives are typically penicillinase-inducible, and respond rapidly to treatment with the antibiotic by increasing rates of enzyme formation up to 300 times the "basal" level. No permanent genetic change is involved, and the cultures revert to their usual uninduced level of production after a period of growth in the absence of inducer (see Pollock, 1959).

I do not propose to deal further with this well-known phenomenon of enzyme induction here. It is as vital a part of resistance to the antibiotics as direct enzymic action itself.

(b) As mentioned previously, there is another method by which wild-type "micro-constitutive" strains—both among Gram-negatives (Eriksson-Grennberg *et al.*, 1965) and Gram-positives (Sneath, 1955)—can increase their rate of penicillinase formation: what I have called a *populational adaptation*, involving an apparently spontaneous mutational event in a very small proportion of a population, derepressing the penicillinase structural gene to allow its full expression, followed by selection of such mutationally altered cells in the presence of a penicillin concentration which will suppress the growth of the rest of the population.

Although the change is genetically fairly stable, it will materialize rapidly, and there are grounds for regarding it as a physiological type of adaptation when applied to the whole population.

2. Genetic Control

(a) The populational adaptation referred to above can also, of course, in another context, be regarded as a genetic type of acquisition of increased penicillinase activity.

(b) More fashionable, and better studied at the moment, is the mechanism by which cells can acquire penicillinase activity—from scratch, so to speak—by acceptance of extrachromosomal factors (episomes or plasmids) which can carry the β -lactamase gene complex in a state that is partially autonomous from the chromosome, but otherwise functions in the coding and control of formation of the enzyme as do the chromosomal genes.

In coliforms the penicillinase genetic system may constitute part of an extrachromosomal "R" or resistance factor, which, by linkage up with a "T" or transfer factor, may pass from one cell to another spontaneously (not necessarily within the same species) in the process referred to as "infectious heredity" (Datta and Kontomichalou, 1965).

In *Staph. aureus*, "penicillinase" plasmids can be transferred from one cell to another—not (so far as is known) spontaneously, but by transduction through an infecting bacteriophage (see Richmond, 1965a; Novick, 1967). It is possible, with staphylococci, for the cell to possess more than one type of penicillinase plasmid at the same time. And in this organism it seems likely that the same or analogous penicillinase genes can, in certain strains, exist fully integrated on the chromosome (Asheshov, 1966), though there is yet no clear evidence that they can pass reversibly from the extrachromosomal to the chromosomal state like episomes.

3. Evolutionary Origin

When we come to consider the problem of evolution we enter the realms of high speculation. In spite of the fact that we accept the fact of organic evolution unquestioningly—at least I *suppose* we do—we know extremely little about its mechanism. Yet so many biologists seem tacitly to assume, rather uncritically, its neoDarwinian basis and its occurrence through a process of natural selection operating on random "spontaneous" mutations and recombinational events in the genome.

With the rise of molecular biology it is now possible to visualize possible steps at a chemical level and be a great deal more precise in our hypotheses.

Unfortunately we do not yet know the exact amino-acid sequence of any type of penicillinase—though such an analysis for one of the staphylococcal varieties is only just short of completion (R. P. Ambler, private communication). Nothing, of course, is known about the base sequences in the relevant deoxyribonucleic acid of its gene. So speculations must be linked to rather more general considerations of function and properties.

At the beginning of this lecture I emphasized the variety in properties of the different penicillinases, particularly in immunology, substrate profile (relative activities on various penicillins and cephalosporins), and overall amino-acid composition.

I now wish to do the reverse and point out the similarities which are (perhaps a little tendentiously) stressed in Table II (see also Pollock, 1967). The number of individual amino-acid residues may differ considerably, but the combined basic and combined acidic amino-acids are fairly similar; cysteine is absent; the specific activities range only over a factor of 10 (which is very narrow considering the wide range of values for enzymes in general) and the "physiological efficiencies" (previously defined) only fourfold.

TABLE II.—Properties of Penicillinases from Different Bacterial Species

	<i>B. cereus</i>	<i>B. licheniformis</i>	<i>Staph. aureus</i>	<i>E. coli</i>
No. of varieties examined	2	2	2	1
Molecular weight	31,000–35,000	28,000	29,000	16,700
N-terminal amino-acid	Asp.	Lys.	Lys.	
Amino-acid composition (No. of residues per molecule):				
Cysteine	0	0	0	
Lysine + arginine	40–43	38	48–49	
Aspartic + glutamine	60–69	64–66	57–64	
Total hydrophobic	67–85	75	66–75	
Differential rate of synthesis (μ g. enzyme/mg. dry bacterial weight)	9–11	11–12	8–9	1.0
Molecular activity $\times 10^6$ (No. molecules benzylpenicillin hydrolysed/molecule enzyme/min. at 30° and pH 7)	1.5	0.2–1.1	0.2	0.19
Physiological efficiency $\times 10^6$ (for definition, see text)	5–6	5–6	16	4

From data summarized by Citri and Pollock (1966).

Though the amino-acid compositions of the *B. cereus* and *B. licheniformis* varieties are as different from each other as either is from the staphylococcal enzyme, there is a striking though quantitatively slender immunological cross-reaction between these two (Pollock, 1967), which would indicate some partial homology in tertiary structure and therefore probably elements of amino-acid sequence resemblances which may also occur in other types. There are, however, no similar peptides found on tryptic hydrolysis of the staphylococcal and *B. licheniformis* enzymes (R. J. Meadway, private communication).

The molecular weights of the varieties from Gram-positive organisms are almost identical, whereas that from *Escherichia coli* (Datta and Richmond, 1966) is about half that of the

others. There is good evidence that in all varieties there is only one N-terminal amino-acid residue, and therefore a single peptide chain, and it could be argued (as in the case of haemoglobin chains—Fitch, 1966) that the Gram-positive variety originated from an "internal" duplication of the more primitive Gram-negative chain.

There is perhaps significant evidence supporting some extent of common pathway in the evolutionary history of these enzymes. It seems unlikely that the degree of biological and structural similarity evidenced could have occurred from a purely convergent line of development.

Be that as it may, we shall assume for the moment that the penicillinases have had a common evolutionary origin, though it is not strictly necessary to do so for the argument I shall develop.

I shall also accept two other propositions, both of which are reasonable and in fashion—but very far from being proved:

(a) That the structural genes for most existing enzymes have evolved through modification of pre-existing structural genes for other enzymes which must inevitably be closely related in amino-acid sequence and therefore probably similar in biological specificity.

(b) That the most plausible mechanism for ensuring the stability of useless intermediary steps in the evolution of one enzyme from another during the period before a significantly useful version had emerged would be through preservation of the existing enzyme by an initial duplication of the relevant gene. In diploid organisms this might not be necessary, at least not at the first stage. In haploids it would be immediately essential and in diploids eventually so, except in so far as such evolution could be by substitution rather than by addition. The expansion of the genome through phylogeny must imply that most evolution has been through addition.

The mechanisms by which the "second copy" is modified need not really concern us here. It could be through genetic shuffling: by recombination, translocation, deletion, or inversion; but in most cases probably through a sequential series of point mutations.

In what direction do these two assumptions point?

Taking the latter first, it is implied that evolution might proceed faster in diploids because initial modifications to one allele would be automatically protected in their early "useless" stage, at least in heterozygotes, without having to wait for linear reduplication. Homozygotes, however, would become lethal and highly disadvantageous, and so duplication would tend to follow at some stage.

So far no bacterial species have been found to be completely diploid, but temporary partial diploids are frequent in staphylococci (Novick and Richmond, 1965; Novick, 1967)—either in the sense of two allelic extrachromosomal plasmids or plasmids plus chromosomal alleles. In that sense—which could, however, be relatively unimportant—the situation may have

been favourable for the evolution of penicillinase, whose genes are now known to be capable of forming diploids—at least under laboratory conditions (Richmond, 1965b).

The first assumption implies that we should look for the evolutionary origin of penicillinase among enzymes attacking or combining with molecules resembling penicillin. And where better should this be done than among those dealing with the biosynthesis of the cell-wall mucopeptide, a process we know to be specifically inhibited by penicillin (see Park, 1966) and one of whose enzymes, therefore, is a likely candidate?

Fashions change in the interpretation of penicillin antibiosis. At the moment the reactions in cell-wall synthesis which have most attention in staphylococci are ones directly involving the exchange of the terminal D-alanine residue of the oligopeptide chain attached to muramic acid, with the first glycine of the pentaglycyl peptide attached to L-lysine of a near-by oligopeptide chain. This reaction, which may be one of the last of the sequence in cell-wall synthesis, thus forms a cross link between two such peptide chains (see Fig. 3). It has in fact been shown to be extremely sensitive to inhibition by penicillin *in vitro* (Wise and Park, 1965).

It has also been pointed out (Collins and Richmond, 1962) that *N*-acetylmuramic acid shows a strong three-dimensional structural analogy to penicillin (though superficially there is little resemblance between their chemical formulae). Tipper and Strominger (1965), however, stress rather the analogy with d-ala-d-ala, emphasizing that penicillin is a modified peptide, and that the penicillin-sensitive transpeptidation reaction itself is a type of peptidase (which, it has been argued, is also true of penicillinase). Ironically, Wise and Park (1965) and Park (1966) stress rather the L-alanyl-γ-D-glutamyl part of the cell-wall molecule as being most closely analogous to penicillin.

It has in fact been claimed in Saz's laboratory—as mentioned previously—that extracts of *B. cereus* cell wall can induce penicillinase in this organism. Induction tests are very sensitive, and they are easier to perform than tests for substrates. They can thus reasonably be taken, if properly controlled, to indicate the possibility of enzymic affinity for the substances as substrates; though it certainly does not necessarily follow that inducers are substrates—or indeed complexants of any kind—for the enzyme. (We have, however, tested *N*-acetylmuramic acid and the d-ala-d-ala dipeptide as inducers for the enzyme in *Staphylococcus* and *B. cereus* without finding a trace of activity.)

If the *N*-acetylmuramic acid/penicillin analogy is significant another candidate for ancestry would be the extracellular bacterial lysozyme first described in *Bacillus subtilis* (Richmond 1959) but probably also produced by many other species. Like the lysozyme from egg-white, this enzyme probably attacks the cell-wall mucopeptide by hydrolysing the *N*-acetylmuramic acid/*N*-acetyl glucosamine bond. It might therefore conceivably be structurally related to penicillinase.

Indeed, following the elucidation of the tertiary structure of egg-white lysozyme by Blake *et al.* (1965) it was reported by Johnson (1967) that this enzyme does indeed bind penicillin to a significant extent, at a site which also binds derivative of *N*-acetylmuramic acid. Penicillin, moreover, was also found to inhibit the action of lysozyme. The groups of the molecule that appear to be involved in this binding reaction with lysozyme are not, however, apparently those originally thought to form the basis for the postulated homology with *N*-acetylmuramic acid (Collins, 1967). The significance of this reaction remains therefore uncertain.

Other interesting candidates would be: (a) the enzymes in lysostaphin (Schindler and Schuhardt, 1964, 1965) among which may be some peptidases responsible for splitting the d-ala-gly bond that is formed by the transpeptidase previously mentioned as being specifically inhibited by penicillin; and (b) the "competase" described by Young *et al.* (1964) which splits the link between *N*-acetylmuramic acid and the L-ly-

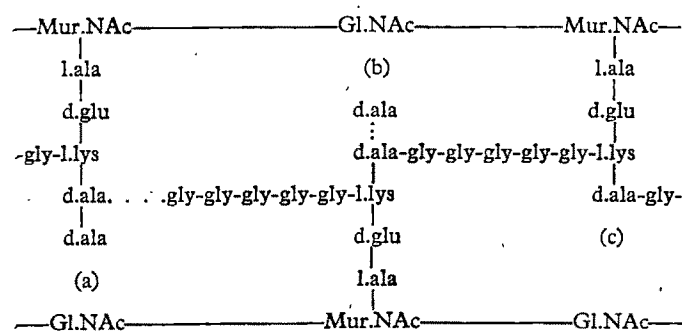


FIG. 3.—Basic unit structure of staphylococcal cell wall, drawn to indicate the two last steps (a and b) in the specific penicillin-sensitive transpeptidation reaction which completes the bridge (c) between the two different oligopeptide chains, and thus finally rigidifies the whole macromolecular complex into a stable molecular exoskeleton for the cell. Based on an article by Wise and Park (1965). Mur.NAc=*N*-acetylmuramic acid. Gl.NAc=*N*-acetyl glucosamine. Abbreviations for amino-acids as suggested by the *Biochemical Journal*, 1967, 102, 3.

residue that is the first of those making up the peptide "side-chain," and confers transformation competence on *B. subtilis*.

What of course is needed here is the isolation and characterization of these cell-wall enzymes in order to see if there are any amino-acid sequence homologies or other types of resemblances between them and the relevant penicillinase.

However, the fact remains that penicillin does inhibit a step or steps in cell-wall biosynthesis quite specifically, and this must almost inevitably mean that it combines specifically with one of the enzymes involved. Moreover, penicillin is known to combine with high affinity, and very specifically, with some sort of receptor site (the P.B.C. or "penicillin-binding-component"—see Cooper, 1956) which is present only in those organisms that are highly susceptible to penicillin. This component could logically be one of the cell-wall synthesizing enzymes, and it is not unreasonable to suppose it might have evolved, through modification of the site that combines with penicillin, to become capable of hydrolysing the antibiotic instead of simply being inhibited by it. This possibility, and related ones, have been discussed recently by Boman *et al.* (1967).

Evidence

In attempting to tackle the general problem of penicillinase evolution itself, is it possible to obtain any direct evidence of the mechanism?

We have made efforts along these lines of approach as follows:

(a) Palaeoenzymological Evidence

In a survey of a wide range of different present-day isolates of *B. licheniformis* from all over the world, strains could be sharply classified into two groups according to the properties of the penicillinase they produced (Pollock, 1965b). The enzyme occurred in two related but quite distinct molecular types, differing by only a very few (probably two or three) amino-acid residues and a number of enzymological properties.

Accordingly, when Sneath (1962) revived some spores of *B. licheniformis* which had lain dormant in the dried soil stuck to the roots of some plant specimens preserved untouched in the British Museum since 1689, the opportunity was seized of examining the properties of the penicillinase produced by the strains found (M. R. Pollock, unpublished experiments). They all fell clearly into one of the two types existing at present: their substrate profiles and immunological reactions indicating that no evolutionary change had occurred at least during the last 270-odd years—a short enough time, of course, in absolute terms; but in terms of the maximum possible number of cell generations, equivalent to 100 million years or so on the scale of human generation time, and therefore presumably long enough for evolution to have occurred if cell generations were the main operative factor.

(b) Laboratory Studies

"Blind training" of the existing penicillinase genome by serial subcultures of *B. licheniformis* in marginally inhibitory concentrations of the new penicillins, such as methicillin, did not give rise to cells producing penicillinase with increased ability to hydrolyse the compounds in question.

Attempts to follow sequential mutations in the penicillinase structural gene, isolated after mutagen treatment of *B. licheniformis*, that might have some physiological significance in changed enzyme specificity yielded nothing of interest. It was, however, possible to show that single-step, presumptive point mutations, supposedly involving single amino-acid residue substitutions in the molecule, could produce a complete inversion of relative penicillinase and cephalosporinase activities (M. R. Pollock, unpublished observations). In other words, a single-step mutation could result (in two instances: see Fig. 4) in an enzyme originally predominantly

a cephalosporinase. But in neither case was there a clearly significant absolute increase in specific activity. It could therefore hardly be claimed that the change was one that must have evolutionary significance. Nevertheless, it might be the first step in a significant evolutionary sequence, and these instances at least indicate the considerable alteration in substrate specificity that may result from a single mutation, and can be regarded as possible examples of the sort of event that may be occurring in the process.

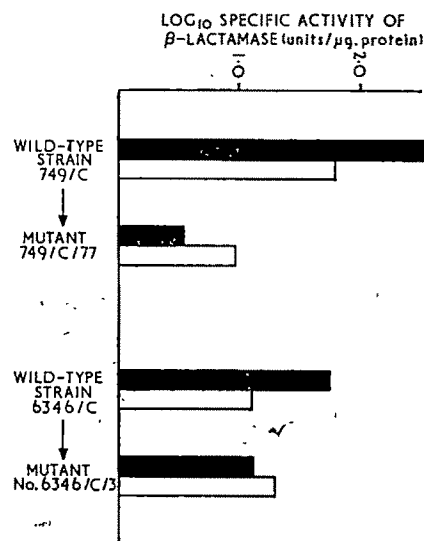


FIG. 4.—A mutational "conversion" of penicillinase into cephalosporinase. Comparisons of specific activities (units/μg. protein) in hydrolysing penicillin and cephalosporin of wild-type and mutated penicillinases produced by two different strains of *B. licheniformis*. ■ Penicillinase (benzylpenicillin as substrate). □ Cephalosporinase (benzyl ceph. C as substrate for 6346 strains and cephaloridine for 749 strains).

It is conceivable that the type of modification observed here is not far removed from the naturally developed change that may be presumed to have occurred in the past in the evolution of the two extracellular β-lactamases of *B. cereus* recently separated and characterized by Kuwabara and Abraham (1967). These two types (one of which is predominantly, if not exclusively, a penicillinase (β-lactamase-1: the original α-penicillinase) whereas the other has approximately equal activity on cephalosporins and penicillins (β-lactamase-2)) differ in thermostability, activation by Zn⁺⁺ and other characters. Their comparative structural properties are so far unknown. But in their response to induction and the simultaneous conversion of the systems controlling their formation to constitutivity, by a single mutational step, they behave as if their genes were components of one operon—that is, contiguously located on the chromosome and under a single control system. They may therefore, for this reason alone, be considered to be possibly evolutionarily related.

(c) Field Survey

The advent, and therapeutic use on a wide scale, of the new penicillins, such as methicillin, cloxacillin, and oxacillin, which are very resistant to hydrolysis by staphylococcal penicillinase, raised the possibility that the organism might respond by developing a modified enzyme that would more effectively destroy these compounds. The prospect of following the evolution of a new enzyme with biochemical and genetical checks at every stage seemed an interesting possibility. Accordingly, a systematic biochemical survey of newly isolated strains of staphylococci showing increased resistance to methicillin was instituted at the Central Public Health Laboratory, Colindale.

The results so far have been unequivocally negative. Increased methicillin-resistance has undoubtedly occurred, and the number of isolates showing some rise in resistance to methicillin has increased. But no new type of enzyme has emerged, and there has been no significant increase in the quantity of enzyme produced (Richmond, 1966; K. G. H. Dyke, unpublished results).

The increase in resistance, which in any case has been modest, is of the "intrinsic" variety and could be due to a cell-wall

synthesizing machinery with a greater capacity for standing up to the penicillinase-resistant penicillins than that predominating in pre-methicillin days. Its biochemical nature and the mode of its emergence remain a mystery.

The most important single factor contributing to the development of penicillin resistance in staphylococci in recent years would appear to be probably the infectious spread of penicillinase plasmids mentioned previously.

Conclusion

All these scrappy and indecisive points, the indirect and circumstantial evidence, and the speculative and perhaps tendentious arguments may seem rather naive and primitive attempts for tackling so difficult and huge a problem as biochemical evolution, albeit of a single enzyme-type. But here and there a few indications and direction pointers have emerged, most of them leading towards a demand for greater information on the amino-acid sequences of more and more enzymes. And if the time-scale for evolution may still be wrong for a direct experimental approach (we really do not know about this) it is through the analysis of bacterial proteins at a biochemical level that we may still hope to have the best chance of obtaining some significant results.

Summary

The enzyme, generally known as "penicillinase," that hydrolyses the β -lactam bond of penicillins and cephalosporins, with production of the antibiotically inactive penicilloic and cephalosporic acids, exists in a number of different forms, produced by a wide range of Gram-positive and Gram-negative bacterial genera (*Bacillus*, *Staphylococcus*, *Escherichia*, *Klebsiella*, etc.).

Despite some striking chemical and biological differences, there are probably significant resemblances between most of the varieties of penicillinase that have been studied in purified preparations. This supports the hypothesis of a common or closely related evolutionary origin.

The restricted specificity and high detoxifying activity of most penicillinases suggest that their physiological functions and evolutionary pathways are specifically related to the antibacterial action of the penicillins and cephalosporins. Moreover, the production of these antibiotics is more widespread among soil and dermatophytic microfungi than is commonly supposed, and the natural distribution of penicillin-producing micro-organisms seems to correspond fairly closely to that of penicillinase-producers.

The recent demonstration of significant penicillin production by *Penicillium* growing in soil unsupplemented by "artificial" nutrients suggests that previous scepticism regarding formation of the antibiotic "in nature" may not be justified, and that the penicillin/penicillinase relationship may be of importance in soil ecology.

Consideration of the evolutionary origin of penicillinase remains highly speculative, though it is clear that the various forms of the enzyme, as we now know them, pre-existed the therapeutic penicillin era, the only effect of which, in this context, has been to increase by natural selection the proportion of bacteria producing them.

Search for a possible penicillinase-ancestor is focused on the only other known class of protein that must, on a priori reasoning, be capable of specific combination with penicillin—that is, one or other of the enzymes involved in biosynthesis

of the mucopeptide of the bacterial cell wall, a reaction known to be specifically inhibited by this antibiotic.

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Direct Exchange Blood Transfusion in Treatment of Hepatic Coma

J. A. McLEAN,* M.D., M.R.C.P., F.R.A.C.P., M.C.P.A.; H. A. LUKE,* M.B., D.D.R., F.C.R.A., F.F.R.

Brit. med. J., 1967, 4, 78-80

The first recorded case of recovery from hepatic coma after an exchange blood transfusion was that of Lee and Tink (1958). They gave two exchange transfusions of fresh blood to a boy aged 13 who was deeply jaundiced and comatose. After the first transfusion of 3,260 ml. his condition was unchanged, but when a second exchange of 3,140 ml. was given he improved and recovered completely.

Trey *et al.* (1965) reported seven cases treated by exchange transfusion. Approximately twice the patient's blood volume was exchanged. Freshly donated heparinized blood was administered under pressure on the venous side while blood was simultaneously removed from an artery. Five of the seven cases recovered completely. They were fully reported by Trey *et al.* (1966). Berger *et al.* (1966) put on record another recovery from fulminating hepatitis after exchange transfusion.

In the above cases fresh heparinized blood was used, and it is the purpose of this paper to describe a technique for directly giving large quantities of unmodified blood.

Materials and Method

Rotary pumps designed by Julian Smith (1941) for direct transfusion were used. Rubber tubing was replaced by polyvinyl tubing (Portex size 12E), which gives a better flow rate and is translucent. A disadvantage of polyvinyl tubing is that at low temperatures it is inelastic, so sterilization is carried out in boiling water immediately before the transfusion to ensure that the tubing is warm and elastic when used. Julian Smith transfusion needles with an inside diameter of 1.6 mm. and highly polished internal surface are used to withdraw blood from the donors.

Plastic catheters for the recipient are prepared from Teflon tubing with an internal diameter of 1.5 mm. Percutaneous catheterization of veins is performed with the Seldinger (1953) technique.

The rotary pumps are mounted on two bridges—one on each side of the patient. On the donor side a clamp for holding a flask of sterile normal saline is attached to the bridge.

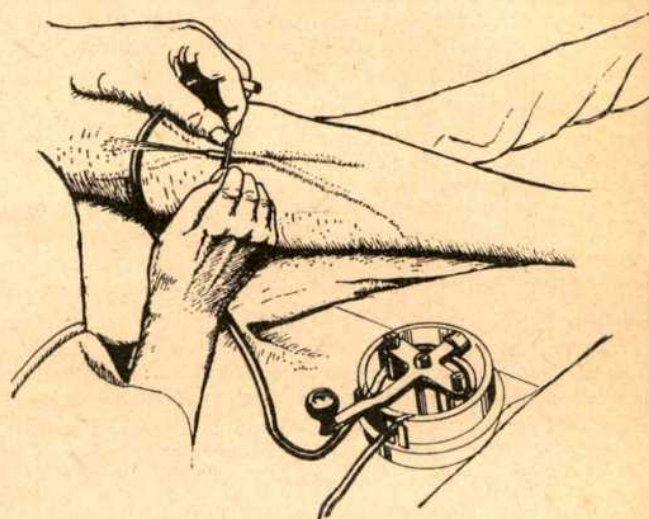
Exchange transfusions are performed under local anaesthesia. Usually from 8 to 11 donors were used, and they were examined and tested for compatibility immediately before the transfusion was begun.

The patient lies on his back with one pillow under the head and a small pad under the sacrum. The thighs are slightly abducted and local anaesthesia is injected in the skin and subcutaneous tissue just medial to the femoral artery. A small incision is made in the skin and a Seldinger needle is inserted into the femoral vein. With the usual technique the Teflon catheter is guided into the femoral vein by the flexible wire, which is then removed. The catheter is connected to polyvinyl tubing fitted in the pump, while the other end of the tubing passes into a transparent measuring cylinder into which the blood flows.

A second Teflon catheter is inserted into a vein on the other side of the patient. If there is no suitable vein at the elbow the catheter may be inserted in the other femoral vein so that it passes into the inferior vena cava proximal to the first catheter.

In the meantime polyvinyl tubing has been fitted into the second rotary pump and the tubing filled with normal saline. One end of the tubing is then taken out of the saline and connected to the Teflon catheter, which will transfuse blood into the patient.

The first donor is brought in and lies on a trolley adjacent to the patient. The transfusion needle is usually inserted in a distal direction and is not connected to the polyvinyl tubing until it is well placed in the vein (see illustration). With this technique a small amount of blood is spilt.



Blood transfusion rotary pump with polyvinyl tubing and insertion of transfusion needle in donor.

The transfusion is started by rotating both pumps simultaneously so that blood is removed from the patient at the same rate at which it is transfused. The usual rate of a direct blood transfusion is 500 ml. in four minutes. The needle is removed from the arm of the donor, who is immediately taken to a rest-room. The flask of saline is replaced and a fresh vinyl tube is fitted into the pump. The second donor comes in to give blood, and the procedure is repeated with each donor in turn until the operation is finished. Throughout the transfusion the volumes of blood infused and removed are checked and the clinical condition of the patient is assessed. The volume of saline must also be noted, and can be kept to a minimum by not connecting the vinyl tubing from the donor until the saline has been pumped out.

After completion of the transfusion the two catheters are removed and the sites of entry compressed for a few minutes.

Results

We have given direct exchange transfusions to four patients in hepatic coma. The first suffered from cirrhosis of the liver with oesophageal varices, and coma occurred after massive haemorrhages. In the other three patients coma was due to fulminating hepatitis. The clinical reports are briefly as follows.

* Alfred Hospital, Melbourne

Case 1

A man aged 53 was admitted to the Alfred Hospital on 1 July 1962. Recent investigation had shown oesophageal varices, and laboratory tests gave the following results: bilirubin 3.0 mg./100 ml.; cephalin flocculation positive (+++); S.G.O.T. 132 units; S.G.P.T. 70 units; prothrombin 60%. On the day of admission he passed three melaena stools. Haemoglobin was 7 g./100 ml. An intravenous drip was set up and he was given 4 units of acid citrate dextrose blood, 1 litre of 5% dextrose, and 0.5 litre of 0.9% saline. His condition deteriorated; he became mentally confused and had further melaenas. A second transfusion of 2 units of acid citrate dextrose blood, 1 litre of 5% dextrose, 1 litre of 0.9% saline, and 1 litre of Hartmann's solution was given, but there was no improvement. He was then given a direct blood transfusion from one donor (500 ml.), and his condition improved—he was more alert and able to answer questions intelligently. Three days later there was further haemorrhage and he became deeply jaundiced and comatose. On the eighth day after admission he was given a direct exchange transfusion from seven donors (volume 3.5 l.), but there was no improvement in his coma. He began to have convulsions, and died eight hours after the transfusion. A complete necropsy was not performed, but the abdomen was opened and the stomach and upper bowel were examined. There had been no recent haemorrhage. Histological section of the liver showed portal cirrhosis and nodular hyperplasia.

Case 2

A man aged 61 was admitted to Fairfield Hospital on 9 April 1966 suffering from infectious hepatitis. After admission his condition deteriorated—jaundice became deep, and foetor hepaticus, ascites, and flapping tremor occurred. He became increasingly drowsy, proceeding to a precomatose state. Melaena stools were passed and he vomited blood. He was given a direct exchange blood transfusion from eight donors (volume of blood 4 l.). Results of laboratory tests before and after the transfusion were as follows. Prothrombin increased from 27 to 51%. The platelets rose from 44,000 to 116,000/cu. mm. Bilirubin fell from 46.8 to 29.4 mg./100 ml. Serum protein increased from 3.7 to 4.9 g./100 ml. Clinical improvement was shown by less drowsiness, disappearance of foetor hepaticus, and no further bleeding. Two days later deterioration occurred. He developed signs of a chest infection and candida were grown from sputum and blood culture. He became anuric and died on 18 May. At necropsy the liver was shrivelled with surface abscesses. The lungs were congested, with consolidation in the upper lobes.

Case 3

A woman aged 38 was admitted into the Royal Melbourne Hospital on 4 August 1966. On admission she was drowsy and deeply jaundiced. She had foetor hepaticus and liver flap. Two days later her condition deteriorated; she became mentally confused and developed ascites. Peritoneal dialysis was begun, but without any improvement, and eight days after admission she was deeply comatose. At this stage, when extremely ill, she was given a direct exchange transfusion from eight donors (volume transfused 4 l.). Blood values showed an improvement; the bilirubin fell from 33 to 17 mg./100 ml. and platelets rose from 90,000 to 125,000/cu. mm. There was no clinical improvement, however, and she died seven hours later. At necropsy the liver was small with a wrinkled capsule (weight 730 g.). Nodules of regenerating tissue could be seen among areas of necrotic liver substance.

Case 4

A woman aged 31 was admitted to Fairfield Hospital on 15 July 1966. Eighteen days previously she had noticed jaundice, which progressively deepened. On admission she was mentally confused, with foetor hepaticus and a flapping tremor. The following day she was stuporous, jaundice was deeper, and the liver had become impalpable. On the third day after admission she became comatose and was given a direct exchange blood transfusion from 11 donors (volume transfused 5.5 l.). Laboratory tests showed an improvement—the bilirubin fell from 32 to 15 mg./100 ml., the prothrombin increased from 15 to 56%, and the platelet count rose from 180,000 to 260,000/cu. mm. Two days later, while comatose,

she was given an exchange transfusion of heparinized blood (5.5 l. was exchanged). There was no improvement in her mental state, while the platelet count fell from 169,000 to 125,000/cu. mm. and prothrombin was 34% before the transfusion and 34% at the end. Two days later another exchange transfusion of 5.5 l. of heparinized blood was given. The platelet count fell from 101,000 to 83,000/cu. mm., while prothrombin increased from 24 to 37%. There was no immediate clinical improvement, but 36 hours later she was mentally alert and rational and made a complete recovery. A further gastrointestinal haemorrhage occurred, and was controlled by a direct transfusion from two donors.

Discussion

The first and third patients were given direct exchange transfusions when in a terminal state, but in both there was no further bleeding after the infusion of unmodified blood. The main advantage of direct transfusion over heparinized blood is its better effect as a haemostatic. This was indicated by the blood tests before and after transfusion in Case 4. Both platelet count and prothrombin increased after the direct exchange transfusion, while the platelets were less numerous after heparinized blood and the prothrombin remained the same. It has been said that serious liver disease is a contraindication to heparin therapy and heparin should not be given to patients with potential or actual gastrointestinal bleeding (Griffith and Boggs, 1966).

In hepatic coma the use of citrated blood is contraindicated because of the danger of citrate intoxication and the possibility of enhanced bleeding from massive transfusion. The terminal liver failure in the first patient may have been contributed to by massive haemorrhages and replacement by citrated blood. If direct blood transfusion had been given initially bleeding could have been controlled.

Platelets and coagulation factors transfused by the direct method have a limited survival period and if bleeding is persistent repeated transfusions are necessary. In the treatment of hepatic coma repeated exchange transfusions have been advocated. In the second case, where only one exchange transfusion was given, death occurred subsequently from infection; whereas in the fourth patient a direct exchange transfusion was followed by two heparinized blood transfusions and a further small direct transfusion. This patient probably recovered because she was kept alive long enough for regeneration of a sufficient number of liver cells.

Direct exchange of unmodified blood has advantages but also the disadvantage of a more difficult technique. Firstly, suitable donors must be obtained, and in Melbourne the Red Cross Blood Transfusion Service has a special list of donors available for emergency. Secondly, the technique must be learnt and practised—it is not suitable for occasional use only.

With plastic materials and a rotary pump there is minimal difficulty from blood-clotting, and the only hazard is the donor, who must have good veins to ensure a rapid flow of blood. The usual practice is for the donor to wait in the rest-room with his forearm immersed in an arm bath of hot water.

In cases of hepatitis the risk of infection of donors is to be considered and special precautions are necessary. The donor is separated from the patient by a plastic screen—he is in the room for a few minutes only and does not have contact with the recipient except through the polyvinyl tube. Obviously the flow of blood must be in the one direction, but even if it was accidentally reversed it would take several turns of the pump to bring blood from the patient to the donor.

We have successfully given more than 100 direct exchange transfusions without risk to the donors.

Summary

The technique of exchange blood transfusion by the direct method is described. Two transfusion pumps are rotated

simultaneously to give blood from donors and remove blood from the patient. Polyvinyl tubing and Teflon catheters are used to lessen the risk of blood-clotting. In four patients suffering from hepatic coma this method of treatment was given. Blood values showed improvement and one patient recovered. It is postulated that unmodified blood transfusion has a place in treatment of liver failure particularly when associated with severe bleeding.

We wish to thank Dr. Morris C. Davis and Dr. J. L. Frew for permission to report Cases 1 and 3 respectively, and to Dr. J. A. Forbes for permission to report Cases 2 and 4.

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Survey of Influenza Antibody in England by the Strain-specific Complement-fixation Test

MARGUERITE S. PEREIRA,* M.D.; PRATIMA CHAKRAVERTY,* B.SC.

T. M. POLLOCK,† M.B., M.R.C.P.GLASG.; J. G. POPE,† B.SC.

Brit. med. J., 1967, 4, 80-82

The susceptibility of a community to current strains of influenza virus is an important factor in the development of epidemics of influenza. Predictions of the likelihood of such epidemics and therefore recommendations for the use of vaccines against influenza should be based on what is known of the susceptibility of the population at risk and on the identity of circulating virus strains.

The influenza antibody survey described here was made to estimate the susceptibility to influenza viruses of all age groups in populations in several areas of England.

The laboratory tests previously used to determine antibody to influenza have certain drawbacks. Thus the haemagglutination inhibition test is sometimes difficult to interpret, since virus strains vary in their avidity for antibody and in their sensitivity to nonspecific inhibitors present in serum. Also the serum neutralization test in tissue culture is laborious and expensive.

By contrast the complement-fixation test is simple, and, as a microtest, economical in reagents. This test may be done by using as antigen either the type-specific S antigen or the subtype or strain-specific V antigen (Lief and Henle, 1956). The former is excellent for the diagnosis of acute influenzal illness, but because the antibody titre declines soon after infection it cannot be used to detect residual antibody. In addition to this limitation the soluble antigen is common to all influenza A viruses and will not react solely with influenza A₂ antibody.

By the development of the V antigen, strain-specific reactions were obtained in the complement-fixation test. Henle *et al.* (1958) demonstrated the value of this test for the antigenic analysis of influenza virus and showed also that antibody detected with the V antigen would persist for several years after infection. It seemed likely that this would indicate the proportion of a population which had already experienced influenza A₂ virus infection. The strain-specific complement-fixation test was therefore employed in this investigation.

Materials and Methods

Public health laboratories in five different locations in England sent samples of serum each week to the Virus Reference Laboratory during the period October 1965 to May 1966. These samples were selected by the sending laboratory from

the number submitted for various routine tests, the majority being for the estimation of antistreptolysin O titres or for Wassermann reactions. Sera from patients with acute respiratory illness were excluded. From October 1965 to January 1966 a first series of 729 sera were examined, and from January to May 1966 a second series of 1,054 sera.

Virus Strains.—In the first series sera were tested against a single V antigen prepared with influenza A₂/England/7/65 virus. For the second series three V antigens were prepared with the influenza A₂/Singapore/1/57, A₂/England/129/66, and B/England/5/66 viruses.

Antigens.—These were prepared by the methods of Lief and Henle (1956). Allantoic fluids were harvested from eggs inoculated 48 hours previously with the strains of influenza virus. The virus harvests were adsorbed to fowl cells at 0° C., followed by elution into small volumes of phosphate-buffered saline at pH 7.2 over a period of three to four hours. This cycle was repeated two or three times. The final eluates were then tested quantitatively for specific complement fixation by the chessboard method against a homologous antiserum prepared in ferrets and against an S specific antiserum prepared in guinea-pigs. The dilution of each antigen for use was taken to be that which fixed complement with the highest dilution of homologous ferret antiserum. This varied between 1/4 and 1/32. If there was fixation of complement with the S specific antiserum, further adsorption-elution cycles were done.

Complement-fixation Test.—The method was described by Pereira *et al.* (1964). It used 0.025 ml. unit volumes of the reagents in W.H.O. plastic plates and overnight fixation at +4° C. Sera were diluted in fourfold steps and mixed with the optimal dilution of the appropriate V antigen. Titres were recorded as the reciprocal of the highest serum dilution producing 50% fixation with the antigen.

Results

There was no indication of any appreciable difference in the results of tests on the sera from the different laboratories. In the analysis all the results have therefore been combined.

* Virus Reference Laboratory, Central Public Health Laboratory, London N.W.9.

† Epidemiological Research Laboratory, Central Public Health Laboratory, London N.W.9.

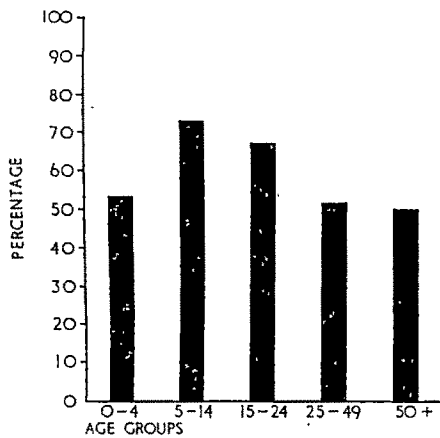


FIG. 1

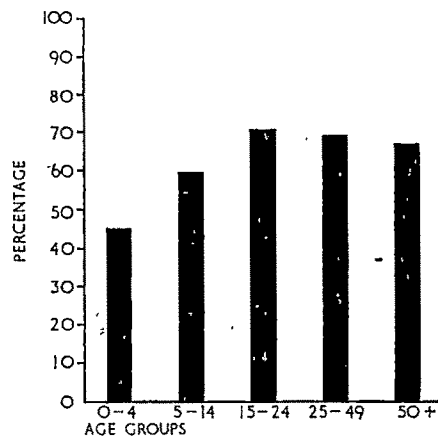


FIG. 2

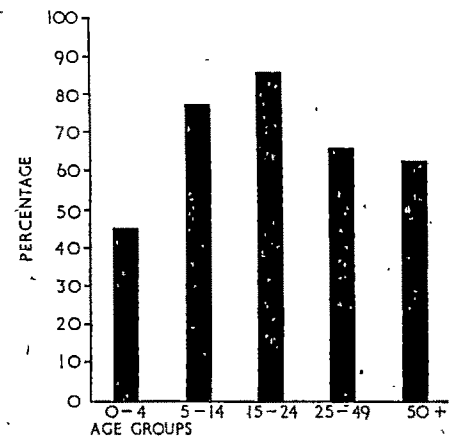


FIG. 3

FIG. 1.—Percentage of individuals with antibody to A₁/65 V antigen by age groups—all areas. October 1965 to January 1966. FIG. 2.—Percentage of individuals with antibody to A₂/England/66 by age groups—all areas. January to May 1966. FIG. 3.—Percentage of individuals with antibody to A₁/Singapore/57 by age groups—all areas. January to May 1966.

As shown in Tables I-III and in Figs. 1-3, a substantial proportion of sera from each age group contained antibody to each of the influenza A antigens. Antibody to the earliest strain, A₂/Singapore/1/57, was found most often. In persons aged 5-24 years few were without demonstrable antibody, and their sera included the greatest number with high titres against all the strains tested.

The antibody titres to each of the two A antigens in sera from 49 children under 5 years of age are shown in Fig. 4. Despite the antigenic shift of the influenza A strains since 1957 considerable crossing was found and antibody could be demonstrated in most instances against both variants. In the majority the titres were higher against the more recent strain.

TABLE I.—Specific Antibody to Influenza A₂/England/7/65 V Antigen. All Laboratories—October 1965 to January 1966

Age Group	Antibody Titre									Total
	<4	4	8	16	32	64	128	256	512	
0-4	19 (46%)	3	5	2	2	1	2	7	—	41
5-14	52 (27%)	14	13	27	30	29	14	9	1	189
15-24	47 (32%)	7	13	16	21	24	8	9	1	146
25-49	103 (48%)	15	12	19	19	17	17	11	3	216
50+	68 (50%)	6	10	17	13	11	6	6	—	137

TABLE II.—Specific Antibody to Influenza A₂/England/129/66 V Antigen. All Laboratories—January to May, 1966

Age Group	Antibody Titre								Total
	< 8	8	16	32	64	128	256	512	
0-4	27 (55%)	3	2	7	3	2	3	2	49
5-14	104 (41%)	22	16	39	24	11	23	13	252
15-24	64 (29%)	19	21	35	34	15	9	23	220
25-49	76 (36%)	26	22	31	49	21	14	15	254
50+	93 (33%)	32	37	32	36	25	14	10	279

TABLE III.—Specific Antibody to Influenza A₁/Singapore/1/57 V Antigen. All Laboratories—January to May 1966

Age Group	Antibody Titre								Total
	< 8	8	16	32	64	128	256	512	
0-4	27 (55%)	4	4	7	2	3	1	1	49
5-14	57 (23%)	20	26	36	54	18	29	12	252
15-24	30 (14%)	17	37	35	46	15	21	19	220
25-49	88 (34%)	32	26	36	35	10	18	9	251
50+	106 (38%)	26	35	41	41	12	14	4	279

TABLE IV.—Specific Antibody to Influenza B/England/5/66 V Antigen. All Laboratories—January to May 1966

Age Group	Antibody Titre								Total
	< 4	8	16	32	64	128	256	512	
0-4	37 (75%)	3	2	2	2	1	1	1	49
5-14	144 (57%)	20	12	25	15	13	8	15	252
15-24	81 (37%)	24	14	35	21	20	10	14	219
25-49	123 (48%)	37	11	39	19	15	6	4	254
50+	155 (55%)	36	11	35	14	18	5	5	279

In Table IV and Fig. 5 the presence of antibody against influenza B is shown to be relatively infrequent in sera from preschool children, but this incidence has increased sharply in the older children, reaching a peak among the young adults. The outbreaks of influenza B infection which occurred in many schools throughout the country in the early months of 1966 may have had a considerable influence on the formation of this pattern.

Discussion

Though the presence or absence of immunity to the current virus strains is a principal influence in the development of epidemics, there have been few attempts in England to assess

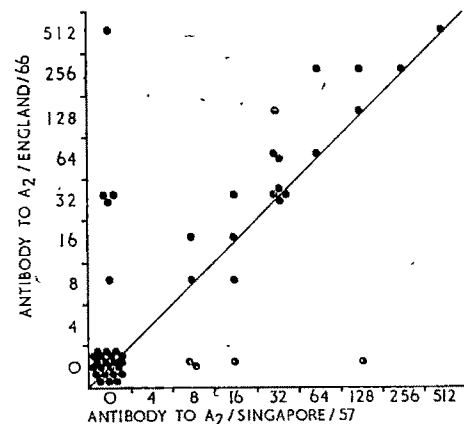


FIG. 4.—Antibody titres to A₂/57 and A₂/66 in individual children under 5 years.

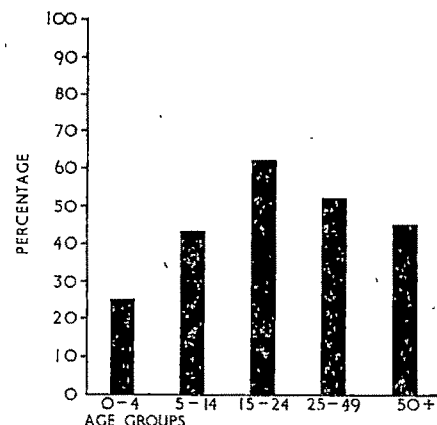


FIG. 5.—Percentage of individuals with antibody to B/England/66 by age groups—all areas. January to May 1966.

the prevalence of immunity in the population by a survey of the influenza antibody titres over a wide range of age groups. In the present investigation these titres have been estimated in samples of serum from a large number of individuals of various ages in five areas of England.

More than 1,700 sera were tested, but the numbers of samples from most of the age groups were rather limited. A more selective investigation in additional areas would be necessary to confirm that the results obtained were truly representative of the titres in the general population. However, the results give a general indication of the proportion of persons with antibody in many areas in England.

The strain-specific complement-fixation test was found in practice to be very suitable for a survey of this kind, since it is simple and quick with a clearly recognizable end-point.

A previous investigation (to be published) showed that infection with influenza A₂ virus was followed by the production of antibody which could be detected equally well by the haemagglutination inhibition, serum neutralization, and strain-specific complement-fixation test and which persisted for at least nine years. In a few instances the complement-fixing and haemagglutination-inhibiting antibody had declined to a low titre by this time and occasionally even became undetectable, whereas neutralizing antibody could be demonstrated convincingly on all occasions. On this basis the results obtained by the present complement-fixation tests must be regarded as providing a modest estimate of the proportion of the population that possess antibody.

If, as seems probable, the presence of circulating antibody is accepted as indicating some degree of resistance to influenza, the findings clearly indicate that a substantial proportion of each age group in England is protected against the current strains of influenza virus. It follows, therefore, that until the antigenicity of the influenza strains is altered a widespread epidemic of influenza is unlikely in England.

The investigation demonstrated the heterogeneity of antibody to the influenza A₂ strains because antibody to one strain may

appear after infection with another. This is evident from the findings in children under 5 years old. In this group most of those with antibody to the A₂/England/129/66 strain also had antibody to the A₂/Singapore/1/57 strain, though the children could not have been infected with the A₂/Singapore/1/57 strain, because it had disappeared from England before many of them were born; moreover, most of them were too old for maternal antibody to the A₂/Singapore/1/57 strain to have persisted.

Summary

To obtain information on the susceptibility of communities to influenza-viruses serum samples from 1,783 persons of all ages living in five different areas of England were examined. Strain-specific complement-fixation tests for antibody to influenza viruses were used.

The results indicated that antibody to both early and late antigenic variants of influenza A₂ virus and to influenza B virus is widespread in all age groups. An epidemic due to the current strains is unlikely.

The strain-specific complement-fixation test was found to be highly suitable for this type of investigation.

We are grateful to Drs. B. Moore, C. E. D. Taylor, J. O'H. Tobin, and J. E. M. Whitehead, from the public health laboratories of Exeter, London, Manchester, and Coventry respectively, for sending us serum samples, and to Dr. T. Skeoch and Mr. H. Bell, of the Central Clinical Laboratory, Middlesbrough, for their help. We would like to thank two visiting workers from New Zealand, Dr. Jack Burton and Miss Marjorie Bennett, for their part in this investigation.

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Antibodies in Children's Sera for Serologically Different Recently Isolated Strains of Influenza Viruses A₂ and B

G. C. SCHILD,* B.SC., PH.D.; C. H. STUART-HARRIS,† C.B.E., M.D., F.R.C.P.

Brit. med. J., 1967, 4, 82-84

The natural antigenic variation of the influenza viruses and its probable significance in relation to the sequence of epidemics and pandemics of human influenza is well known. In the case of the influenza A, A₁, and A₂ viruses the variation from one major antigenic form to another has occurred every ten or more years, but in between these happenings there have been minor variations with a progressive deviation from the prototype. In the case of the influenza B viruses it has not proved possible to group strains into families arranged in a chronological sequence of occurrence as with influenza A viruses, and the variation appears to have been relatively haphazard. The serological impact of the various races of both influenza A and B on the population has been studied by many workers. Davenport *et al.* (1953) were the first to show that different age-cohorts of the population exhibit different serological spectra against the major influenza A virus families. They attributed their findings to a dominating influence on the

immunological mechanism of childhood infection by the particular virus serotype then prevalent. Reinforcement of this antibody production by subsequent exposure to other serotypes occurs during adult life. Their doctrine of "original antigenic sin" or serological recapitulation of childhood antibodies has received support from numerous observations, including those derived from prospective studies on the same persons (Schild and Stuart-Harris, 1965).

The serological effects on man of minor antigenic variations occurring in interpandemic periods have, however, received little attention. Zhdanov (1967) has attempted to predict the occurrence of epidemics by examining sera with different serotypes represented by viruses isolated recently and from less recent epidemics. In such work children's sera are likely to yield more definitive information than those of adults because of the relatively specific character of the antibody response in childhood. The success of the Russian method in predicting the 1965 epidemic of A₂ and the 1967 outbreak of B influenza (Zhdanov *et al.*, 1966; Zhdanov, 1967) indicates that it is

* Department of Bacteriology, University of Sheffield.

† Department of Medicine, University of Sheffield.

worthy of wider exploration. Experience over prolonged periods of time will probably be necessary to assess its value. A start has been made on this in Sheffield by examining sera from children with recently isolated and serologically variant strains of influenza A₂ and B. The sera were collected at intervals from May 1965 onwards, and the period of study preceded and followed the mixed A₂ and B influenza epidemic of January to March 1966.

Materials and Methods

Sera were obtained from the laboratories at the Children's and Royal Hospitals in Sheffield, either from patients in the wards or from specimens from children living in the Sheffield hospital region, and submitted for antistreptolysin O titres or blood-grouping. With the consent of their parents, 30 sera were obtained from healthy children attending a welfare clinic in the West Riding. Sera were stored frozen at -20°C . in screw-capped bottles.

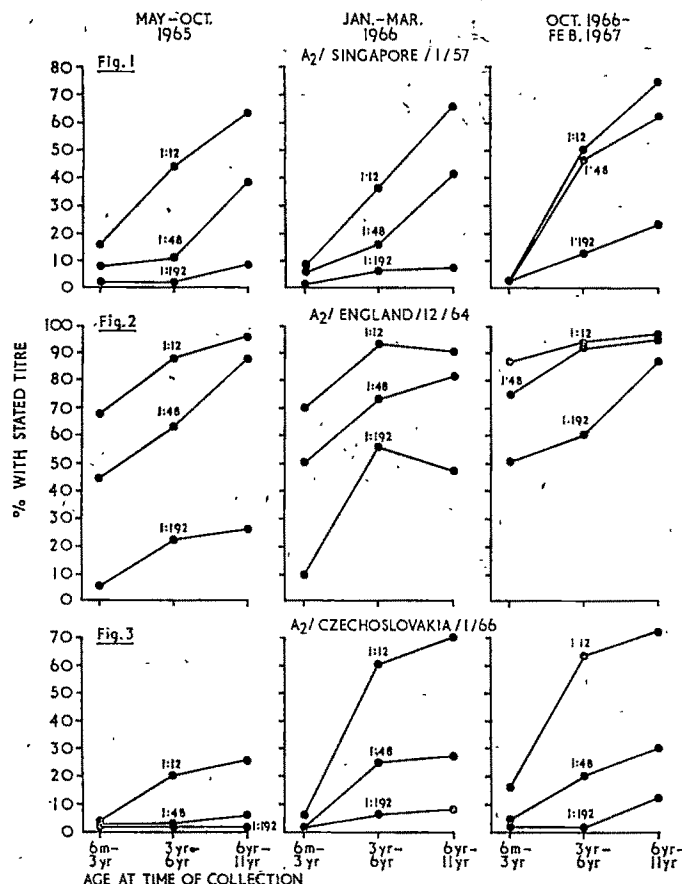
Virus Strains.—The A₂ viruses were the prototype 1957 strain A₂/Singapore/1/57, the A₂/England/12/64 representative of the variants occurring in 1964–6 (Pereira *et al.*, 1964), and A₂/Czechoslovakia/1/66 isolated in December 1966 and kindly supplied by Dr. H. G. Pereira, of the World Influenza Centre in London. The influenza B viruses were B/Lee/1940; B/England/939/59, B/England/101/62, B/Taiwan/4/62, and B/England/13/65. They were received from Dr. D. Hobson, of the University of Liverpool. B/Sheffield/66 was recovered in Sheffield in May 1966 from a patient with influenza. Pools of viruses were made by allantoic inoculation of 10-day embryonated eggs from stock cultures diluted 10^{-3} to 10^{-4} . After incubation at 35°C . for 48 hours the allantoic fluids were harvested, pooled, and stored frozen at -70°C .

Haemagglutination-inhibition Tests.—These were carried out in perspex trays by conventional methods (W.H.O., 1953), using 8 haemagglutinating units of virus and twofold serum

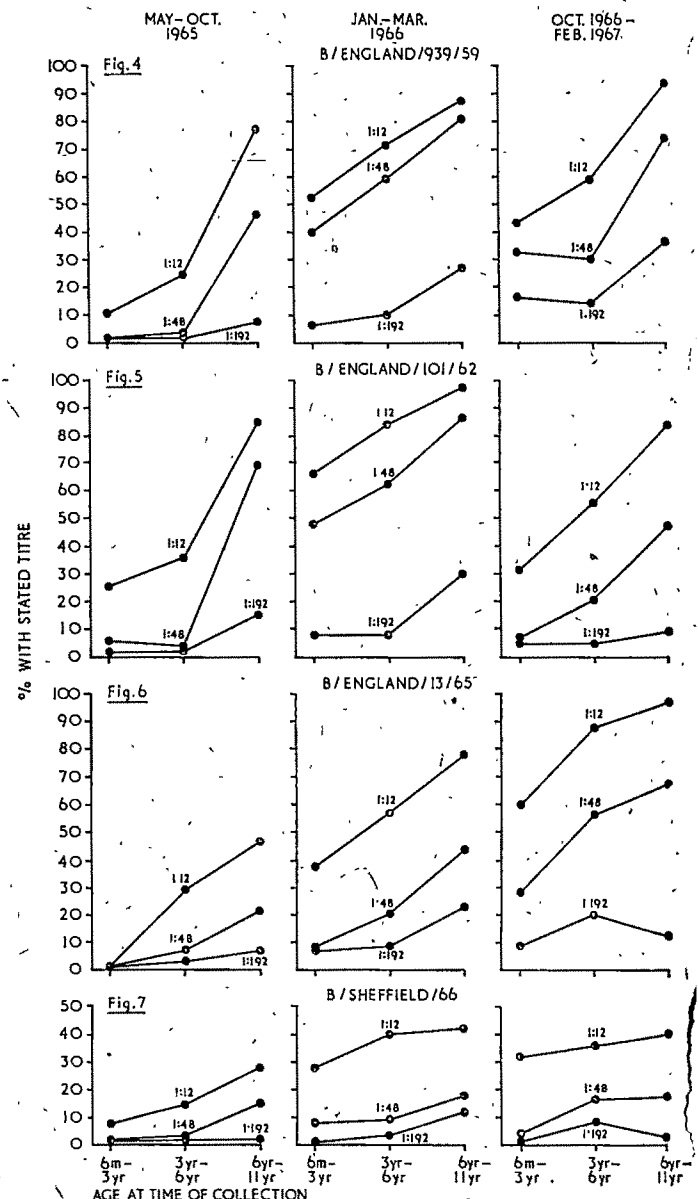
dilutions. All sera were treated before test to remove non-specific serum inhibitors by incubation overnight at 37°C . with 5 vols. of cholera filtrate (N.V. Phillips Roxane or Burroughs Wellcome Ltd.). They were subsequently heated at 56°C . for one hour to destroy the receptor-destroying enzyme.

Results

The ages of the children from whom the specimens were received varied from 6 months to 11 years at the time of collection. The serum collections were made in three periods—May to October 1965, January to March 1966, and October 1966 to February 1967. Not all the sera were tested against all the viruses, because of the actual volume of available serum. Figs. 1 to 7 show the proportion with antibodies for the appropriate viruses in each of these three serum collections. They represent at three titre levels the proportions with antibodies during and after the epidemic period (A₂ and B) of 1966. Though the serum specimens came from different children in each of the three periods of time, the figures for each period show the percentage of sera with positive haemagglutination-inhibition at 1 in 12, 1 in 48, and 1 in 192 dilutions. In each period of time the results from the children are shown at three separate ages of 6 months to 3 years, 3 to 6 years, and 6 to



FIGS. 1-3.—Percentage of children of various ages with haemagglutination-inhibition antibody at the stated titre to influenza A₂ virus strains.



FIGS. 4-7.—Percentage of children of various ages with haemagglutination-inhibition antibody at the stated titre to influenza B virus strains.

11 years at the time of collection. The relation between ages and dates of birth are shown in Table I.

TABLE I.—Range of Birth Dates of Serum Donors in the Various Age Groups of Children Studied

Date of Serum Collection	Age of Donors at Time of Collection of Serum		
	6 Months–3 Years	3–6 Years	6–11 Years
May–Oct. 1965	May 1962–May 1965*	1959–62	1954–9
Jan.–March 1966	Jan. 1962–Oct. 1965	1959–62	1954–9
Oct. 1966–Feb. 1967	Oct. 1963–Sept. 1966	1960–3	1955–60

* Range of birth dates.

A₂ Virus Antibodies

Table II and Figs. 1 to 3 show respectively the proportion of children with antibodies and the antibody distributions for the A₂ strains recovered in 1957, 1964, and 1966 and indicate definite differences in the results with the various viruses. Against the prototype A₂ virus shown in Fig. 1 there were relatively few differences between the various serum collections. The oldest children in each group who were alive during the earliest epidemics of the A₂ era in 1957 and 1959 show the greatest proportion of positive results (60 to 70%) and the greatest number with high-titred sera (10 to 20%). Relatively few sera from the youngest children born from 1962 onwards gave positive results with the Singapore virus, and all of the sera from those born since October 1963 were negative. The 1966 epidemic appeared to have had little effect on the titre distributions except that the proportion of sera positive at a 1 in 48 dilution was greater in the most recent than in the earlier collections.

TABLE II.—Antibodies to Influenza A₂ Viruses

Virus Strain	Serum Collections and No.	No. and Proportion of Sera Inhibitory at 1 in 12 Dilution or Higher					
		6 Months–3 Years		3–6 Years		6–11 Years	
		No.	%	No.	%	No.	%
A ₂ /Sing./57	May–Oct. 1965 (180)	7/45	16	30/70	43	35/65	46
	Jan.–Mar. 1966 (79)	2/16	12	13/34	38	19/29	66
	Oct. 1966–Feb. 1967 (65)	0/14	0	13/25	52	20/26	77
A ₂ /Eng./64	May–Oct. 1965 (180)	31/45	69	61/70	87	62/65	95
	Jan.–Mar. 1966 (60)	9/13	70	21/23	96	21/24	87
	Oct. 1966–Feb. 1967 (65)	11/14	78	23/25	92	25/26	96
A ₂ /Czech/66	May–Oct. 1965 (120)	1/30	3	11/55	20	9/35	26
	Jan.–Mar. 1966 (80)	1/15	7	21/35	60	21/30	70
	Oct. 1966–Feb. 1967 (65)	2/14	14	16/25	64	19/26	73

Antibodies against the A₂/64 virus (Fig. 2) were present in a higher proportion of sera in all three periods and at higher dilutions than with the A₂/57 virus. Indeed, the sera were so consistently inhibitory at 1 in 12 in all three collections that it is probable that A₂/64 virus is more avid for antibody than A₂/57. The results obtained by Dr. H. G. Pereira with convalescent ferret sera (Table III) did not, however, suggest the existence of an undue avidity of the A₂/64 virus, and the human results could also be explained on the basis of the cross-relationship of A₂/64 with the A₂/57 and A₂/66 viruses, together with the effects of the 1964 and 1966 epidemics. Thus 85% of the sera from the oldest children (6 to 11 years of age) exhibited antibodies for A₂/64 virus at 1 in 192 dilution in the 1966–7 collection; 50% of sera collected during January to March 1966 and only 25% of the 1965 sera were positive at 1 in 192. An increase of high-titred sera against A₂/64 virus also occurred in the groups of children under 3 years of age between the collection of sera early and later in 1966. These results probably indicate the effect of the outbreak of influenza in that year.

TABLE III.—Haemagglutination-inhibition Tests for Influenza A₂ Viruses with Immune Ferret Sera

Virus Strains	Sera		
	A ₂ /Singapore/1/57	A ₂ /England/12/64	A ₂ /England/1/66
A ₂ /Singapore/1/57 ..	2,560	160	160
A ₂ /England/12/64 ..	320	3,840	2,560
A ₂ /England/1/66 ..	240	960	1,920
A ₂ /Czechoslovakia/1/66	240	960	1,920

The results with the A₂/Czech/1/66 virus (Fig. 3) contrast with both the other A₂ viruses in that only a low percentage of the sera collected before January 1966 inhibited the virus. Even among the sera from the oldest children from the 1965 collection only 25% exhibited antibody demonstrable at 1 in 12 dilution, compared with 70% positive at the same dilution in both collections of sera from 1966. This result was surprising in that tests with convalescent ferret sera (Table III) showed only slight antigenic differences between A₂/England/12/64 and A₂/Czech/1/66 viruses. Nor did they suggest that the latter strain was significantly non-avid in the haemagglutination-inhibition test. In addition, the titres obtained with the ferret antisera show that A₂/Czech/66 is serologically closely related to an A₂ virus (A₂/England/1/66) isolated in Great Britain during the same year.

Influenza B Viruses

Antibodies were present in children's sera against each of the four B viruses isolated in England from 1959 to 1966 (Table IV), though the proportions and titres varied at different ages and in the different serum collections. Few sera contained demonstrable antibodies against the B/Lee/1940 and B/Taiwan/4/62 strains. Those which did so react with these viruses were almost invariably from the oldest children among the several groups in whom 10 to 30% were positive at 1 in 12. Such sera usually also possessed high antibody titres to the other influenza B strains, and particularly to B/England/13/65, thus suggesting that the antibodies to the Lee and Taiwan viruses were heterotypic and resulted from infection by the other B viruses.

Table IV indeed suggests that antibody orientated to B/Taiwan/62 might result from infection by the 1965 B viruses, for sera from ferrets convalescent from infection by the latter reacted also with the Taiwan strain. Similarly, cross-reactions between B/England/59 and Lee ferret antisera, also shown in Table IV, would explain the presence of antibodies against the Lee virus in the sera from children exposed to infection in 1959. In regard to B/England/65 and B/England/66 viruses close serological resemblances were found by Dr. H. G. Pereira (personal communication). These results are borne out by the titres obtained in our own laboratory (Table IV).

TABLE IV.—Serological Relation Between Influenza B Virus Strains in Haemagglutination-inhibition Tests with Immune Ferret Sera

Virus Strains	Ferret Sera			
	B/Lee/1940	B/England/939/59	B/Taiwan/4/62	B/England/5/65
B/Lee/1940	384	192	<12	NT
B/England/939/59 ..	<12	1,536	12	"
B/Taiwan/4/62 ..	<12	<12	192	"
B/England/101/62 ..	<12	192	<12	"
B/England/5/65 ..	NT	NT	NT	1,280
B/England/13/65 ..	<12	48	48	NT
B/Sheffield/66 ..	<12	24	12	960

Table V and Figs. 4 to 7 give the human serological results with the viruses isolated in 1959, 1962, 1965, and 1966, all of which show in varying degree the effect of the B outbreak in 1966. The fact that the older children, aged 6 to 11 years, exhibited higher titres than the infants in each group of sera is best explained by the repetitive effect of infection during the B epidemics in 1959 and 1962 on antibodies acquired before that date. The virus recovered in 1959 (Fig. 4) thus shows

the effect of the 1966 epidemic in that an increased proportion of sera was positive in all three dilutions in the serum collections from 1966 compared with that from 1965. The older children exhibited both an increased proportion of sera positive at 1 in 12 in the latest compared with the earliest collection (from 80% in 1965 to 95% in 1966) and an increased number with higher titres.

TABLE V.—Antibodies to Influenza B Viruses

Virus Strain	Serum Collections and No.	No. and Proportion of Sera Inhibitory at 1 in 12 Dilution or Higher					
		6 Months–3 Years		3–6 Years		6–11 Years	
		No.	%	No.	%	No.	%
B/Eng./59	May–Oct. 1965 (120)	3/30	10	11/55	20	27/35	77
	Jan.–Mar. 1966 (85)	8/16	50	29/39	73	28/30	93
	Oct. 1966–Feb. 1967 (90)	7/18	40	23/38	60	32/34	94
J/Eng./62	May–Oct. 1965 (80)	4/17	24	13/35	37	24/28	86
	Jan.–Mar. 1966 (110)	17/25	68	42/50	84	34/35	97
	Oct. 1966–Feb. 1967 (80)	6/18	33	19/33	58	24/29	83
B/Eng./65	May–Oct. 1965 (120)	0/30	0	16/55	29	16/35	46
	Jan.–Mar. 1966 (110)	10/25	40	28/50	56	27/35	77
	Oct. 1966–Feb. 1967 (90)	11/18	60	33/38	87	33/34	97
B/Sheff./66	May–Oct. 1965 (80)	1/17	8	5/35	14	8/28	28
	Jan.–Mar. 1966 (110)	7/25	28	20/50	40	15/35	43
	Oct. 1966–Feb. 1967 (80)	6/18	33	11/33	33	12/29	40

The pattern of antibodies against the B/England/62 virus (Fig. 5) was not greatly different from that obtained with the B/59 virus, as might be expected from the results with ferret antisera shown in Table IV. With the B/England/65 virus (Fig. 6) antibodies were not found in sera from the youngest children collected in 1965 but were present in 40% of sera from those aged less than 3 years collected in January to March 1966. Of the sera from the youngest children collected in 1966–7, 60% were positive at 1 in 12 and 30% at 1 in 48. The 1965 virus was thus inhibited by sera from the oldest children in all three collections, but a rise in both the proportion of inhibitory sera and in the number with strongly inhibitory properties occurred during 1966. The results with this virus are compatible with the view that the 1966 outbreak was associated with infection by a strain resembling B/England/65, as was indicated also by the results with ferret antisera (Table IV).

However, the B virus recovered in Sheffield in 1966, which yielded results with ferret sera similar to those with both 1965 and other 1966 viruses, gave different results with the children's sera (Fig. 7). In the sera from 1965 28% of the oldest and less than 10% of the youngest children were inhibitory at 1 in 12. Sera positive at 1 in 12 dilution formed from 30 to 40% at all ages of those collected during 1966. The 1966 outbreak thus appeared to have left the majority (60%) of children, whose sera were collected from October 1966 onwards, with no antibodies at all to this virus (Table V). The youngest children in this group also exhibited an almost total lack of antibodies at 1 in 48 or higher, as in the case of the sera from children from 6 months to 6 years of age collected in 1965.

Discussion

The purpose of this study was twofold. The first query was whether children's sera can be used to detect antigenic differences between recently isolated but serologically distinct virus strains. The results abundantly support the view that this is so. Indeed, children's sera appear to detect antigenic differences even more specifically than do sera from convalescent ferrets. The second purpose was to obtain baseline data concerning

the effect of an outbreak of influenza on the distribution of antibodies in children of different ages. Such data might enable one to predict the likelihood of an outbreak. So far as the A₂ viruses are concerned, A₂/England/64 was inhibited by a high proportion of sera collected before the 1966 outbreak, and therefore no indication would have been obtained with this strain of the imminence of an A₂ outbreak. Had the A₂/66 variant been available, however, it would have revealed a low percentage (from 4 to 26) of children of all ages with antibodies in the pre-epidemic period. Thus the likelihood of an outbreak could have been foreseen, but probably only retrospectively, by using the epidemic strain.

In the case of the B viruses the data show once again that there was a deficiency of antibodies in pre-epidemic sera against the virus which caused an outbreak in 1966. Yet, in spite of the known occurrence of localized outbreaks in the January-to-March period of that year, the 1965 B virus showed a similar deficiency of antibodies in the youngest children. Even in the case of children aged 3 to 6 years, only 29% exhibited antibody to the 1965 virus strain. On these grounds, therefore, the likelihood of a recurrence of infection by the 1965 virus or a related strain such as that actually experienced in 1966 might have been considered probable.

It seems clear that further experience with sera from the youngest segment of the population other than those with maternal antibodies may give an indication of the likelihood of an outbreak if a very recently isolated antigenic variant is available. Much more experience will be necessary, however, before this method of prediction can be properly evaluated. For instance, a general lack of antibody to B/Taiwan/4/62 virus existed in the children's sera. This strain, isolated in 1962, was found at that time to be serologically distinct from previously known influenza B strains (Green *et al.*, 1964). Yet it has never again been identified in an epidemic of influenza, a fact which indicates that not all antigenic variants of the influenza viruses are successful pathogenic agents even in the absence of serological immunity. Therefore the recovery of a new variant may not predicate the immediate likelihood of an outbreak of that virus.

Summary

A survey has been carried out on the incidence of haemagglutination-inhibiting antibody to influenza A₂ and B virus strains isolated between 1957 and 1966 in sera collected from children aged 6 months to 11 years. Evidence of recent infection in the community with the various test viruses was indicated by changes in the frequency of occurrence of antibody in sera collected at different periods of time during the study. Serological differences were demonstrated between influenza virus strains even when the latter were closely related in tests with immune animal sera. The study provides baseline information on the effect of outbreaks of influenza on the distribution of antibodies in children's sera and raises the possibility of using such data in the prediction of future influenza epidemics.

We wish to thank Dr. H. G. Pereira, of the World Influenza Centre, London, for the provision of virus strains and immune animal sera and for helpful discussion. Dr. D. Hobson, of the University of Liverpool, kindly provided other virus strains. We are grateful for the excellent technical assistance of Miss K. Cullen and Miss J. A. Waite.

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Measurement of Blood Loss by Means of a Whole-body Counter

J. M. HOLT,* M.D., M.R.C.P.; F. G. H. MAYET,*† M.D.; G. T. WARNER*;
S. T. CALLENDER,* M.D., F.R.C.P.

Brit. med. J., 1967, 4, 86-88

In the investigation of patients with hypochromic anaemia the assessment of the part played by gastrointestinal or menstrual blood loss is often extremely difficult. This paper describes a method for the measurement of blood loss over periods of up to three months by means of ^{59}Fe and the simple whole-body counter recently designed in this department (Callender *et al.*, 1966). The principles involved are that 7 to 10 days after the administration of ^{59}Fe all or most of the dose will be incorporated into circulating red cells. In normal males and postmenopausal females the whole-body radioactivity will remain stable and any loss in total body radioactivity must represent loss of blood. The technique was evaluated by studying patients with polycythaemia from whom known quantities of blood were removed by venesection. Its clinical use is illustrated by studies of five patients with hypochromic anaemia.

Methods

The design of the whole-body counter and its uses in measuring absorption have been described in detail elsewhere (Warner and Oliver, 1966; Callender *et al.*, 1966). The majority of subjects studied were given an intravenous tracer dose of ^{59}Fe ferric citrate with 1.5 to 1.0 μCi activity; subjects in whom additional information on the ability to absorb iron was required were given an oral dose of 5 mg. of ferrous iron labelled with approximately 5 μCi ^{59}Fe .

Patients Studied.—Four patients who had recovered from a myocardial infarct agreed to act as control subjects. All were outpatients and none was receiving anticoagulant drugs. They were studied over a period of three months in order to measure the normal daily iron loss as blood and to assess the week-to-week variation of the whole-body counter. Twelve patients with polycythaemia who required therapeutic venesection were studied; three were postmenopausal females and nine were males. Ten had polycythaemia vera and two had secondary polycythaemia. Plasma iron disappearance curves were plotted and used for estimation of blood volume. Seven to 10 days after the injection of ^{59}Fe (day zero of the experiment) the whole-body radioactivity was measured. Thereafter venesections were carried out at varying intervals of a few hours to three weeks. The whole-body radioactivity was measured immediately before and after each venesection. Five patients with iron-deficiency anaemia in whom either gastrointestinal bleeding or excessive menstrual loss was suspected were investigated. The proportion of the oral dose retained at 10 days was a measure of iron absorption. Thereafter the total body activity was measured at intervals.

Calculation of Blood Loss.— L =Percentage loss of whole-body radioactivity between counts. BV =Blood volume in ml.

$$\text{Blood loss in ml.} = \frac{L}{100} \times BV$$

In control subjects and patients with iron-deficiency anaemia the blood volume was taken to be 65.6 ml./kg. body weight (Wasserman *et al.*, 1951). For the purpose of this calculation it was thought reasonable to assume that in polycythaemia and

iron-deficiency anaemia the red-cell utilization of ^{59}Fe could be taken as 100%. This was verified in a number of subjects. When 100% utilization was not expected—for example, in control subjects—the utilization was measured and the appropriate correction made.

Results

Control Subjects

The whole-body counts expressed as a percentage of the count on day zero were plotted against time in days (Fig. 1). The mean loss of ^{59}Fe per day was $0.031\% \pm 0.039\%$. The calculated blood loss per 100 days was 152, 155, 160, and 182 ml. respectively. After correction for the amount of blood removed for blood sampling the losses were 142, 105, 90, and 132 ml. (mean 117 ml.).

Patients with Polycythaemia

A total of 39 venesections were carried out in the 12 patients, and the calculated volume of blood lost on each occasion was compared with the known volume of blood removed by venesection. The difference, or error, was expressed as a percentage of the known volume removed. In 10 instances between 100 and 300 ml. of blood was removed; the mean error was -10% , the range -48% to $+63\%$, and the standard deviation of the errors $\pm 36\%$. On the other 29 occasions between 395 and 520 ml. of blood was removed; the mean error was -12% , the range -60% to $+50\%$, and the standard deviation of the errors $\pm 26\%$.

Venesections Carried Out Over Periods of up to 97 Days. The Known and Calculated Losses are Compared

Period of Study in Days	Blood Removed (ml.)	Calculated Blood Loss (ml.)	Difference (ml.)	Error (%)
1	688	586	-102	-15
1	715	662	-53	-7
2	725	825	+100	+14
37	1,190	1,162	-28	-2
40	1,235	968	-267	-22
84	1,630	1,606	-24	-1
90	1,850	2,280	+430	+23
6	2,025	2,231	+206	+10
97	2,820	2,761	-59	-2

The Table concerns the nine patients in whom blood was removed by repeated venesection, carried out at intervals during periods of from 1 to 97 days. The sum of the calculated blood losses in each case is compared with the total volume removed by venesection. In these calculations only the whole-body count before each venesection was used in order to simulate the situation in which a patient with continuous blood loss was having single whole-body counts at intervals. The mean error was -0.2% , the range -22% to $+23\%$, and the standard deviation of the errors $\pm 14\%$.

In order to demonstrate the relation between whole-body ^{59}Fe activity and blood loss the results from one patient are shown in Fig. 1, where the graph is compared with that from the control subjects.

* Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford.
† Present address: Department of Medicine, University of Natal, Durban.

Patients with Hypochromic Anaemia

The results are shown in Figs. 2-6, where whole-body counts expressed as a percentage of the whole-body count on day zero are plotted against time in days. The percentage absorption of the orally administered dose and the blood loss are recorded.

One patient had occult gastrointestinal bleeding from telangiectases due to scleroderma, and Fig. 2 shows how most of the bleeding occurred during the first 21 days of the study. In 15 weeks 1.8 litres of blood was lost, but as she can absorb oral iron well her haemoglobin can be maintained at a satisfactory level by continuous treatment.

The second patient had recurrent iron-deficiency anaemia. Her iron absorption was normal and her anaemia was attributed to menorrhagia. The magnitude of the bleeding was not, however, fully appreciated until this study showed a loss of 870 ml. during a single menstrual period. Hysterectomy was therefore advised. Fig. 3 shows that the operation was performed without much loss of blood and that thereafter there was no significant fall in whole-body radioactivity, confirming that menorrhagia was the sole cause of her anaemia.

The third patient was an 18-year-old boy who complained of increasing shortness of breath and cough with haemoptysis. He was found to have a severe hypochromic anaemia, and a chest radiograph showed diffuse opacities in both lower lobes. Fig. 4 shows that the whole-body radioactivity remained con-

stant despite a fall in haemoglobin, indicating that blood loss was not the cause of the anaemia. Later, iron-containing macrophages were found in the sputum and a diagnosis of idiopathic pulmonary haemosiderosis was made. Though blood was being lost from the circulation, it was being sequestered in the lung, thereby explaining why the whole-body radioactivity did not fall.

The fourth patient was a 16-year-old boy with the Ehlers-Danlos syndrome who had recurrent iron-deficiency anaemia. Fig. 5 shows that he lost 1.3 litres of blood in 92 days from the gastrointestinal tract, and though it was not practicable to measure absorption of iron he was able to maintain a satisfactory haemoglobin provided he took iron by mouth continuously.

The fifth patient was a 53-year-old man with ankylosing spondylitis who had had a recurrent iron-deficiency anaemia for 12 years. During the period of study (Fig. 6) he had been taking between 1 and 2 g. of paracetamol a day to control pain, and it seems likely that the gastrointestinal blood loss, which amounted to 1.2 litres in 105 days, was related to treatment.

Discussion

The method described here is sensitive enough to detect blood loss of the order of 100 to 300 ml. but with only limited

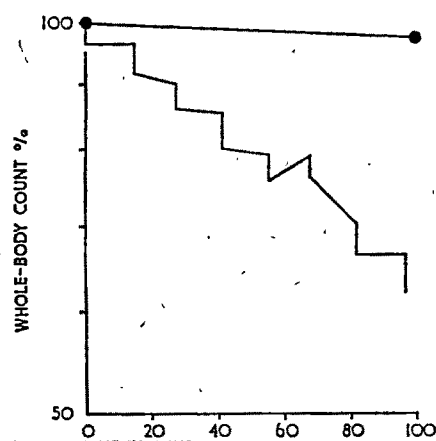


FIG. 1

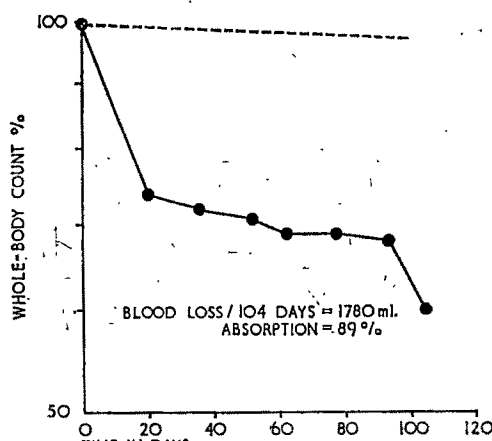


FIG. 2

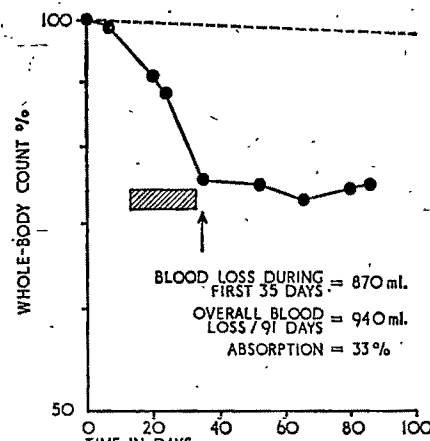


FIG. 3

FIG. 1.—Whole-body count expressed as percentage of the count on day zero plotted against time in days. ●—● Calculated graph from 4 normal subjects (mean ^{59}Fe loss per day, $0.031\% \pm 0.039\%$). — Patient with polycythaemia. The steps correspond with venesections. The apparent rise in activity about day 60 is thought to be due to a combination of counting statistics and counter error. FIG. 2.—Whole-body counts in a patient with telangiectases and scleroderma. ----- Control graph. FIG. 3.—Whole-body counts in a patient with menorrhagia. The arrow indicates hysterectomy and the hatched area a menstrual period. ----- Control graph.

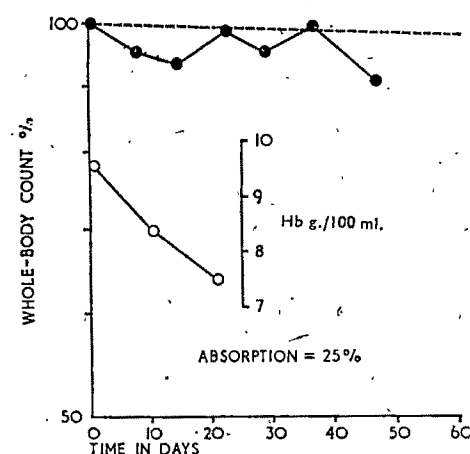


FIG. 4

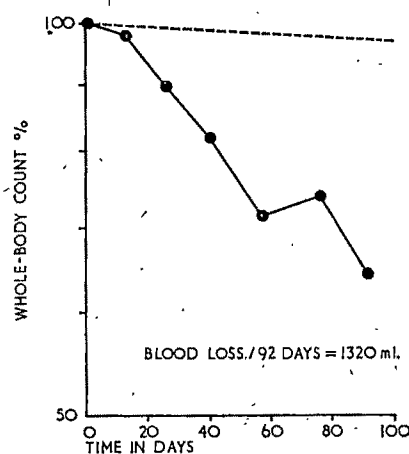


FIG. 5

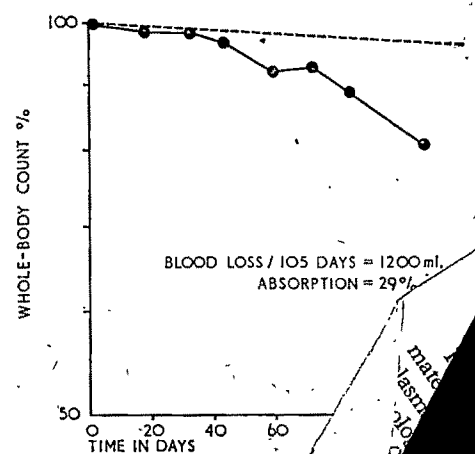


FIG. 6

FIG. 4.—Whole-body counts in a patient with idiopathic pulmonary haemosiderosis. Despite a fall in haemoglobin the activity remained constant, showing that the anaemia was not caused by blood loss. ----- Control graph. FIG. 5.—Whole-body counts in a patient with the Ehlers-Danlos syndrome. ----- Control graph. FIG. 6.—Whole-body counts in a patient with ankylosing spondylitis who was taking paracetamol to control pain. ----- Control graph.

accuracy and reproducibility (mean error -10% , standard deviation $\pm 36\%$). Blood loss of the order of 400 to 500 ml. can be measured with greater reproducibility (-12% , $\pm 26\%$). However, blood loss of the order of 700 to 3,000 ml. computed from consecutive whole-body counts over periods of time ranging from 1 to 97 days can be measured with sufficient accuracy and reproducibility (-0.2% , $\pm 14\%$) to be of use in the quantitative assessment of blood loss in patients with hypochromic anaemia, over periods of up to three months.

Although a whole-body counter has previously been applied to clinical problems of blood loss (Price *et al.*, 1964), the technique has never been evaluated critically. Price *et al.* calculated menstrual blood loss against a direct measurement of the ^{59}Fe content of tampons in one case, and thought an error of 20–40 ml. in losses amounting to 33–59 ml. was likely. Nevertheless it is probably wrong to assume that blood loss occurring clinically can be measured with the same precision as was attained with venesection of patients with polycythaemia. Gastrointestinal or menstrual bleeding may occur erratically and lead to fluctuations in the red cell content of ^{59}Fe and blood volume, both of which cannot be corrected for.

By the above method we are unable to measure reliably blood loss of the order of 100 ml., and an accurate assessment of a single moderately heavy menstrual period is not possible. However, a more accurate measurement is possible if the patient is followed over three or four menstrual cycles.

The ease and simplicity of the technique described here is such that all the studies were carried out on subjects visiting

the department as outpatients. The technique is now available in this hospital as a diagnostic service and is being used to study the mechanism of anaemia in patients with hiatus hernia, ulcerative colitis, and Crohn's disease.

Summary

A method is described for the measurement of blood loss over periods of up to three months by means of ^{59}Fe and a whole-body counter. Patients with polycythaemia from whom known quantities of blood were removed by venesection were studied to evaluate this technique. The method is sensitive and accurate enough for clinical purposes, and blood loss of more than 700 ml. can be measured with reproducibility of $\pm 14\%$. To illustrate its application to clinical problems, studies of five cases of hypochromic anaemia are described.

We wish to thank Miss Marjorie Alcock for technical assistance. The work was in part supported by a grant from the Medical Research Council.

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Effect of Transfusion Materials on Rouleaux Formation and Sedimentation Rate of Erythrocytes

A. J. SALSBUURY,* M.D.

Brit. med. J., 1967; **4**, 88–90

The range and variety of plasma expanders and plasma substitutes are constantly increasing, particularly in the case of dextran solutions (Mollison, 1967; *Brit. med. J.*, 1967). A relatively new dextran is dextran 110, which has a high molecular weight though lower than that of the longer-established dextran 150. Ricketts (1966) has investigated the properties of a modified dextran similar to dextran 110. He found that the effect of this dextran on the red-cell sedimentation rate was substantially less than that of dextran 150 and that red-cell aggregation in the rabbit was minimal. Rouleaux formation was found to interfere with cross-matching in only two out of nine patients who received modified dextran.

In view of these results, it was decided to undertake a series of investigations in vitro to determine the effect of dextran 110, dextran 150, Macrodex, a commercial plasma protein solution, and plasma itself upon red-cell rouleaux formation, blood typing, and cross-matching.

Methods and Results

In the experiments the following standard transfusion materials were compared: (1) reconstituted dried human plasma; (2) a commercial 4.3% plasma protein solution (Serological Products Ltd.); (3) 6% w/v Macrodex in normal saline (Pharmacia (Great Britain) Ltd.); (4) 6% w/v dextran

110 in normal saline (Fisons Pharmaceuticals Ltd.); (5) 6% w/v dextran 150 in normal saline (Fisons Pharmaceuticals Ltd.). As a control, tests were also set up with normal saline in place of one of the above substances. All samples of blood were taken from healthy human volunteers into Sequestrene (sodium edetate). The Westergren sedimentation rate of each sample was 2 mm. in the first hour. Three main sets of experiments were then performed.

Effect of Varying Concentrations of Transfusion Materials on the E.S.R.—The transfusion materials listed above were mixed with blood in dilutions of 1 in 10, 1 in 20, and 1 in 40 (Table I). Five different samples of blood were tested (Tests A–E). Citrate was added to each mixture and the samples were set up in Westergren tubes at room temperature, results being read at the end of one hour. The substitution of plasma or plasma protein solution for saline had no effect on the sedimentation rate (Table I). The substitution of dextran 150 markedly raised the E.S.R. The effect of dextran 110 was less pronounced, but still considerable, while that of Macrodex was moderate. The greater the concentration of Macrodex, dextran 110, or dextran 150, the greater their effect on the E.S.R. This increased effect, however, was much less pronounced with Macrodex than with dextran 110 or dextran 150.

Effect of Transfusion Materials and Anaemia on the E.S.R.—The concentration of transfusion material added to blood was kept constant at 1 in 10. Three different samples of blood were used (Tests I–III). The samples were adjusted by centrifugation and reconstitution of cells and plasma to give haemo-

* Department of Haematology, St. Bartholomew's Hospital, London E.C.1.

globin levels ranging between 30 and 110%, before any transfusion material was added. Westergren sedimentation rates were investigated as in the first set of experiments. The results (Table II) essentially resembled those of the first set of experiments. The sedimentation rate was unaffected by plasma or plasma-protein solution and only moderately affected by Macrodex, even in the specimens with the lowest haemoglobin concentrations. Nevertheless, dextran 110 and dextran 150 produced a striking increase in the E.S.R., which became more pronounced as the haemoglobin concentration in the blood specimen fell.

Effect of Transfusion Materials upon Cross-matching.—Mock saline cross-matching tests were set up in this experiment. Five samples of normal blood were made up as 5% red-cell suspensions in normal saline. Single drops of each suspension were placed in precipitin tubes. To each was added one drop of serum from the corresponding subject, containing a 1 in 10 dilution of the appropriate transfusion material. The tubes were incubated at 37° C. for two hours. At the end of this time any red-cell aggregation visible to the naked eye was noted and the results were read microscopically. No macroscopic red-cell aggregation or microscopical rouleaux formation was observed in the tubes containing saline, plasma, or plasma-protein solution. With Macrodex a fine granularity was visible

to the naked eye and some rouleaux formation was seen on microscopy (Fig. 1). Both dextran 110 and dextran 150 produced a coarse granulation, macroscopically resembling agglutination. Under the microscope, aggregation of red cells into large masses almost impossible to distinguish as rouleaux could be seen. This effect was only slightly less marked with dextran 110 (Fig. 2) than with dextran 150.

TABLE I.—Effect on Erythrocyte Sedimentation Rate of Varying Concentrations of Transfusion Materials

	Citrate (ml.)	Blood (ml.)	E.S.R. (mm. in 1st hour) (Westergren)				
			Test A	Test B	Test C	Test D	Test E
Saline	0.05 ml.	1.95	1	2	2	4	2
	0.1 "	1.90	1	1	2	3	2
	0.2 "	1.80	1	2	3	4	2
Plasma	0.05 "	1.95	2	2	2	2	2
	0.1 "	1.90	2	2	3	3	1
	0.2 "	1.80	2	3	2	4	2
Plasma protein solution	0.05 "	1.95	1	2	2	2	2
	0.1 "	1.90	2	2	2	4	2
	0.2 "	1.80	1	2	2	3	2
Macrodex	0.05 "	1.95	6	5	4	6	3
	0.1 "	1.90	7	7	8	9	6
	0.2 "	1.80	12	9	12	13	10
Dextran 110	0.05 "	1.95	10	15	14	18	17
	0.1 "	1.90	42	49	50	53	47
	0.2 "	1.80	63	62	61	70	59
Dextran 150	0.05 "	1.95	18	18	24	27	19
	0.01 "	1.90	69	67	65	75	70
	0.2 "	1.80	88	85	93	97	82

TABLE II.—Effect on Erythrocyte Sedimentation Rate of Artificially Produced Anaemia. Added Transfusion Material is Present at a Concentration of 1 in 10. 100% = 14.6 g. of Haemoglobin per 100 ml. Blood

Haemoglobin (%)	Test	E.S.R. (mm. in 1st hr.) (Westergren)					
		Saline	Plasma	Plasma Protein Sol.	Macrodex	Dextran 110	Dextran 150
30	I	8	6	7	28	94	129
	II	5	9	5	16	102	118
	III	6	5	8	25	84	113
40	I	8	4	7	27	90	129
	II	4	9	5	16	100	111
	III	6	5	7	23	79	112
50	I	7	5	6	27	89	127
	II	2	8	5	16	95	110
	III	5	5	7	22	72	108
60	I	5	5	5	25	88	119
	II	2	6	3	15	90	110
	III	5	5	6	22	71	103
70	I	4	4	6	24	85	117
	II	2	5	3	12	87	96
	III	3	3	4	18	71	103
80	I	3	2	4	21	80	115
	II	3	5	3	11	85	98
	III	3	3	2	16	69	99
90	I	2	2	3	21	70	108
	II	2	5	3	11	86	97
	III	3	2	2	13	63	95
100	I	2	1	3	18	71	104
	II	2	4	3	11	82	98
	III	2	2	1	13	60	90
110	I	2	2	2	13	70	96
	II	2	4	3	12	80	98
	III	3	2	2	10	59	88



FIG. 1.—Rouleaux formation in a saline cross-match containing Macrodex.



FIG. 2.—Rouleaux formation in a saline cross-match containing dextran 110.

Discussion

The in vitro addition of plasma or plasma-protein solution to blood was found to have a virtually negligible effect upon rouleaux formation and the erythrocyte sedimentation rate. On the other hand, all dextrans tested under these conditions produced some rouleaux formation and an increase in sedimentation rate. Of the dextrans, Macrodex exerted the least effect. Rouleaux formation was slight and the increase in sedimentation rate only moderate. The rouleaux formation was readily recognized microscopically and was unlikely to lead to any difficulty in blood grouping and cross-matching. These findings were in agreement with previous reports on the effect of Macrodex upon blood typing and cross-matching (Turner *et al.*, 1949; Bloom, 1951; Roche *et al.*, 1952; Bowman, 1953; Arndt-Hanser, 1956; Pettenkofer, 1959; Haynes, 1960).

Surprisingly, dextran 110 produced rouleaux formation as readily as dextran 150. The degree of rouleaux formation was

severe enough to cause considerable difficulty in blood grouping and saline cross-matching. There are at present few published accounts dealing with this aspect of dextran 110. Ricketts (1966) found rouleaux formation a hindrance to satisfactory saline cross-matching in only two cases, and then with serum concentrations of modified dextran considerably higher than in the present investigation. Though Ricketts found a moderate increase in E.S.R. with modified dextran in experiments in vitro, this could not be compared directly with the marked increase noted here, since Ricketts used the Wintrobe method for estimating the E.S.R.

There is a critical level of molecular weight so far as rouleaux formation by dextrans is concerned (Thorsén and Hint, 1950). Dextrans with an average molecular weight below 60,000 cause no increase in sedimentation rate. As the molecular weight increases above 60,000, red-cell rouleaux formation appears and the sedimentation rate rises progressively.

Macrodex has an average molecular weight of about 70,000. About 10% of the preparation has a mean molecular weight of 108,000 and 9% of 25,800 (Kjellman, 1965; Rousell, 1966; Nilsson, 1967). Hence on average Macrodex is only slightly above the critical molecular weight. Dextran 110 has an average molecular weight of about 110,000. Ten per cent. of the preparation has a mean molecular weight of 194,000, and 8% of 35,000 (Nilsson, 1967). This is reflected in an increased tendency to cause rouleaux formation and a rise in the erythrocyte sedimentation rate.

Thus from the point of view of effective blood grouping and cross-matching it would seem essential to take blood from a patient for these purposes *before* administration of dextran 110 or dextran 150. If immediate transfusion before withdrawal of blood is required Macrodex will cause little interference, and plasma or plasma-protein solution no interference, with blood grouping and cross-matching.

Summary

Plasma, plasma-protein solution, Macrodex, dextran 110, and dextran 150 were compared for their effect upon red-cell rouleaux formation and erythrocyte sedimentation rate in a series of in vitro experiments.

Plasma and plasma-protein solution do not produce rouleaux formation and have no effect upon the sedimentation rate. Macrodex, in concentrations likely to be found in plasma, does not cause marked rouleaux formation. Therefore administration of these substances before the taking of blood is unlikely to lead to any difficulty in blood grouping and cross-matching.

In contrast, both dextran 110 and dextran 150 produce marked rouleaux formation and a considerable rise in the E.S.R. They are likely to interfere with blood grouping and cross-matching, and should be given to a patient only *after* blood has been withdrawn.

Many thanks are due to Professor D. L. Mollin for the great interest that he has shown in this paper and for his many helpful comments.

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Paget's Disease: a Family with Six Cases

J. VERRIER JONES,* B.M., M.R.C.P.; MERVYN F. REED,† M.B., CH.B.

Brit. med. J., 1967, 4, 90-91

Although McKusick (1966) states that 52 families have been reported in which more than one member suffered from Paget's disease, it is a striking fact that there have been only three reports of familial Paget's disease occurring in Great Britain. Kilner (1904) recorded an affected brother and sister, and Smith (1905) an affected father and son. Rast and Weber (1937) described the cases of three affected sisters. The literature on familial Paget's disease has been fully reviewed by Ravault, Lejeune, Robert, and Maitrepierre (1963) and by McKusick (1966). Records have been published of one family with four confirmed and two probable cases (Ravault *et al.*, 1963), two families with six cases (Hanke, 1935; Dickson, Camp, and Ghormley, 1945), and one family with five cases (van Bogaert, 1933). The remainder of the reports are of smaller families. McKusick (1966) draws attention to the difficulty of studying the familial incidence of a disease which is often asymptomatic, and suggests that "it may be that a study of families using alkaline phosphatase determinations as a screening procedure would be productive."

The purpose of this paper is to put on record an English family in which six cases of Paget's disease have occurred in three generations, and in which nine unaffected members of

the family have been studied. Radiological investigations and alkaline phosphatase estimations have been made in 13 members of the family.

The Family

Details of the family are set out in the genealogical diagram and in the Table. Thirteen members of the family were visited. All were examined clinically, x-ray films of the pelvis and tibiae were taken, and the alkaline phosphatase was estimated. In the case of two members of the family who were dead (I 1 and II 3) it was possible to make a diagnosis of Paget's disease with reasonable certainty from the evidence given by the rest of the family. Four living members of the family had clinical Paget's disease (details are given in the Table), and in all of these the alkaline phosphatase was raised. Nine members, ranging in age from 81 to 17 years, had no clinical evidence of Paget's disease, and their bone radiographs and alkaline phosphatase were normal. The age of onset of Paget's disease in this family seems to be in the decade 40 to 50. Three of the unaffected members are in this age group, and are therefore likely to remain unaffected. Of the remaining six (aged 17 to 29) several are likely to develop the disease in later life. This study suggests that there are no early x-ray changes or abnor-

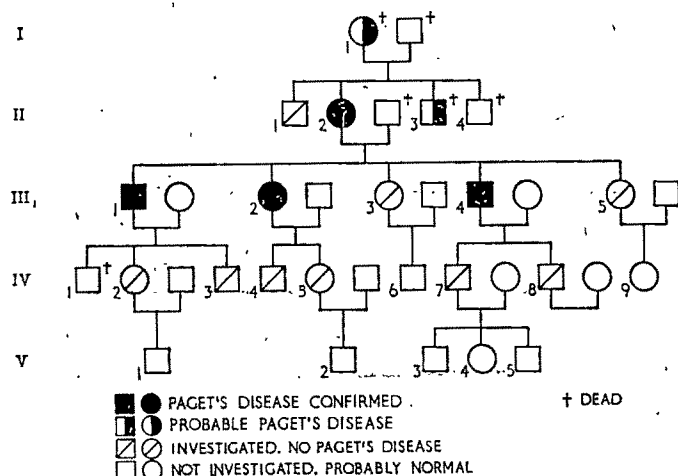
* Senior Medical Registrar, Bristol General Hospital, Bristol.

† Registrar in Obstetrics and Gynaecology, Southmead Hospital, Bristol.

malities of alkaline phosphatase on which it is possible to predict the subsequent development of Paget's disease.

Discussion

Paget (1889), in his original description of osteitis deformans, wrote: "I have tried in vain to trace any hereditary tendency



Genealogical diagram. Details of individual members are shown in the Table.

Details of Family

- I 1. Very bowed legs; had coffin made specially.
- II 1. Aged 81. Normal. Alkaline phosphatase (A.P.) 9.7 K.A. units/100 ml.
2. Aged 80. Paget's disease left tibia and pelvis. A.P. 26.
3. Legs deformed. Died 1937.
4. Aged 66 at death (1960). No evidence of Paget's disease.
- III 1. Aged 56. Paget's disease right tibia and pelvis. A.P. 36.
2. Aged 54. Paget's disease pelvis, both femora, both tibia. A.P. 54.
3. Aged 53. Normal. A.P. 7.
4. Aged 52. Paget's disease of lumbar vertebrae and pelvis. A.P. 76.
5. Aged 40. Normal. A.P. 6.
- IV 1. Died at age 16 (1957)—accident.
2. Aged 21. Normal. A.P. 14.
3. Aged 17. Normal. A.P. 7.
4. Aged 24. Normal. A.P. 10.
5. Aged 19. Normal. A.P. 6.
6. Aged 20. Not studied.
7. Aged 29. Normal. A.P. 11.
8. Aged 22. Normal. A.P. 7.
9. Aged 10. Not studied.
- V The members of this generation are all below the age of 10, and have not been studied.

to the disease. I have not found it twice in the same family." Rosenkrantz, Wolf, and Kaicher (1952), in a review of 111 cases, do not mention a familial form of the disease. Most of the previous reports of families with Paget's disease have been from France, Germany, or the U.S.A. The family reported here seems to be the largest family group reported in Great Britain.

All previous reports suggest that the pattern of inheritance is compatible with an autosomal dominant gene with incomplete penetrance, with the exception of Ashley Montagu (1949), who suggested that it was inherited as a sex-linked recessive. Our findings are consistent with an autosomal dominant inheritance.

Clinically the disease in the family studied seems limited to the tibiae, pelvis, and lumbar spine. No case involving the skull has been encountered. The cases are all reasonably benign, with only minor symptoms in most cases and no instance of cardiac failure. This is comparable with the case reports in the literature.

Summary

An English family is reported in which six cases of Paget's disease have occurred in three generations. Nine unaffected members of the family have also been studied. There is no evidence of radiological abnormality in the clinically unaffected members, and alkaline phosphatase levels are normal. The disease is mild (with onset of symptoms in the fifth decade), and appears to be inherited as an autosomal dominant.

We are grateful to Dr. E. Rhys Davies and to the radiology department, Bristol General Hospital, for radiological studies on most of these patients. It is a pleasure to acknowledge the assistance of the patients' general practitioners.

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Preliminary Communications

Evidence for Autonomic Denervation in Familial Dysautonomia, the Riley-Day Syndrome

Brit. med. J., 1967, 4, 91-92

The clinical features and experimental findings in familial dysautonomia have been summarized by Riley (1957), Riley and Moore (1966), and Goodall *et al.* (1967). Vasomotor instability, poor muscular co-ordination, impairment of sweating lacrimation and temperature control, and defective taste all point to a widespread neurological disorder. The absence of a flare in response to intradermal histamine and the exaggerated response to infusions of methacholine or noradrenaline offer further evidence of faulty autonomic control, as does the potentiated miosis following instillation of methacholine drops into the conjunctival sac.

Pupil responses to sympathomimetic amines have recently been used in studies on surgically induced sympathetic denervation and to evaluate the mode of action of adrenergic blocking drugs, such as guanethidine (Sneddon and Turner, 1967). Smith, Dancis, and Breinin (1965) investigated some of the ocular responses to autonomic drugs in familial dysautonomia, and concluded that there was evidence of parasympathetic but not of sympathetic denervation. The pupil responses in a female patient aged 18 months with this condition, reported in detail elsewhere (Goodall *et al.*, 1967), are here described, the results extending and differing from previous accounts.

METHOD

The experimental procedure is that described by Sneddon and Turner (1967). The eyes of the patient, and of four control children taking no drugs and who were matched for

age and eye colour (dark brown), were photographed under standard lighting conditions. The nature of the procedure was fully explained to the parents of these children, and their permission was obtained in every case. A Nikon F single lens reflex camera was used, mounted on a movable stand with bellows attachment. The camera settings were fixed and the whole camera was moved for focusing, resulting in a constant magnification of $\times 2$ when the patient's pupils were in focus. Four photographs of each subject were taken within a 15-second interval every 10 minutes for 30 minutes after the instillation of one drop of the drug under investigation into the conjunctival sac. In the subsequent measurements of pupil size the negatives were projected on to a white screen at a final magnification of $\times 8$. Pupil diameters were measured as the transverse diameter of this image and mydriasis or miosis was expressed as the percentage increase or decrease in pupil diameter from control values determined before drug instillation.

The drugs used were eye-drops containing methacholine 2.5%, physostigmine 0.5%, phenylephrine 10%, or ephedrine 2%. The experiments were carried out over four weeks, a different drug being administered each week.

RESULTS

The results are shown in the Table. Methacholine and physostigmine produced a greater miosis in the patient than in the control subjects. The mydriasis produced by phenyl-

Percentage Miosis and Mydriasis at 30 Minutes After Administration of Drugs into the Conjunctival Sac of One Eye in Four Control Subjects and a Patient with Familial Dysautonomia. The Results are the Means of Four Readings From Each Subject

	% Miosis				% Mydriasis			
	Methacholine 2.5%		Physostigmine 0.5%		Phenylephrine 10%		Ephedrine 2%	
	Mean	S.E.	Mean	S.E.	Mean	S.E.	Mean	S.E.
Controls	0	0	44	7	25	4	33	5
Patient	39	5	72	7	61	2	0	0

ephrine was also much greater in the patient, but ephedrine, which produced a mydriasis in the controls, did not have a measurable effect in the patient.

DISCUSSION

The mydriatic action of sympathomimetic amines is less in subjects with dark irides than those with light irides (Obianwu and Rand, 1965). It is therefore important to match subjects for eye colour.

Methacholine acts directly on parasympathetic end-organ receptor sites. The exaggerated response to this drug in our patient is characteristic of denervation (Emmelin, 1961) and indicates that usually her pupil has little if any parasympathetic tone. When the anticholinesterase drug physostigmine is given it is apparent that the pupil also reacts to endogenously released

acetylcholine. Physostigmine prevents its breakdown, and the miosis following its administration is good evidence that acetylcholine is being synthesized in parasympathetic nerve endings, though the rate may be reduced or its release impaired. Unfortunately there is no parasympathomimetic drug available analogous to ephedrine on the sympathetic system which releases stored acetylcholine from nerve endings. These findings agree with those of other workers and indicate a partial parasympathetic denervation phenomenon.

The response to phenylephrine, a sympathomimetic drug acting directly on sympathetic end-organ receptor sites, has not previously been documented. Together with the response to ephedrine, which releases noradrenaline from granules in postganglionic sympathetic nerve endings, the responses are similar to those found in surgically induced Horner's syndrome and in chronic treatment with local guanethidine (Sneddon and Turner, 1967).

This is good evidence that the response in familial dysautonomia parallels sympathetic denervation produced artificially. Though this conclusion differs from other reports, it is in agreement with the increased sensitivity to noradrenaline infusion found in this condition (Smith and Dancis, 1964). The absence of ephedrine mydriasis indicates absent or reduced transmitter stores in the sympathetic nerve ending.

We did not use adrenaline eye-drops as absorption is unpredictable, nor cocaine, as it was thought undesirable to anaesthetize the eyes of control subjects of this age. This has been done in older children and a mydriasis reported (Smith *et al.*, 1965), but the degree of dilatation compared with control subjects was not stated.

SUMMARY

Denervation phenomena both in the sympathetic and in the parasympathetic control of pupil diameters are reported in a child with familial dysautonomia.

Exaggerated responses were demonstrated to parasympathetic and direct-acting sympathomimetic agents.

We thank Dr. Dennis Cottom for permission to study patients under his care at the Hospital for Sick Children, Great Ormond Street, London W.C.1.

ELLIOT SHINEBOURNE, M.B., M.R.C.P.

J. M. SNEDDON, B.Sc.

PAUL TURNER, M.D., B.Sc., M.R.C.P.

St. Bartholomew's Hospital,
London E.C.1.

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Medical Memoranda

Corrosive Damage to Stomach Simulating Carcinoma

Brit. med. J., 1967, 4, 93-94

Lesions of the stomach after the ingestion of corrosives are reported infrequently in the British surgical literature. Such lesions are apparently more common in the United States and Europe.

The case reported is of interest in that it has unusual features but at the same time illustrates some of the classical points found after corrosive injury. It is unusual in the diffuse nature of the gastric damage produced and the way in which it was treated. It shows, on the other hand, the following classical features: the history of mental disease, the sparing of the oesophagus, the ulceration, and the difficulty found in differentiating corrosion from carcinoma. The similarity between cancer and a corrosive lesion was here so striking that at operation a confident diagnosis of the linitis plastica type of carcinoma was made.

CASE REPORT

A 57-year-old carpenter was brought to the accident unit on 20 February 1965, having drunk a quarter of a pint (140 ml.) of yellow fluid from a bottle labelled "turpentine." This fluid was used as a soldering flux and was found to contain a high proportion of hydrochloric acid. The patient had been under the care of a psychiatrist for a depressive illness for one year. He had twice been admitted to a mental hospital for electric convulsion therapy, and was due for readmission on 21 February. After drinking the fluid he had vomited and become drowsy, and complained of pain in the abdomen. When examined in the accident unit he had hypotension, abdominal tenderness, and a blackened tongue. His blood pressure rapidly returned to normal. He was given sodium bicarbonate to

drink and was admitted. After a few days' observation, he was discharged to the mental hospital.

On 4 March he was again brought to the accident unit. He had vomited fresh blood twice during the previous six hours. His blood pressure was 110/90 mm. Hg, and there were no abnormal physical signs. On direct questioning he admitted having had indigestion for some weeks. Barium studies showed a small, aperistaltic, rapidly emptying stomach with a small ulcer on the lesser curve of the pyloric antrum, the appearances being consistent with a diffuse scirrhus carcinoma (Fig. 1). Surgical opinion was sought and a laparotomy was undertaken on 24 March. A thoracoabdominal incision was made through the bed of the seventh rib, dividing the diaphragm to the hiatus. The stomach appeared to be of a dark red colour, and its walls felt thick and of firm consistency. The whole organ was adherent to the neighbouring viscera. There were hard lymph nodes in the splenic hilum and in the gastrohepatic omentum. The liver and other viscera were normal. A confident diagnosis of carcinoma of the stomach was made and a total gastrectomy was decided on. The body and tail of the pancreas, spleen, and greater and lesser omenta were removed en bloc with the stomach. Reconstitution was made by a Roux-en-Y oesophagojejunostomy, and a jejunojejunostomy was performed distal to the anastomosis. A Ryle tube was left across the anastomosis and the pleural space was drained to an underwater seal. Recovery was uneventful and he was discharged 19 days after operation.

The pathologist's report on the excised stomach was as follows: "A subacute gastritis involving most of the stomach and characterized by ulcers with a floor of granulation tissue lacking the usual zone of necrosis seen in peptic ulceration (Fig. 2). Infiltration most marked in the mucosa and submucosa with lymphocytes, plasma cells, and eosinophils. Occasional small epithelioid cell and giant-cell granulomata, with giant cells in the superficial granulation tissue. Small cysts filled with fatty material and extensive endarteritis and endophlebitis fibrosa. Nonspecific catarrh in the lymph nodes." The pathologist was of the opinion that such a lesion could have been due to the consumption of corrosive material some weeks previously.

COMMENT

Many agents can cause corrosive gastritis. Hydrochloric acid is the commonest in England; usually it is found in soldering flux. Others are sulphuric and nitric acids, more rarely lysol and formaldehyde. The first case in the world literature was reported by Robert in 1828. His patient drank sulphuric acid. The case of a patient who drank formaldehyde was reported in Britain by Vinson and Harrington (1929).

Corrosives are drunk most commonly by people with mental disorders, as in this case. They may also be taken by mistake

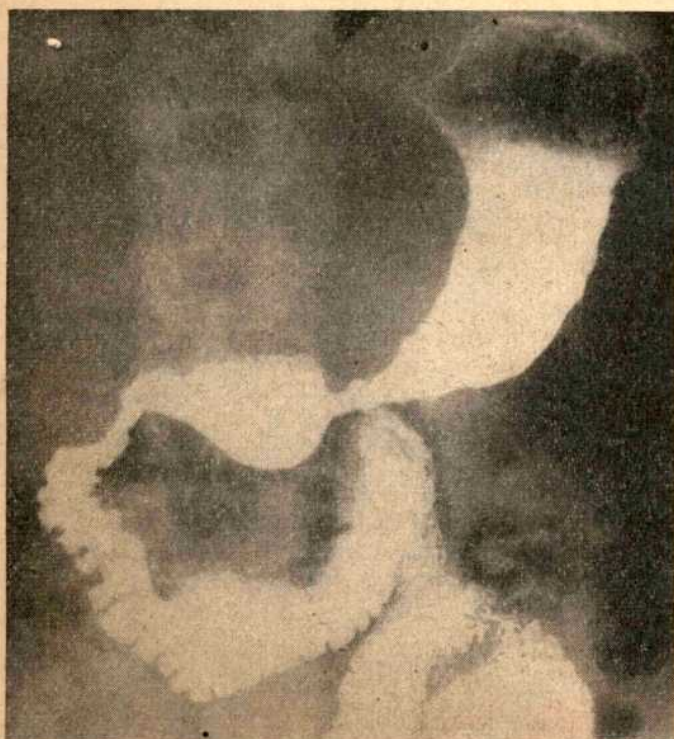


FIG. 1.—Photograph showing steerhorn stomach and a lesser-curve ulcer at pyloric antrum.

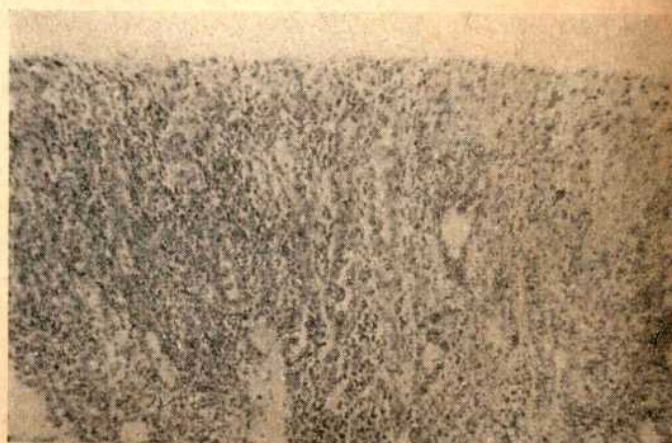


FIG. 2.—Floor of ulcerated area to show granulation tissue heavily infiltrated with inflammatory cells and without a superficial zone of necrosis. (H. & E. $\times 135$.)

and by children (Tucker and Gerrish, 1960). Few patients survive after taking sulphuric acid (Gray and Holmes, 1948). Robert's patient lived for nine weeks.

In corrosive damage to the stomach the usual lesion is pyloric stenosis of rapid onset. There is a characteristic histamine-fast achlorhydria. One is particularly likely to make a diagnosis of carcinoma from the radiographs. The possibility of carcinoma may force a laparotomy for a decision. Even at operation the condition may resemble carcinoma to a remarkable degree.

In 80% of lesions of the upper gastrointestinal tract due to acids the oesophagus is spared; 20% have concomitant gastric and oesophageal lesions. Ingestion of alkalis damages the stomach and oesophagus equally or spares the stomach (Skapinker and Crawshaw, 1954). Moynihan's (1926) series all had pyloric lesions. Strode and Dean (1950) described the microscopical lesion, which was similar to that in our case.

Treatment consists of emergency and resuscitative measures and surgery for the results of the damage. The acid should be neutralized with magnesium bicarbonate. Tracheostomy or intubation may be necessary for glottic oedema. Intravenous fluid and electrolyte and calorie intake maintenance will be required for some time.

Surgery is undertaken for the results of the corrosion. Local plastic procedures in the region of the pylorus—for example, pyloroplasty or gastroduodenostomy—are unsatisfactory because of the poor tissues and progressive fibrosis. Gastroenterostomy was the usual treatment before 1948. Gray and Holmes (1948), reviewing 139 cases, could find only three treated by partial gastrectomy. Gastroenterostomy, though often satisfactory, has a number of disadvantages—poor tissues and advancing fibrosis, stomach ulceration later, and gastric mucosal metaplasia. Strode

and Dean (1950) reported two cases treated by partial gastrectomy. Strange *et al.* (1951) and Skapinker and Crawshaw (1954) performed total gastrectomies. Hodgson (1959) advocated partial gastrectomy.

From these reported cases the best management of corrosive gastric injury appears to be partial gastrectomy. It is occasionally necessary to perform a total gastrectomy for the more unusual diffuse lesion.

We would like to thank Mr. A. B. M. Currie for allowing us to publish this case and for his help; and Dr. R. G. F. Parker for advice and his interpretation of the histological sections.

S. C. KENNEDY, M.B., F.R.C.S.
A. E. BAVAKI, M.D.

East Birmingham Hospital

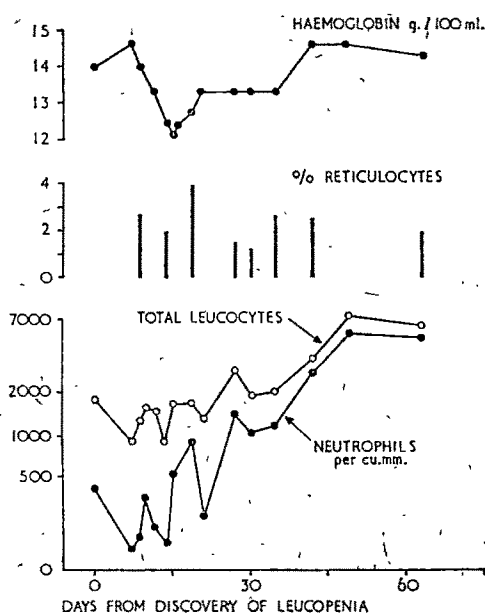
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Haemolysis and Agranulocytosis Complicating Treatment with Methyldopa

Brit. med. J., 1967, **4**, 94

Methyldopa occasionally causes autoimmune haemolysis (Worledge, Carstairs, and Dacie, 1966). Agranulocytosis has also been attributed to this drug (Hallwright, 1961). A case is presented showing both these complications with demonstrable autoantibodies on the red and white cells.



CASE HISTORY

A man aged 71 suffering from hypertension had been treated with methyldopa (2 g. daily) for 16 months. For the last six of these he had also received chlorpropamide (200 mg. daily) on account of mild diabetes. When admitted to hospital his liver and spleen were found to be enlarged and both drugs were stopped, but no active treatment was given for the haematological disturbance discovered.

The results of the haemoglobin, reticulocyte, and white cell estimations are summarized in the Chart. The bone marrow showed normoblastic hyperplasia, active granulopoiesis to the metamyelocyte stage, and excessive iron storage. The half-life of ^{51}Cr -labelled red cells ($T_{1/2}^{51}\text{Cr}$) was reduced to 20 days. The serum bilirubin was 1.4 mg./100 ml. The red cell osmotic fragility was normal. The direct antiglobulin test was positive and the eluate showed anti-e and nonspecific components.

The mixed antiglobulin reaction (Chalmers, Coombs, Gurner, and Dausset, 1959) for autoantibodies on the patient's white cells was repeatedly strongly positive during the early recovery phase. Both the red and white cells remained weakly sensitized after five months.

Comment.—As the complications found in this patient bear little resemblance to the few blood disorders attributed to chlorpropamide (Grace, 1959; Karlin, 1960; White, 1962), this drug seems unlikely to have been the cause. The immune haemolysis discovered is readily attributable to methyldopa, and the agranulocytosis, associated with an autoantibody, suggests that a similar process affected the white cells.

King's College Hospital,
London S.E.5.

K. G. A. CLARK, M.B., B.S.

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Goodpasture's Syndrome: Survival after Acute Renal Failure

Brit. med. J., 1967, 4, 95

Goodpasture's syndrome, the combination of haemoptysis and nephritis, is being recognized with increasing frequency (Davidson *et al.*, 1966). In its classical form it comprises a distinct clinical entity to which the term "lung purpura with nephritis" has been applied (Rusby and Wilson, 1965). This paper provides the first report of a patient with this condition who recovered after an episode of acute renal failure.

CASE REPORT

A 27-year-old mechanical engineer was admitted to hospital on 9 October 1965. He gave a history of persistent haemoptysis for seven months, increasing breathlessness for three months, macroscopic haematuria for one week, and failure to pass urine for 36 hours. He was afebrile, pale, and orthopnoeic. The blood pressure was 110/70 mm. Hg and there were crepitations over the right lower chest.

Investigations.—Blood urea 170 mg./100 ml.; serum Na⁺ 129 mEq/l.; K⁺ 3.4 mEq/l.; HCO₃⁻ 17 mEq/l.; calcium 9.2 mg./100 ml.; phosphate 6.0 mg./100 ml. Liver-function tests normal. Serum proteins: total 6.1 g./100 ml. (albumin 2.6 g., globulin alpha₁ 0.4 g., alpha₂ 1.2 g., beta 0.5 g., gamma 1.4 g.). Hb 8.7 g./100 ml.; P.C.V. 30%; M.C.H.C. 29%; E.S.R. 94 mm./1st hour (Westergren); W.B.C. 13,700/cu. mm. (normal differential count); reticulocytes less than 1%; prothrombin time 17 seconds (control 11 seconds). Blood coagulation mechanism otherwise normal. Serum iron 25 µg./100 ml., total iron binding capacity 435 µg./100 ml. Coombs test, antinuclear factor, L.E. cells all negative. Antistreptolysin titre less than 100 Todd units; blood cultures negative; sputum and throat culture, a few beta-haemolytic streptococci (Lancefield group A). The E.C.G. was normal, but chest x-ray examination showed patchy consolidation at both lung bases. Numerous haemosiderophores were present in the sputum. Bronchoscopy and bronchography were normal, as were cystoscopy and retrograde pyelography.

Histological examination of renal tissue obtained on 12 October and reported by Dr. M. K. McDonald showed a moderately severe acute proliferative glomerulonephritis, with epithelial crescent formation, a few small foci of glomerular necrosis, but no generalized obliteration of glomerular structure. There was some evidence of acute tubular necrosis. Arteritis was not demonstrable.

He was treated with penicillin but continued to have haemoptyses and remained anuric. Four days after admission the blood urea had risen to 266 mg./100 ml., and peritoneal dialysis was begun with rapid improvement. On 27 October he passed urine for the first time for 20 days. On 29 October dialysis was discontinued. The blood urea which had fallen to 76 mg. rose to 138 mg., but then fell spontaneously as renal function steadily improved. During this period he had another episode of haemoptysis associated with sore throat, radiological evidence of further intrapulmonary haemorrhage, and the antistreptolysin O titre rose to greater than 2,000 Todd units. A further course of penicillin was given, and by discharge on 20 December he was clinically well and has remained well. The blood pressure was 140/90 mm. Hg, Hb 17.4 g./100 ml., E.S.R. 7 mm./1st hour, blood urea 29 mg./100 ml., and creatinine clearance 100 ml./min. There was no haematuria but moderately heavy proteinuria persisted. A second renal biopsy, performed on 29 November 1966, showed complete hyalinization of a small number of glomeruli: the remainder showed only a minor degree of endothelial swelling and focal endothelial cell proliferation and no crescents were visible.

COMMENT

Goodpasture's syndrome can be distinguished histologically from polyarteritis nodosa by the absence of significant arteritis, and is thought by some to be related to idiopathic pulmonary

haemosiderosis (Elder *et al.*, 1965). The cause is obscure, though there is evidence to suggest a hypersensitivity or immunological reaction (Duncan *et al.*, 1965). Streptococcal infection is not thought to be important, though cases with high antistreptolysin O titres have been described (Lundberg, 1963; Spreccace, 1963; McCall *et al.*, 1965).

In 1964 Benoit *et al.* reviewed 52 cases, by 1966 Davidson *et al.* increased the number to 105, and there are at least 38 further cases in the literature, bringing the total to 143. Goodpasture's syndrome is often fatal, death resulting either from massive pulmonary haemorrhage or from renal failure. Eighteen of the many patients reported as dying of uraemia have been dialysed, sometimes inadequately by present standards. Two patients who had been dialysed were still alive at the time of reporting: one has been maintained by intermittent haemodialysis (Freeman *et al.*, 1966), and the other was alive 16 months after renal transplantation (Cleveland *et al.*, 1964). Twenty-one other reported cases of Goodpasture's syndrome have survived (Bloom *et al.*, 1965; Duncan *et al.*, 1965; Elder *et al.*, 1965; McCall *et al.*, 1965; Pasternack *et al.*, 1965; Portwich and Encke, 1965; Sybers *et al.*, 1965). In the majority the renal involvement, where detailed, comprised proteinuria and haematuria without deterioration of renal function. Thirteen were treated with steroids, seven improved spontaneously, and details of therapy are not mentioned in the others.

In the present case the course of the illness was initially characteristic of Goodpasture's syndrome, but the severity of the renal failure seemed disproportionate to the pathological appearances in the glomeruli and may have been partly accounted for by the coexistent tubular changes. None the less, recovery after prolonged anuria or oliguria due to any form of glomerulonephritis is said to be very uncommon (Persoff, 1965). This is the first reported case of Goodpasture's syndrome where such recovery has occurred. With adequate dialysis other patients may survive and all uraemic patients with Goodpasture's syndrome should be treated as if suffering from potentially reversible acute renal failure.

Our patient received neither steroids nor immunosuppressive therapy, and there is no evidence to suggest that these drugs are of value during the acute uraemic phase.

J. F. MUNRO, M.B., M.R.C.P.ED.
A. M. GEDDES, M.B., M.R.C.P.ED.
W. L. LAMB, M.B., F.R.C.P.ED.

Royal Infirmary, Edinburgh 3.

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Acquired Ichthyosis from Breast Cancer

Brit. med. J., 1967, 4, 96

Non-metastatic skin manifestations of malignant disease are well recognized (*Med. Clin. N. Amer.*, 1965). They include acquired ichthyosis, which is not uncommon in association with malignant lymphomas (Sneddon, 1955) but is rare in patients with cancer. Van Dijk (1963) described one case with lung cancer and from the literature collected 28 others associated with malignant disease, only one being cancer, and this was of the breast.

A case is described of disseminated breast cancer and acquired ichthyosis.

CASE REPORT

A 67-year-old woman was admitted to hospital under the care of Dr. E. W. Skipper in May 1966 with increasing pain in the shoulders, ribs, and spine of six months' duration. Her skin had been dry and itchy for three months. She denied any visual impairment.

On examination she was moderately obese with no signs of weight loss. Spinal movements were extremely painful, and the thoracic spine was kyphotic from compression fractures. The liver edge was palpable, and there was a small left pleural effusion. The



Photograph of patient's legs on admission, showing ichthyosis.

eyes were normal except for slight conjunctival injection. The skin showed generalized scaliness and dryness, and was slightly red and pigmented (see Fig.) A large carcinoma of the right breast was present with enlarged axillary lymph nodes, one of which showed metastatic breast cancer on biopsy. Malignant cells were found in the pleural effusion. Skin biopsy from the right arm was consistent with ichthyosis, and no carcinoma cells were seen. Spine

and chest x-ray films showed extensive osteolytic deposits. The fasting serum carotene and folate activity were 13 $\mu\text{g.}/100\text{ ml.}$ and 1.3 $\text{m}\mu\text{g.}/\text{ml.}$ respectively on admission and 86 $\mu\text{g.}/100\text{ ml.}$ and 3.9 $\text{m}\mu\text{g.}/\text{ml.}$ in November 1966. Faecal fat excretion over six days averaged 3.1 g./day. Other investigations, including full blood count, urinalysis, liver-function tests, blood electrolytes, cholesterol, iron, calcium, and phosphate, were essentially normal.

Stilboestrol 20 mg. daily was started on admission, and soon after she needed bendrofluazide 5 mg. daily to control leg oedema. A course of deep x-ray therapy was given to the spine, and a spinal support was supplied. One halibut oil tablet and 15 mg. of folic acid daily were given in addition for the first month. She responded well to treatment, and within six weeks her pruritus and ichthyosis disappeared and her bone pains cleared, leaving her with discomfort on spinal movements only. She remained in satisfactory health with no return of ichthyosis six months after admission.

COMMENT

There seems no doubt that the ichthyosis in this patient was related to the malignancy. On suppressive therapy her symptoms abated, general health improved, and the ichthyosis disappeared. The cause of ichthyosis in association with malignant disease is obscure. The fact that it may regress after treatment of the malignancy, as in this patient, suggests either that the neoplasm produces a metabolite causing the skin reaction or that it results from a deficiency of some substance taken up in high quantities by the neoplastic process.

Low serum vitamin-A levels as in this case have been noted in some patients. The reason is obscure and the low levels may be incidental. Our patient's dietary intake of vitamin A appeared normal, and she showed no evidence of malnutrition. Liver damage with impairment of vitamin-A storage has been suggested as a cause (Glazebrook and Tomaszewski, 1947), but it is unlikely in our patient. Vitamin-A absorption from the intestine is reduced in steatorrhoea, and Stephens and Rhodes (1964) reported the case of a patient suffering from ichthyosis, abdominal Hodgkin's disease, and steatorrhoea in whom histology of jejunal mucosa was characteristic of idiopathic steatorrhoea. Vitamin-A levels were not ascertained. No evidence of disordered bowel function was present in our patient. Ichthyosis has been reported after the use of cholesterol-lowering drugs, but our patient received no drug treatment before admission. High uptake by the cancer may have been the cause.

Ichthyosis is not described as a manifestation of vitamin-A deficiency. The skin may be dry, but hyperkeratinization in follicular and visual symptoms is usually the earliest manifestation. The absence of eye symptoms and signs and the marked skin involvement would not suggest low vitamin-A levels per se as the cause of the ichthyosis in the above case.

I wish to acknowledge with thanks the permission of Dr. E. W. Skipper to allow me to report this case, and for his help and criticisms in the preparation of this paper.

A. R. HASTE,* M.B., M.R.C.P.,
Medical Registrar, Royal Infirmary, Sheffield 6.

* Present address: Senior Medical Registrar, Royal Infirmary, Leicester.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Dyspepsia

N. F. COGHILL,* M.A., M.B., F.R.C.P.

In spite of all that has been written about dyspepsia the condition remains ill-defined. Dyspepsia and indigestion are commonly and justifiably used as synonyms, and in the *Shorter Oxford English Dictionary* the meaning of dyspepsia is given as "Difficulty or derangement of digestion; indigestion." In practice most of us use these two words more to describe a group of clinical syndromes than a physical or functional state or derangement.

History-taking is helped by getting the patient to define his terms so that he and the doctor are talking about the same thing. By "stomach" most patients mean abdomen. Pain and discomfort, as felt by the patient, need to be carefully assessed. Patients sometimes use the word "vomiting" for acid regurgitation, or even merely retching. "Wind" to them may mean excessive belching or passing of flatus, or feelings of abdominal distension or discomfort.

Patients do not always recognize that they are suffering from indigestion; others use this term to describe symptoms which obviously have nothing to do with the alimentary tract. To establish the relationship, if any, of the patient's symptoms to his intake of food it may be necessary to construct a timetable of his day. The symptom-time relationships which come to light are sometimes news to the patient.

Assessment of Clinical Manifestations

Some patients with a peptic ulcer causing actual pain will give a clear succinct history leaving the diagnosis hardly in doubt. Even then there are pitfalls: the radiologist may fail to find an ulcer, or the patient may be suffering from other important physical, psychological, or social disease. Quite a number of cases need time and a sense of leisure for the history-taking that is not always immediately available in a busy out-patients.

It is good practice to try to assess whether a patient has pain or not. Though organic disease may cause no more than discomfort, it is unwise, without thorough investigation, to discount such disease when the patient experiences pain. It may be difficult to appraise the patient's chief symptom. "Terrific pain" may turn out in the end to be merely discomfort. Much will depend on the severity of the chief symptom; and on the patient's pain sensibility, his state of apprehension, and even his intelligence. Most patients understand that pain arises when something is actually hurting them, and that otherwise it is fair to speak of discomfort only. But some patients cannot categorize their abdominal sensations in this way.

A wide variety of epithets are used to describe the pain (or discomfort) of peptic ulcer, but about 7% of patients with dyspepsia are unable to describe it. In a recent survey¹ we found that only one in six patients with gastric or duodenal

ulcer complained of gnawing pain, usually thought of as common in these conditions, but that half of these patients had either gnawing or aching pain. We found that in non-ulcer dyspepsia gnawing pain was much less frequent and a feeling of distension twice as frequent as in peptic ulcer.

Some people believe that they cannot digest certain foods, often either on inadequate evidence or merely because a doctor has told them to stop eating such food. Nevertheless, fried foods upset about 50% of patients with non-ulcer dyspepsia,² but fewer (about 40%) of patients with peptic ulcer. Many patients with gall stones or chronic cholecystitis can eat butter with impunity, though cooked fats upset them.

Wind and flatulence are symptoms often complained of by dyspeptic patients. They suggest biliary disease but may occur in about half the patients with peptic ulcer and non-ulcer dyspepsia, and not infrequently accompany small intestinal disease and even heart disease; so that assessment of their clinical relevance is difficult. Nausea may occur in nearly half the patients with either peptic ulcer or non-ulcer dyspepsia, but vomiting, which used to be thought rare in uncomplicated peptic ulcer, may be seen in a quarter to one-third of such patients. Persistent vomiting may occur in patients with gall stones, duodenal obstruction, or gastric carcinoma, or as a hysterical symptom. A good appetite is commoner in duodenal ulcer than gastric ulcer, and is uncommon in gastric carcinoma.

Sometimes a dyspeptic patient loses weight. When the history is short, particularly when there is anorexia and atypical pain and the patient is a middle-aged man, the possibility of carcinoma of the stomach springs to mind. But such patients may be suffering merely from anxiety, perhaps inflamed by a family history of cancer. The loss of weight is due mainly to deficient food intake: the clue lies in obtaining from the patient other symptoms of anxiety, perhaps among them the story that although he feels hungry before a meal he feels full as soon as he starts to eat it.

Changes in Symptoms

When, after a long time, new and more severe symptoms appear it is wise to redouble the search for an organic disorder, which may prove difficult to find.

Many years ago I saw a man of 43 who for 18 years had had intermittent heartburn, flatulence, and epigastric discomfort 1-1½ hours after eating. Alkalis relieved him. For one month he had had new symptoms—nausea, and persistent lower abdominal pain unrelieved by alkalis. Full investigation, including laparotomy, failed to reveal a cause for any of his symptoms. Later he was admitted to another surgical ward as an emergency with severe pain. A registrar, nonplussed by the case, told the patient his symptoms were caused by mental illness. The patient was angry and discharged himself. Later still, at another hospital, secondary carcinoma was found in a cervical gland, and a small seminoma was

* Consultant Physician, West Middlesex Hospital, Isleworth.

discovered. The patient had lived in a house overlooking the garage where I kept my car and his widow used to come out and talk about suing the surgeon who had misdiagnosed her husband's case. Fortunately she did not do so.

It is essential for the patient to show the site of pain or discomfort when stripped. The position indicated with the clothes on is frequently misleading. If the unclothed patient with epigastric pain can "put one finger on it," indicating its localized nature, "it" is more likely than not to be due to a peptic ulcer.

Certain points in the assessment of the case will have a bearing on the treatment advised—the severity and duration of symptoms; the patient's pain sensibility (difficult to measure); the time his symptoms have kept him off work; the number of cigarettes he smokes per day; his mode of life; and his work and how he copes with it.

Diagnosis

The physical findings in most forms of dyspepsia are scanty, and for prolonged periods they may be absent. It is this, combined with the overlap of symptoms in gastric ulcer, duodenal ulcer, and non-ulcer dyspepsia, that has so far made it impossible in the majority of patients, even with computer-analysis of symptoms, to establish the diagnosis exclusively by clinical means. In about a fifth of patients with peptic ulcer the history is so atypical that it may not at first even suggest that diagnosis.³ Once it is decided that the patient has dyspepsia a barium meal examination should be performed. This will not give the diagnosis in every case, for a small number of peptic ulcers and gastric carcinomas will be missed. Gastroscopy or the use of the gastro-camera and even laparotomy may be required to make the diagnosis. In the case of patients with long histories who have been investigated in different hospitals one should avoid being unduly influenced by previous conceptions about the case, although examination of others' findings is naturally helpful. If appropriate investigation fails to reveal the diagnosis the record must be gone over again, if necessary at an extended consultation.

There is some evidence¹ that the symptom pattern in non-ulcer dyspepsia may be more helpful diagnostically than that in gastric or duodenal ulcer.

During the last 20 years hiatus hernia and its associated oesophageal reflux has become recognized as a common cause of dyspepsia. Unfortunately radiological demonstration of hernia, reflux, or both is often difficult. The condition should be suspect whenever there is complaint of heartburn and acid regurgitation in association with epigastric pain, particularly when they are influenced by posture (including lying down). Difficulties arise when peptic ulcer and hiatus hernia, both common conditions, are present in the same subject. Heartburn is probably commoner in a patient with a hiatus hernia who also has a normal mucosa or a duodenal ulcer than in one with atrophic gastritis associated with reduced gastric acidity.

Dyspepsia affects many people in whom no physical disorder can be found to explain it. Thorough search should be made for nervous causes, and this involves unhurriedly talking with the patient. The physician must appear to be interested in, and to understand, the patient's problems. Sometimes the experienced physician can sort these out, and offer adequate advice, at one consultation. Indeed, negative findings on examination and investigation may be all the patient needs for reassurance and the loss of his symptoms, particularly when there is unjustified cancerphobia. But it may be necessary to set aside adequate time by making another appointment. The medical social worker or dietitian may give valuable assistance in some of these patients, but for the most part they are the responsibility of the physician. Only occasionally will they need to be referred to a psychiatrist. Aetiological relationships

are not made less obscure by the finding, in our previously quoted survey, that worries occupying patients' minds for a large part of their waking hours beset as many patients with peptic ulcer as with non-ulcer dyspepsia. About three-quarters of all these patients related their dyspepsia to their worries.

The question of whether gastritis can cause dyspeptic symptoms is still unresolved. We have found some evidence¹ that idiopathic chronic atrophic gastritis may cause dyspepsia in some patients, but little to support the suggestion⁴ that gastritis can cause a specific dyspepsia.

Other Alimentary Causes of Dyspepsia

Disease of the biliary tract frequently causes indigestion. Gall stones or chronic cholecystitis may cause pain or discomfort in the epigastrium or right hypochondrium, and, as in gastric ulcer, duodenal ulcer, and gastritis, pain may also be felt in the back. There is usually associated flatulence and often vomiting. With gall stones the pain may be severe and prolonged and is not a true colic; "biliary colic" is a misnomer for this pain. The symptoms of carcinoma of the gall bladder, bile duct, or ampulla of Vater are usually more insidious. Jaundice is likely to appear at some stage with all disorders affecting the biliary tract; unfortunately in carcinoma it is not infrequently a late sign.

Any condition which interferes with the ability of the small or large bowel to pass food residues onward may give rise to flatulent dyspepsia and even pain after eating. Such disorders include Crohn's disease and other forms of obstruction of the small intestine, carcinoma of the colon, and ischaemic disease of the intestine. The use of new techniques for measuring intraluminal pressures in the large bowel^{5,6} has shown that some patients with unexplained abdominal pain or discomfort occurring soon after meals have irregular and increased post-prandial motility of the colon.⁷ These patients are often constipated and have what used to be termed "spastic colon," or "irritable colon." In the light of new knowledge their condition is better referred to as "functional colon disorder." Though our understanding of this condition has increased, treatment remains rather unsatisfactory.

A high serum calcium level is associated with anorexia, nausea, vomiting, abdominal discomfort, and hyperchlorhydria. Hyperparathyroidism not infrequently causes dyspepsia, and many patients with it develop duodenal ulcers.

Other, less common, causes of indigestion are intestinal worms (especially giardiasis), and hypertrophic gastritis.⁸ When dyspepsia is associated with weight loss, anaemia, hypoalbuminaemia and oedema carcinoma of the stomach or hypertrophic gastritis (Menetrier's disease) should be considered. Gastrectomy will cure the oedema in either case, for it is due to protein-losing gastropathy.

Duodenal diverticula are believed seldom to cause symptoms unless very large. Duodenitis is still a condition of unknown clinical and pathological importance. Few people now believe that dyspepsia is caused by chronic appendicitis.

Drugs

At a time when iatrogenic disease is on the increase it is well to remember that aspirin, corticosteroids, phenylbutazone, indomethacin, potassium chloride, ammonium chloride, and ferrous salts are commonly used drugs that, in the form of tablets, may cause dyspepsia (and worse) in susceptible individuals. Symptoms are less likely if these substances are taken a few minutes before a meal, which suggests that some of them cause dyspepsia by the production of a high local concentration of soluble salt or drug; if this is so it conflicts with currently held ideas about the insensibility of the gastric mucosa.

Non-alimentary Causes of Dyspepsia

Renal Disease.—Patients with renal disease are not infrequently sent first to a gastroenterologist. Renal infection or stone, or hydronephrosis, may be missed when the patient presents with dyspepsia. Pyelonephritis may of course occur in a patient with a duodenal ulcer or some other cause of dyspepsia.

Anaemia.—Patients with severe untreated Addisonian pernicious anaemia, or hypochromic anaemia, often suffer from indigestion, which always disappears, if there is no other cause for it, when their anaemia is cured.

Heart Disease.—Vague dyspepsia is associated in some patients with ischaemic heart disease (sensations of "wind round the heart," abdominal flatulence and aerophagy), or congestive heart failure (pain over the congested liver, and anorexia and possibly discomfort from a congested stomach). Diagnosis is especially difficult when, as is not rare, heart disease and hiatus hernia occur together in the same patient. The perfusion of hydrochloric acid through the oesophagus has been found^{9,10} to be a reliable test for differentiating oesophageal from cardiac ischaemic pain.

Other Conditions.—Patients with anxiety and/or depression often develop dyspepsia. It is usually not very suggestive of physical disease but often needs investigating, if only as part of the treatment of the nervous condition.

Uraemia causes anorexia and sometimes indigestion. "Fibrositis" of the abdominal wall, and a small epigastric midline hernia can also cause much confusion in the diagnosis of dyspepsia.

Accounts of dyspepsia commonly refer to a long list of other aetiological factors. In the light of present knowledge it is questionable whether, for example, allergy, unhygienic eating

habits, or an irregular mode of life (whatever that may mean) should be seriously considered as causes.¹¹

Tertiary syphilis has become rare and gastric crises now seldom trap the unwary into a diagnosis of peptic ulcer. If pulmonary tuberculosis ever did cause indigestion it was probably through associated asthenia, much as it is presumably caused in patients with untreated anaemia.

The relationship of indigestion to a variety of organic and nervous conditions has been interestingly and amusingly discussed by Alvarez.¹² Accounts of dyspepsia commonly list numerous causes of "functional" indigestion. It is tempting to speculate about the real relationship, for example, of physical fatigue, frustration, and anger with dyspepsia. Sometimes such states of mind or body must be coincidental; sometimes perhaps they and the dyspepsia have a common cause. The anxious, depressed, obsessional dyspeptic, whose overactivity is a substitute for peace of mind, is like those whose chief characteristics are their power of sustained unthinking activity, and their lack of curiosity about their destinations.¹³ Does this provide a clue about aetiology and therapy for some types of dyspepsia?

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MEDICINE TODAY

Management of Rheumatoid Arthritis

"*Medicine Today*" is the television series for doctors produced by the B.B.C. Advice on the preparation of the programme is given by the Association for the Study of Medical Education.

The programme on B.B.C. 2 on 10 October was on the subject of rheumatoid arthritis. Printed below is an article prepared with the help of expert contributors to complement the television programme, which will be repeated on B.B.C. 1 on 18 October at about 11.20 p.m.

Anyone unfortunate enough to acquire rheumatoid arthritis should be given as intelligent an understanding of the disease as possible. Ten minutes of conversation can lay the foundation of many years' effective care. There are many aspects of the disease which the patient should clearly grasp from the beginning—what is going on in the joints and what are the principles of treatment, together with the facts that inflamed synovia and erosions can heal, and that in most people the disease, even if it remains active over a long period, need not progress to serious incapacity. This last piece of reassurance is particularly important after a depressing visit to a hospital outpatient department, where the most severe forms of the disease are displayed. Yet it sometimes happens that all this gets left out; the general practitioner may have obtained a consultant opinion, and each has left the job of explaining things to the other. It is quite certain that there will be a good deal of advice from elsewhere. Friends, acquaintances, books, and women's magazines, acting from one motive or another, all add their quota of misinformation, and it is

as well for the doctor to get in first. However, not all the books that have been written for patients are bad, and a few are quite useful, one of the best and simplest being *Rheumatoid Arthritis*, a handbook for patients published by the Arthritis and Rheumatism Council.*

Among the questions many patients ask are those relating to the effect of weather and diet, the value of various irregular forms of treatment (a newspaper cutting is usually produced at this stage), and the place of rest and exercise in the management of the disease. There is little doubt that symptoms in certain patients are exacerbated by weather conditions. Most dislike cold and damp, but a few find hot weather trying. Rheumatoid arthritis, however, occurs in all parts of the world, and there is no reason to suppose that climatic factors have any influence on the progress of the disease. Similarly, diet has no specific effect. Some patients with advanced disease may be unable to purchase or prepare their meals properly. A regimen of cups of tea and bread-and-butter will contribute towards iron deficiency and avitaminosis, so that where necessary arrangements must be made for proper meals, with supplementary vitamins and iron. With regard to "fringe" treatments, one can only sympathize with the desire to turn to any source of possible cure, but a firm hand sometimes has to be taken with foolish or expensive nonsense.

* Obtainable free by doctors only from the Secretary, Arthritis and Rheumatism Council, Faraday House, 8-10 Charing Cross Road, W.C.2.

Rest and Exercise

The question of rest and exercise is a difficult one on which to generalize, and both play a part in management. There is no doubt that local and general rest can lead to improvement, with diminution in joint pain and swelling and fall in sedimentation rate. This is particularly so in the early phases of the disease. A patient with moderate or severe early active rheumatoid arthritis should be given the benefit of a few weeks' rest in bed, preferably in hospital, where the break from work or household cares is complete, and where supervised physiotherapy, assessment of drug treatment, and investigative measures are more easily undertaken. Admission to hospital is not always practicable, however, nor is it necessarily desirable. Established daily routines, sometimes acquired with difficulty and practice, should not be interrupted, and older people are usually better off mobile and out of hospital. Whatever the circumstances, the posture in bed should receive careful attention. The mattress should be firm, prolonged flexion of the neck should be avoided by the use of a rigid back-rest during the day and restriction to one pillow at night, pressure on the legs and feet may be prevented by the use of a bed cage, but the use of pillows under the knees is prohibited.

Such measures help towards prevention of deformity and maintenance of function, which is the aim of treatment in rheumatoid arthritis. This is also accomplished by suitable exercises, supplemented where necessary by splinting. Exercises should be taught early and continued indefinitely. The particular movements to be emphasized depend to some extent on the individual pattern of joint involvement. Flexion contracture of the knees can be prevented by quadriceps exercises, contracture of the wrists by exercises of the forearm muscles and so on. Most of these exercises are straightforward enough, but sometimes some apparatus is desirable—for example, a rope over a pulley, easily fixed to a wall at home, can be very useful for shoulder movement. Formal exercises should be performed two or three times daily, but practised activity of many muscle groups can be carried out for a few moments at any time.

The patient should also be educated in the use of rest-splints for knees and wrists, which prevent prolonged flexion during the hours of sleeping. To summarize the rest and exercise problem: general and local rest are usually indicated during the acute onset or exacerbation of disease, and during subacute or chronic phases it is as well to avoid fatigue, taking a midday rest if possible, while active exercises must be carefully taught and continued as a habit. It is no exaggeration to say that scrupulous attention and encouragement by the practitioner in this regard can do more than anything else to maintain function in a patient with rheumatoid disease, while the plight of countless chairbound or bedbound arthritics is a testimony to the neglect of these simple measures.

Drug Treatment

Drug treatment was discussed in the television programme, and most of the principles are generally appreciated and accepted. The use of analgesics in maximum tolerated dosage is advisable in many patients, because relief of pain permits exercise and thereby assists in maintenance of function. However, pills should not be forced upon people who have a high threshold for pain and who are seen to be doing well without drug treatment. Despite all that has been written about its side-effects, aspirin is a relatively safe drug and its long-term use in rheumatoid arthritis is perfectly justified, but for patients who cannot tolerate it there are a number of alternative analgesics. Efficient analgesia and physical treatment of the sort already outlined are all that is required in the majority of patients with rheumatoid arthritis. Other anti-inflammatory agents—mainly gold salts and corticosteroid hormones—are necessary only where there is progressive and disabling disease

activity. The enthusiasm for gold salts in the thirties and for corticosteroids in the fifties has been replaced by a healthy respect for their potential dangers. The schedule of dosage for gold indicated in the programme is reasonably safe provided that a careful clinical and haematological watch is kept for incipient dermatitis, proteinuria, or blood dyscrasia. In the same way the dangers of corticosteroids are widely known, but serious trouble has usually been confined to patients on high dosage. Prednisolone 2.5–7.5 mg. daily is very unlikely to cause toxicity, and in this dosage it can often be withdrawn if the activity of the disease subsides. The drug should be considered when it confers increased mobility and functional performance and relief from severe morning stiffness, if these are unobtainable by any other means.

Long-term Management

Still, however, we are faced with the core of patients in whom the disease progresses, and where chronic disability poses various further problems in long-term management. Certain limitations of physical performance may now have to be accepted and environmental adaptation must be carefully planned. For the housewife there are numerous appliances which can be used in the house to help with cooking, housework, and personal activities. Details of these, and information about where they can be obtained, are given in another book published by the Arthritis and Rheumatism Council called *Your Home and Your Rheumatism*.† For the manual worker the necessity may arise of modification in his work, an invalid motor vehicle, or a complete change of employment, and here the help and advice of the disablement rehabilitation officer of the Ministry of Labour must be sought. And over the years there must be constant observation for various local complications which may need attention. Excessive synovial proliferation in a dorsal tendon sheath on the hand requiring excision; sudden weakness of extension of a finger due to tendon rupture requiring early suture; painful paraesthesiae in the fingers indicating a carpal tunnel syndrome, amenable to injection or to operation; progressive pain and instability in a single joint such as the wrist indicating the need for a work splint or arthrodesis; recurrent joint effusion requiring local injection of corticosteroids or synovectomy; exacerbation of joint pain raising the possibility of secondary infective arthritis; early flexion contracture of a knee requiring serial plasters in hospital; painful metatarso-phalangeal subluxation requiring suitable footwear or perhaps remedial surgery; ischaemic ulceration on the legs—these and many other problems may arise from time to time, and their early detection and successful handling play an important part in the management of the patient and the maintenance of physical, economic, and mental independence.

† This can be ordered by members of the public from the Arthritis and Rheumatism Council, Faraday House, 8–10 Charing Cross Road, W.C.2. Price 1s. 6d.+6d. postage.

B.M.J. Publications

The following are available from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1. The prices include postage.

<i>Is There an Alternative?</i> ...	Price 7s. 6d.
<i>Treatment of Common Skin Diseases</i> ...	Price 10s.
<i>Obstetrics in General Practice</i> ...	Price 32s. 6d.
<i>Child Care</i> ...	Price 32s. 6d.
<i>Charles Hastings and Worcester</i> ...	Price 3s. 6d.
<i>Health Centres and Group Practices</i> ...	Price 3s. 6d.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Albinism

Q.—A woman aged 34 is an albino with nystagmus and poor eyesight. One of her three brothers and one of her three sisters are albinos and one sister died at 10 weeks with spina bifida. Only one of her own five pregnancies has produced a live baby, and this boy died at 6 days with spina bifida. The other four pregnancies ended in miscarriages at either 9 or 26 weeks. The husband's family history is relatively unremarkable, except that one of his three sisters has congenital heart disease and a cousin on his mother's side is "mentally handicapped." What are the chances of this couple having a normal child?

A.—The recurrent abortions in this case are probably not due to genetic factors, and the risk of recurrence of miscarriage will depend on the underlying obstetric cause. If a pregnancy goes to term the risk of a neural tube malformation (anencephaly or spina bifida) is about 5%. If, however, a neural tube malformation is noted in any of the fetuses which miscarry the risk would be increased to about 1 in 10.¹

The albinism in the family is autosomal recessive and so is unlikely to appear in any offspring, provided that the marriage is not a consanguineous one. The congenital heart malformation in the husband's sister gives little or no increased risk to the children of the marriage.

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Overhung Bite

Q.—What is the treatment for a child aged 9 months who has an overhung bite? The two lower central incisors overlap the upper central incisors. At what age should treatment begin?

A.—There are two possible causes for the condition. One is that a slightly aberrant path of eruption has produced a backward slope of the upper primary incisors and/or a forward slope of the lower, leading to a reversal of their normal occluding relationship. The true relation may in fact be an edge-to-edge incisor bite, but, since this would be neither stable nor comfortable, the infant reflexly adopts a slightly protrusive mandibular position as the teeth are brought fully together.

A case of this type rarely requires treatment, since it has no harmful effect. The condition may be self-eliminating by normal wear of the incisal edges during the next few years or after stimulation of such wear by dental operative grinding of the teeth. Generally, however, it disappears when the primary teeth are shed and replaced by their permanent successors at about 7 years of age.

The second and more likely cause is a fault in the antero-posterior relation of the mandible to the maxilla, which is reflected in the relationship of the dental arches. The facial

skeletal pattern—of which this is one aspect—is established early in life, normally by 3 months after birth at the latest,¹ and thereafter does not usually change to any clinically significant extent. One can therefore expect the abnormal relation of the teeth to be perpetuated in the occlusion of the permanent teeth.

Numerous radiographic analyses of the facial growth patterns of children undergoing orthodontic treatment for dental malocclusions of all types have failed to show any resultant beneficial changes in the shape or relationships of the basal jaw structures. Before this evidence became available it was common for children with structural faults of the type under discussion to be fitted with an orthopaedic type of appliance which applied backward traction to the chin by elastics from a skull cap. Despite the belief of some clinicians, careful investigation has produced no proof that this treatment either changes the shape or inhibits the growth of the mandible,² and these must therefore be considered unrealistic treatment objectives.

A later modification of the traction appliance replaced the rigid chin cup with a fabric strap across the front of the lower jaw between lip and chin, and it has been successfully used on infants to correct a reversed bite of the primary incisor teeth.³ Its effect is solely to produce retroclination of the lower primary incisors by pressure through the lower lip, but it does not alter the underlying facial skeletal pattern. While doing no harm, this treatment is in the main a waste of time, since it has little or no effect in preventing eventual malocclusion of the permanent teeth.

The differential diagnosis of the condition is best undertaken by an orthodontist (a dental surgeon specializing in malocclusion of the teeth), and could well await complete eruption of the primary dentition.

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Trichomonal Vaginitis

Q.—What alternative treatment is there for persistent trichomonal vaginitis in patients in whom metronidazole causes a rash or other side-effects? Would giving antihistamines at the same time as the trichomonicide overcome the difficulty?

A.—Side-effects of metronidazole are very uncommon, though rashes are known. Such rashes are probably of the toxic kind rather than allergic, so that the administration of antihistamines would probably be ineffective.

When toxic effects are observed with metronidazole it would seem wise not to continue with the drug, for there is no threat to life from trichomonal vaginitis. Since metronidazole is the only oral form of therapy, the only alternative is some form of pessary. There are many of these dealt with in standard works of gynaecology.¹ Many

authorities would recommend acetarsol pessaries one every night for six weeks—even during menstruation, when recurrence is very common—and a further two courses of one pessary every night for ten nights at the next two menstrual periods. The efficacy of treatment should be regularly checked by pathological investigation.

Other side-effects of metronidazole therapy are leucopenia, abdominal discomfort, headache, depression, nervousness, and insomnia.²

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Serotonin in Foods

Q.—In what foods is serotonin mainly contained, and which items contain the most?

A.—Information on the distribution of serotonin, or 5-hydroxytryptamine, in common foods is not readily available, presumably because it is of little interest to dietitians concerned with the nutrition of normal subjects. It is formed from tryptophan by the action of micro-organisms.

Cheeses, which owe their attractive taste to products formed by micro-organisms, contain substantial amounts of serotonin, and Camembert cheese seems particularly rich. Serotonin is also found in brain, and the enzyme necessary for its formation is present in liver, kidney, and intestines. A more exotic source of serotonin is the salivary gland of the octopus, which may possibly be eaten as a delicacy in Italy. Bananas and pineapples have also been mentioned for their high contents of serotonin and other monoamines.

In the normal subject serotonin, after ingestion in the food, is detoxicated by monoamine oxidase, an enzyme normally present in the intestinal flora. When this enzyme is inactivated by certain drugs, notably the tranquillizer tranlycypromine and drugs based on the hydrazide molecule, unchanged serotonin may be absorbed into the system, producing severe hypertensive effects. For the benefit of patients treated with these drugs more extensive knowledge of the distribution of serotonin would certainly be useful in order to tell them what foods to avoid.

Triple Vaccine

Q.—Should the pertussis component be omitted from the triple vaccine when beginning a course of immunization in a child aged 4 months who is convalescing from whooping-cough?

A.—It is irrational to administer pertussis vaccine to a child who has already had whooping-cough. He should be immunized with three doses of absorbed diphtheria/tetanus toxoid (D.T./Vac/P.T.A.H.) given at intervals of not less than four weeks and six months respectively, starting at the age of 9 months. There is no need to give the combined toxoids early in infancy. Triple vaccine (D.T.P./Vac) is given early solely on account of the hazards of whooping-cough in the very young. The antibody response, however, is improved by delaying immunization until towards the end of the first year of life.

Book Reviews

The Very Stuff of Anaesthesia

Clinical Anaesthesia Conferences. Edited by Lester C. Mark, M.D. (Pp. 326+xii. £5 5s.) London: J. & A. Churchill. 1967.

In spite of the scientific advances in anaesthesia, nothing can take the place of continuous careful observation of the patient. What is seen, however, must be interpreted so skilfully that complications can be forestalled and accidents prevented. There is a real danger just now that young anaesthetists may concentrate their attention on the more "scientific" aspects of anaesthesia to the exclusion of the more mundane but equally important ones, which draw on an accumulated store of clinical experience and knowledge. Anaesthesia still causes preventable deaths and serious complications, the majority of which are usually due to crude and preventable things, of which respiratory obstruction, drug overdose, inhalation of vomit, and circulatory failure are but a few examples.

Descriptions of these and many, many, more are to be found in the case reports gathered together in this book. These reports are based on the clinical anaesthesia con-

ferences which are published regularly in the *New York State Journal of Medicine* and which have been a feature of that journal for some ten years. The cases make fascinating reading, for not only is the discursive style used—admirably suited to the subject material—but each case report is followed by a terse and apt commentary, frequently flavoured with the unique tang of American colloquialism to drive home a point. The complications, by no means always fatal, which are described, fall under the headings of respiration, cardiovascular system, blood transfusion, regional anaesthesia, muscle relaxants, obstetrics, urethral surgery, errors in technique, and others.

This book is the very stuff of anaesthesia, and those in training will get more value out of it than many a systematic textbook. An anaesthetist is more likely to be judged incompetent in his specialist examination or in his hospital practice for failure to recognize, prevent, or treat the complications of

anaesthesia exposed here, than for his knowledge at some more abstruse level, important though that may be. The experienced anaesthetist is bound to read this book with delight, for he will find set out the excitements and triumphs as well as the disappointments which make clinical anaesthesia such a worthwhile occupation. Other physicians too will read this book with interest if not with profit. It is not only good armchair reading, but it demonstrates clearly the value, in terms of life and limb to a patient undergoing surgery, of having a competent and well-trained anaesthetist. The case reports show that anaesthesia is not simply a matter of the repetitive performance of a few technical procedures, but of the involvement of every aspect of the training that goes into a good doctor.

This is a good medical book in its own right, for it recounts clinical experience in a skilful manner. If its lessons are taken, it will benefit those who read it and their patients, and it will perhaps act as a stimulus to groups of anaesthetists in this country to do more actively what the New York anaesthetists have already been doing for so long.

W. W. MUSHIN.

Fair Play for Pharmaceuticals

Medicine at Risk. The High Price of Cheap Drugs. By F. H. Happold. (Pp. 212. 18s. Paper 12s. 6d.) London: Queen Anne Press. 1967.

History is most fascinating when presented by prejudiced rather than by impartial historians, provided one has time to consult the works of their rival protagonists. The same applies to most controversial questions; one gets a better—or certainly a more stimulating—impression by reading the views of ardent controversialists rather than by consulting the anaemic representations of impartial students.

The modern pharmaceutical industry seems to stimulate not only commissions of inquiry but also passionate controversy. For years critical onslaughts on it have been published which, though the industry in certain respects is susceptible to justifiable criticism, have often been intemperate, sensational, and hysterical. We have also had references from noble ladies in the House of Lords to "the vultures of the pharmaceutical industry making their unholy profits at the expense of the community," and even from more eminent politicians in the House of Commons that the industry has "grown fat at the expense of the public purse."

More recently the industry has found a number of apologists, of whom Mr. Happold is one. It must be confessed that their apologies are much less intemperate than the denunciations of their opponents. The author has relied on four main lines of argument, and has produced some cogent evidence to

support them: firstly, that industry has been mainly responsible for the great therapeutic progress of the last 50 years; secondly, that the drug bill forms a relatively modest and constant proportion of the cost of the National Health Service; thirdly, that financial decisions can be taken rapidly by industry without those in charge having to fear the odium of having wasted public money should the project fail; and, lastly, that the important drugs which the manufacturers produce constitute a saving to the national economy in diminishing mortality and morbidity besides contributing very significantly to the export drive.

The book is well written and traces in an interesting fashion the history of the therapeutic revolution of the last 30 years, and explains—possibly from a somewhat biased point of view—the complexities of prices, profits, and patents. This short and inexpensive volume can be confidently recommended to the many who are interested in the subject.

DERRICK DUNLOP.

Immunity Phenomena

Delayed Hypersensitivity. By J. L. Turk. (Pp. 252+ix. 80s.) Amsterdam: North-Holland. 1967.

This valuable monograph appears at a time when cell-mediated immune reactions are beginning to be understood, and it is greatly to the credit of Dr. Turk that he has succeeded in writing a book which is extremely readable and at the same time provides a serious critical analysis of present knowledge on this difficult topic.

The tuberculin or Mantoux reaction reflects complicated and long-lasting immunity phenomena, yet is independent of circulating antibodies in the accepted sense. Other examples of the dermal expression of this type of immune reaction are the virus exanthems and chemical or toxic contact sensitivity dermatitis. Of more crucial importance to human pathology is the central role played by delayed hypersensitivity phenomena in the rejection of grafted organs. A fuller understanding of this phenomenon in transplantation immunity is essential to the future development of one of the most exciting new branches of surgery, and immunological studies have already greatly contributed to the success of kidney transplantation. Delayed hypersensitivity phenomena may also be of importance in the understanding of many diseases, such as the connective tissue disorders, in which there appears to be an underlying abnormality in immunological responsiveness.

In the organ-specific type of autoimmune disorders many of the pathological changes cannot be explained by the effects of circulating antibodies alone, and the role of cell-mediated reactions is being intensively studied at the present time. Another aspect in which delayed hypersensitivity might be implicated is the defence of the organism against cancer. In all these fields research is advancing rapidly, although it is still mostly concentrated on the fundamental aspects which are being studied in experimental animals. Dr. Turk has himself contributed important original papers on the cytological events in delayed hypersensitivity skin reactions and other experimental aspects of the subject, so

that he is able to assess critically the work of others. His experience in human pathology is more limited, and discussion on what is known of delayed hypersensitivity in disease is somewhat sketchy throughout the book. This is not a serious omission considering the incomplete state of the data obtained so far in human patients.

All the experimental aspects of cellular immunity are clearly and fully reviewed and an extensive bibliography is given up to 1966, which is a credit to the speed of publication. This book will be read with interest and pleasure by all who would like to understand the basic principles underlying immunological responsiveness, and all that this implies in terms of the causation of diseases. It will be particularly useful to immunologists, immunopathologists, and workers in the transplantation and cancer immunity fields.

DEBORAH DONIACH.

Home Refresher Course in Ophthalmology

Current Concepts in Ophthalmology. By Bernard Becker, M.D., and Robert C. Drews, M.D. (Pp. 265+x; illustrated. £6 10s.) London: Henry Kimpton. 1967.

In recent years a number of publications, mainly of American origin, have appeared which provide concise and up-to-date information about some aspects of a specialty which are currently arousing interest. Such books cannot be comprehensive reference works, and, especially when of multiple authorship, they tend to devote an undue amount of space to one small subspecialty while doing less than justice to others.

Current Concepts in Ophthalmology is the combined product of 20 members of the Oscar Johnson Institute in St. Louis. Each is an authority on his subject, and most of the 21 chapters are about the length of an average paper in an ophthalmological journal. Thus they are convenient to read and digest whenever short intervals of time become available. It may be that rather too much space has been devoted to the recognized shortcomings of indentation tonometry and instruction in the use of the more accurate optical aplanation method now in very general use. Great emphasis has been placed on the value of tonography, for the gradual decrease in tension when the eye is compressed by a measured weight gives a more accurate assessment of problems of defective aqueous outflow than do simple readings of intraocular pressure. It is surprising that such a complicated method of examination calling for a close personal relationship between examiner and patient to ensure accurate results seems usually to be left to a technician, but pressure of work which renders lengthy investigations impracticable is no doubt the reason. There are good chapters on diabetic retinopathy and attempts to treat this currently little-understood disease. There is a full account of blow-out fractures of the orbit. On the other hand, there is little about retinal detachment surgery.

This book, well written and produced, is a very worthy addition to the home refresher courses which any ophthalmic surgeon can

study with advantage. It is a credit to the ophthalmic surgeons of St. Louis.

HAROLD RIDLEY.

Disorders of the Cervical Spine

Cervical Spondylosis. And Other Disorders of the Cervical Spine. Edited by Lord Brain, D.M., LL.D., D.C.L., D.Sc., F.R.C.P., F.R.C.S., F.R.C.O.G., F.R.S., F.R.R., and Marcia Wilkinson, D.M., F.R.C.P. (Pp. 232+ix; illustrated. 55s.) London: William Heinemann. 1967.

Cervical spondylosis is one of the most common diagnoses made in a neurological outpatient clinic at the present time, especially as a cause of pain in the arm, lesions of the cervical segments of the spinal cord, and recurrent episodes of vertigo. Twenty years ago this condition, even under its earlier name of cervical osteoarthritis, was only rarely recognized as the cause of these conditions. The importance of cervical spondylosis as a cause of neurological disorder is largely due to the observations of Lord Brain and his co-workers, in particular Dr. Wilkinson. Cervical spondylosis as shown radiologically is common, and the demonstration of it does not necessarily mean that the patient's symptoms are due to it. This excellent book puts the condition into perspective.

The outstanding chapter is that by Professor Ruth Bowden and her colleagues from the Royal Free Hospital on the anatomy of the cervical spine and its relation to the spinal cord, emerging nerve roots, and the vertebral artery, and it would be worth buying the book for this chapter alone. There is, however, much more of value. The accounts of pathology by Dr. Wilkinson and on radiology by Dr. A. C. Young are first class. The chapters on treatment, including a review of surgical treatment by Mr. D. W. C. Northfield and Mr. H. Osmond-Clarke, are informative, but the account of prognosis of the condition is rather disappointing in view of the authors' great experience in the disorder.

The production of the book, in particular the illustrations, is of the highest class, but there is a somewhat macabre misprint on page 117 in the description of Fig. 89.

J. W. ALDREN TURNER.

Trying to Keep Abreast

Current Therapy. 1967. Edited by Howard F. Conn, M.D. (Pp. 844+xxv. £4 11s.) Philadelphia and London: W. B. Saunders. 1967.

Three hundred and thirty-two contributors, 12 consulting editors, and an editor-in-chief have combined to produce the 19th edition of *Current Therapy*. It weighs something over 5 lb. and is clearly meant for the doctor's office rather than for his pocket. It is divided into 15 sections covering infectious diseases, internal medicine, genitourinary conditions, venereology, allergy, dermatology, neurology, rheumatic disease, obstetrics and gynaecology, and injuries due to physical and chemical agents. There are useful addenda on the contents of the

doctor's bag, electrolyte balance, and normal laboratory values. Subjects in the main sections are arranged roughly alphabetically, and each is discussed by the chosen contributor under the heading "Method of . . ." The stated object is to present the "latest approved methods of treatment for the practicing (sic) physician."

A few examples taken at random will show that the book does not always meet with the approval of at least one practising physician. Should tincture of belladonna really be recommended for the treatment of heart block? And should therapy of myxoedema begin with 2 gr. thyroid extract a day—and why not thyroxine? Three different dosage regimens are mentioned for the initial treatment of pernicious anaemia, the largest being 250 µg. cyanocobalamin on alternate days. Bethanidine is not included among the drugs used for the treatment of hypertension (it may not of course have been approved in the United States), nor is the haemolytic reaction to methyl dopa mentioned. Finally, is it necessary to place so much emphasis on quinidine dosage schedules now that cardio-version is increasingly available?

Such criticisms do not invalidate what is by any standard a most impressive performance, but they raise two questions. Is it possible to write a book on treatment which will satisfy everyone? And is it really necessary to publish such a book every year when the time interval between writing and production will put some of it out of date? Perhaps it would be better to concentrate on *standard* forms of treatment arrived at by the consensus of opinion, rather than try to present the latest, knowing that such a task is impossible.

A. PATON.

Alcoholism

Out-Patient Treatment of Alcoholism. A Study of Outcome and its Determinants. By Donald L. Gerard, M.D., and Gerhart Saenger, Ph.D. (Pp. 249+xviii. 60s.) London: Oxford University Press. 1967.

This volume reports an ambitious collaborative project for the evaluation of treatment given in a sample of outpatient clinics for alcoholics supported by State funds in the U.S.A. Eight clinics and 797 patients were included in the final analyses. Throughout the text there is an understandable emphasis on the methodological difficulties that arose in this prospective study.

Follow-up was of necessity limited to a single interview one year after the first attendance, but the authors argue the special value of progress reports on alcoholics obtained at this interval of time. The findings are extensively tabulated and there is an evident preference for simple statistical techniques. The proportion of patients abstinent for six months before follow-up interview was 13%; controlled drinking was noted in 5%, and some improvement in drinking pattern in another 12%. Against these and other ratings of improvement the authors scrupulously offset evidence of deterioration in a smaller percentage of patients. As to prognostic factors, "social stability" (a combined measure of work record and residential and marital arrangements) was by far the most significant, the

socially most disestablished having the worst outlook. There was a slight tendency for older patients to do better than younger ones, but (surprisingly) there was no difference in outcome that could be correlated with sex or education.

Most doctors treating alcoholics subscribe to the dogma that once "loss of control" (in a technical sense) has set in, moderation in drinking can never be attained thereafter, and the alcoholic must choose between total abstinence or deterioration. Drs. Gerard and Saenger join those who challenge the universal truth of this proposition.

The clinics studied and reported on in this book were among the best-financed of their type in the United States, but the authors tell us that they had grave staffing difficulties, were short of community support, and all "suffered from the burden of their task." Drug treatment was used in most cases, but disulfiram alone appeared to improve the chances of control of drinking. The eight clinics differed considerably in their staffing. Patients treated by internists or social workers did better than those treated by psychiatrists, and the clinic with a psychoanalytic orientation had the worst results of all. Patients who became abstinent showed much evidence of continuing maladjustment and unhappiness. The defaulting rate was high: 52% of patients attended on no more than four occasions, and the median duration of contact with the clinic was one month. Addictive alcoholics of previously stable personality (the group so much favoured by Alcoholics Anonymous and by psychiatrists selecting for treatment patients of good prognosis) were clearly a minority among the clientele of the eight clinics. Any service opening its outpatient doors to problem drinkers of all types might find it hard to better these American results.

The literature on alcoholism is in danger of overgrowth, but studies as painstaking as this one are still more than welcome.

DENIS PARR.

Sarah Gamp and her Forebears

English Midwives. Their History and Prospects. By James Hobson Aveling, M.D. Reprint of the 1872 edition, with an Introduction and Biographical Sketch of the Author by John L. Thornton, F.L.A. (Pp. 185+xxxi; illustrated. £7 10s.) London: Hugh K. Elliott, 1967.

James Hobson Aveling (1828-92) is known to most medical students as the inventor of a "repositor" that proved useful in cases of uterine inversion, but few are acquainted with his writings and other activities. He wrote several valuable medical historical articles, but is best known for his books on *English Midwives* (1872) and *The Chamberlens and the Midwifery Forceps* (1882). In 1873 he founded, and for three years edited, the *Obstetrical Journal of Great Britain and Ireland*, and he was one of the founders of the Chelsea Hospital for Women.

The book before us consists of "an exact reproduction of Aveling's book" on British midwives, to which Mr. Thornton has added an introduction, a short biography of Aveling with a list of his writings, and a select bibliography of more recent writings on the history of midwifery. Aveling traces the history of English midwives from the sixteenth to the nineteenth century, gives short lives of some of the better-known midwives, but confesses that on the whole "it was a sad story of indifference and neglect, of petty jealousies and sordid interests." He mentions occasions when a man-midwife (a qualified doctor) had to crawl into the lying-in room on hands and knees so that he should not be seen by the patient, to whose aid he had been summoned by the midwife. The final chapter includes a strong plea for the instruction, licensing, registration, and supervision of midwives. England lagged behind other European countries in this respect and it was not till 1902, when the Midwives Act set up the Central Midwives Board, that a new era opened in British midwifery.

This readable little volume was well worth reprinting both for the story it tells and for the light it throws on the life and work of rather a neglected figure in English obstetric history.

ZACHARY COPE.

Surgical Technique

Nouveau Traité de Technique Chirurgicale. Vol. 9. Paroi Abdominale. Sutures Digestives. Laparotomies. By Philippe Dérivé. (Pp. 473; illustrated. 115 F.) Paris: Masson, 1967.

Nouveau Traité de Technique Chirurgicale. Vol. 13. Système Porte. Rate. By Lucien Leger and Jean Patel. (Pp. 332; illustrated. No price given.) Paris: Masson, 1967.

These two volumes are part of a series of 15, each concerned with surgical technique in different regions. The authors are a number of distinguished French surgeons under the editorship of Professor Jean Patel and Professor Lucien Leger. Of the two books under review, volume 9 is concerned with herniae, techniques of intestinal anastomosis, and various indications for laparotomy, while volume 13 describes the operative treatment of portal hypertension by Leger and the surgery of the spleen by Patel.

The production is of high quality, with good print, good paper, and many excellent illustrations of the various steps in operative technique, which are described in considerable detail. There are, for example, some good drawings of the various knots tied by surgeons, and probably no method of joining two pieces of bowel together has been omitted. The illustrations of the surgery of portal hypertension and of the spleen are particularly good, and if all the volumes are of the same standard it will certainly form a valuable contribution to the literature of operative surgery, though its size may tend to make it a work of reference in a library rather than one of personal purchase.

EDWARD G. MUIR.

Books Received

Review is not precluded by notice here of books recently received.

Problems of Psychotherapy. By Herbert Zucker. (Pp. 194+viil. 48s.) London: Collier-Macmillan, 1967.

Reproduction and Man. Contemporary Science Paperback 3. By R. J. Harrison, M.A., M.D., D.Sc. (Pp. 134+vii; illustrated. 7s. 6d.) Edinburgh and London: Oliver & Boyd, 1967.

Chemical Exchanges in Man. A Physiological Essay. Contemporary Science Paperback 10. By B. F. Matthews, B.Sc., M.B., Ch.B. (Pp. 136+vii; illustrated. 7s. 6d.) Edinburgh and London: Oliver & Boyd, 1967.

Ambroise Paré. Surgeon of the Renaissance. By Wallace B. Hamby, M.D. (Pp. 251+xxi; illustrated. \$9.50.) St. Louis, Missouri: Warren H. Green, 1967.

Pharmacology. Concise Medical Textbook. 2nd edition. By J. L. Pinniger. Revised by J. R. M.D., B.Sc., M.R.C.P., M.R.C.P.E., M.D. (Pp. 279+viii. 21s.) London: Baillière Tindall & Cassell, 1967.

Diseases of the Ear. 2nd edition. By Stuart R. Mawson, M.B., F.R.C.S., D.L.O. (Pp. 554; illustrated. £5.) London: Edward Arnold, 1967.

Review of Medical Physiology. 3rd edition. By William F. Ganong, M.D. (Pp. 621; illustrated. 52s. 6d.) Oxford: Blackwell, 1967.

Handbook of Bacteriological Technique. 2nd edition. By F. J. Baker, F.I.M.L.T., F.I.S.T., F.R.M.S. (Pp. 482+ix. 75s.) London: Butterworth, 1967.

Ekg-Fibel. 7th edition. By Professor Rolf Heinecker. (Pp. 316+vii; illustrated. DM. 22.) Stuttgart: Georg Thieme, 1967.

Diccionario Medicobiologico University. Director: Dr. Alberto Folch Pi. (Pp. 1501+xxxiv. No price given.) Mexico City: Editorial Interamericana, S.A., 1966.

Intravenous Anaesthesia—S.A.A.D. 3rd edition. Based on Postgraduate Course Lectures and Material. Edited by S. L. Drummond-Jackson, T.D., L.D.S. (Pp. 230+ix; illustrated. 40s.) London: Society for the Advancement of Anaesthesia in Dentistry, 1967.

Control of Cellular Growth in Adult Organisms. A Sigrd Jusélius Foundation Symposium. Edited by Harald Teir and Tapio Rytömaa. (Pp. 434+xxiii; illustrated. £5.) London: Academic Press, 1967.

Muscle and Bone. Anatomy and Physiology. Pre-Medical Primer No. 1. By Harry Asher, M.A. (Pp. 134+viil. 7s. 6d.) London: Arlington, 1967.

Engineering in the Practice of Medicine. Edited by Bernard L. Segal, M.D., and David G. Kilpatrick, P.E. (Pp. 482+xvii; illustrated. £8.) Edinburgh and London: E. & S. Livingstone, 1967.

Intra- und Postoperative Zwischenfälle. Vol. 1. Allgemeiner Teil, Thorax. Hals. Edited by G. Brandt, H. Kunz, and R. Nissen. (Pp. 427+xiii; illustrated. DM. 98.) Stuttgart: Georg Thieme, 1967.

Secretory Mechanisms of Salivary Glands. Proceedings of an International Conference held at Birmingham, Alabama, 1966. Edited by Leon H. Schneyer and Charlotte A. Schneyer. (Pp. 389+xvii; illustrated. £5 8s.) New York and London: Academic Press, 1967.

Middle Articles

MEDICAL ETHICS

Experiments on Man

[FROM A SPECIAL CORRESPONDENT]

A round-table conference on "Biomedical Science Facing the Dilemma of Human Experimentation," organized by C.I.O.M.S. (Council for International Organization of Medical Sciences) was held in Paris on 7 October. Opening the conference, the President, Professor M. FLORKIN (Liège, Belgium), sketched briefly the historical background, pointing out that the Declaration of Helsinki was very similar to the Nuremberg Code of 1947, except that the former specified that the subject's consent should be obtained in writing. Even having obtained this, however, the research worker should always consider the underlying motivation, and he cited one investigation at Harvard Medical School which had shown that 60% of volunteers were maladjusted, and were thus completely unrepresentative of the general population.

Discussing experimental procedures on the central nervous system, Sir JOHN ECCLES, F.R.S. (Chicago, U.S.A.), instanced several which in his view were clearly allowable; moreover, the subjects were often the investigators themselves. These included "psychophysics," such as the stimulation of vision, hearing, and balance. No after-results were seen from these procedures, which essentially had to be done in man, since the object of the work was to investigate conscious experience. Similarly, investigations on reflexes and most conditioning and learning experiments in man were acceptable. When full safeguards were taken another category of procedure was also allowable—namely, the stimulation of the exposed brain during neurosurgery. In some cases stimulation might be necessary to determine the site of a lesion and to treat it effectively. In others, however—as in the treatment of Parkinsonism—the procedure might be quite unrelated to treatment. This aspect must be explained fully to the patient, who also must be told of his right to refuse permission. Nevertheless, Sir John continued, a high proportion of patients volunteered to undergo this procedure, which was free from the risk of damage to the brain and had led to some fundamental discoveries about the threshold of consciousness.

He was extremely concerned about certain experiments which had used indwelling electrodes inserted through trephine holes in the skull. These might have multiple leads and be maintained in position for months, and undoubtedly they caused "fantastic" damage to the brain. Since the subjects were often psychotic they could never be expected to understand the procedure fully, and the damage to the brain could not be justified under any circumstances. Concluding, Sir John called for the development of large

colonies of anthropoid apes, in which most of this type of work could be done.

Drug Testing

Professor B. N. HALPERN (Collège de France) said that testing drugs in animals did not necessarily exclude all their risks in man. In particular the metabolism of a drug might be completely different in man from that in most experimental animals. For this reason he felt that preliminary tests with small doses of a new drug should be carried out in man. Once the metabolic pathway had been determined, the drug should be tested extensively in those animals which were known to have similar biochemical processes to man. He emphasized that rigid legislation for human experimentation in therapeutics was impossible, since the risk to be run was proportional to the seriousness of the disease. There was a great need to develop the discipline of clinical pharmacology, which would provide the necessary bridge between the laboratory worker on the one hand and the clinician on the other.

Professor A. GELLHORN (Columbia University, U.S.A.) said that probably the 60–70% of patients with incurable malignant disease constituted the largest identifiable group of persons regularly submitted to therapeutic tests. Patients' families demanded some sort of treatment; the doctor felt he must do something; the patients often volunteered for any form of treatment; while the results of cancer research in animals could be applied to man only rarely. There were two main types of research carried out on patients with cancer: firstly, work which might possibly benefit the individual (such as the use of new drugs and surgical procedures, and non-conventional radiotherapy); and, secondly, work having no relevance to the patient's disease. In his view the latter was never justified. He believed that no form of experiment was justifiable on the basis that the patient was going to die anyway—such experiments on the "hopeless case" might eventually diminish the doctor's concern for human life. If the patient was moribund no useful conclusions could be derived from any results, while, if he was not, how could the doctor be certain of the hopelessness of the position?

Code of Conduct

Continuing, Professor Gellhorn asked two questions. Could there be laws on human experimentation? He thought not. Should decisions about experiments be left to the

individual? Again, he thought not, because it placed too much power in one person's hands. He proposed a procedure for the decisions based on six main points. Firstly, work should be carried out only with the hope of improving the patient's condition. Secondly, there should be a reasonable prospect of success based on animal and other work. Thirdly, a protocol for control work and safeguards should be drawn up. Fourthly, the proposed research programme should be reviewed by the worker's peers who were knowledgeable in the particular field. Fifthly, the results should be systematically collected and analysed by independent observers. Lastly, the patient's written consent should be obtained before any procedure was undertaken. Though he believed truly informed opinion was impossible, this consent would give the patient his rightful status as a person and not as a mere experimental animal.

Kidney Transplantation

Professor J. HAMBURGER (Paris, France) discussed the mortality risks run by the live donor of a kidney, pointing out that a study in Boston had shown these totalled 0.12%—an immediate operative risk of 0.05%, together with a remote risk of 0.07% for subsequent disease which might develop in the remaining kidney. Now that improved techniques had raised the one-year success rate of live-donor kidney transplantation to about 75%, he asked whether it was justifiable to accept the offer of a kidney from a donor. Since this might save a patient's life, people were beginning to revise their critical objections, drawing up a balance sheet between the risks and the prospects of success. Professor Hamburger emphasized that the donor must be an active volunteer—completely warned of all the risks; well-motivated (for example, to save a relative's life); subjected to no moral or financial pressure; and mentally healthy (usually determined by psychological testing). Concluding, he pointed out that in June 1967 Italy had promulgated a law defining the conditions for accepting a live graft which would protect both the donor and the doctor. In his opinion all countries with units undertaking transplantation procedures should follow this example.

Unwise Control

Professor M. B. VISSCHER (University of Minnesota, U.S.A.) considered that progress in knowledge would be seriously restricted if

Professor Gellhorn's criterion of individual benefit was followed, though he emphasized that he was not advocating harmful procedures. At present there were two possible legal checks on wrongful experimentation—firstly, by prosecution for acts already undertaken, and, secondly, by some form of licensing of the experiments. Whereas the latter method was well suited to food-processing, for example, he questioned whether it could be applied to clinical experiments. Professor Visscher cited the British licensing system for experiments on animals, saying that this had saved workers from the harassments of the antivivisectionists; on the other hand, it had virtually barred students from performing a number of types of valuable experiments, as well as hampered surgeons in training. Moreover, British law did much to protect animals, but little to protect man.

Continuing, he said he would deliberately instance some extreme examples of restrictions on research procedures in his own university. There research studies on body fluids—blood, faeces, and urine—could not now be carried out without the informed consent of the patient and approval of the project by a committee of the worker's peers, whether or

not the specimens were to be obtained specifically for the research work or were merely left over from routine testing. Moreover, Professor Visscher thought that more patients were now dying from the want of life-saving drugs which overzealous and cautious departments had delayed in licensing than would have ever been at risk from the drugs themselves. The core of the ethical problem was the propriety of research with real hazards to the patients, and he believed that the solution was to put more of the onus of responsibility on panels of non-Governmental research experts.

Achieving a Balance

Dr. A. E. CONFREY (National Institutes of Health, Bethesda, U.S.A.) said that the underlying principle of the United States Public Health Service was to achieve a balance of Federal and local responsibility for the control of research. The task of the central authority was to lay down general standards, and to require adherence to them, without seeking to define the detailed pro-

cedure for an individual research project. At local level the research project should be reviewed and continually scrutinized by a university or hospital research committee which had no vested interest. Nevertheless, ultimately the research scientist was responsible for the quality of research investigation.

Professor A. DE MURALT (Berne, Switzerland) questioned how many students were getting any training in medical investigations. There was a danger that the availability of money for clinical investigation, the increase of sophisticated machines, and the growing number of new drugs might tempt workers into unethical procedures. Moreover, the large-scale financial support of university laboratories by pharmaceutical companies might tend to diminish the former's independence. Supporting the proposal for the introduction of clinical pharmacology departments on a large scale, he thought that research should be done by large groups on worthwhile problems which had been carefully screened. Though Government regulations might discourage research, permission or a licence by an uncommitted body of the worker's peers would be a justifiable and suitable safeguard.

CONFERENCES AND MEETINGS

British Association of Physical Medicine

[FROM A SPECIAL CORRESPONDENT]

This year's Annual Provincial Meeting of the British Association of Physical Medicine was held at the Nuffield Orthopaedic Centre, Oxford, on 30 September, under its President, Dr. F. S. COOKSEY, with Dr. PHILIP NICHOLS (Oxford) as the host. The theme of the morning session was the rehabilitation of the severely disabled, and included exhibits and demonstrations of many mechanical appliances and aids of all kinds, together with current research projects relating to powered prosthetics being developed in collaboration with the department of engineering science in the University of Oxford.

Suppression of Menstruation

Emphasis was also placed on the importance of clinical assessment of such patients. To illustrate this Dr. ANNE HAMILTON (Oxford) discussed the suppression of menstruation as a technique of particular importance for severely disabled women. She pointed out that the problem of the physical management of perineal toilet during menstruation is one of considerable distress to many severely disabled women. A method of complete suppression of the menstrual cycle by inducing pseudo-pregnancy with ethynodiol diacetate 2 mg. and mestranol 0.1 mg. (Metruken) was described. Experience over the past year had shown that this could be extremely successful. Not only were the patients more comfortable, but in several there was an improvement in their mental

state, a feeling of well-being, a steady rise in the haemoglobin level, and healing of bedsores. Four patients stopped taking the drug, but this was the result of factors outside the immediate clinical management. Dr. PHILIP NICHOLS suggested that in those patients where this method was successful on a short-term basis hysterectomy should seriously be considered, because pregnancy was usually particularly inadvisable.

Degenerative Changes in Hip Joints

Dr. P. G. BULLOUGH (Nuffield Foundation) described the degenerative changes observed in the hip joints in 50 patients examined at necropsy. The first signs of arthritis had been observed in patients as young as 15 years, and they were almost invariably present in every patient over the age of 25. These changes appeared to be confined almost exclusively to two main areas—firstly, on the roof of the acetabulum, and, secondly, on a strip below the head of the femur. Degenerative changes in these sites, however advanced, were not necessarily associated with symptoms, as these were non-weight-bearing areas. Why they occurred and their significance were not clear, but Dr. Bullough noted that once these changes extended on to the weight-bearing surfaces around the rim of the acetabulum and corresponding areas on the head of the femur the clinical picture of osteoarthritis began.

Mr. B. T. O'CONNOR (Oxford) reported a series of experiments designed to maintain a continuous negative charge across an osteotomy site in the metatarsal of a rabbit in the hope that healing would be accelerated. In several of the subjects there was evidence that this occurred, but as yet the techniques of the procedure were not entirely satisfactory.

Management of Haemophilic Arthropathy

Mr. A. W. STEEL (Oxford) said that working in close proximity to a large haemophilia centre had enabled surgeons to gain considerable experience of the management of haemarthrosis in the bleeding disorders. The primary aim of the surgeon was to prevent the severe joint deformities which follow repeated bleeding. Ideally bleeding into joints was treated by plasma transfusion within two to three hours of onset. A total of 414 episodes had been treated in this way as day cases in the last year. About 100 established haemarthroses required admission and were treated by plasma, immobilization, and rapid restoration of function at the earliest opportunity. Aspiration of joints was carried out in many cases under plasma cover. Established contractures and deformities were dealt with by plaster techniques and corrective surgery under cover of anti-haemophilic globulin.

Correspondence

Letters to the Editor should not exceed 500 words.

Laboratory Screening Procedures

SIR,—Your report of the symposium on laboratory screening procedures (30 September, p. 859) raises a number of important points. The problems of population screening are immense, from both the technical and economic viewpoints. Both Professor W. M. Davidson and Professor J. G. Scadding rightly stress that the radiological screening of the population produces benefits to the community beyond that to individuals in that the spread of tuberculosis could be defined and checked. May I suggest that the economic consequences of certain diseases spread beyond the affected individual, and therefore need to be considered as a "fall-out" effect, which is as important today as such factors as the spread of infectious disease. The effect of undetected illness on family income and nutrition at one extreme of the social scale and on the judgement of persons in responsible positions at the other are problems that we have all met at some time or another. The aims and desirability of population screening programmes will be better defined when investigations such as that initiated by Professor L. G. Whitby have been going for some time and their implications for the community digested.

In hospitals we have had screening programmes since the systemization of clinical medicine seriously began in the nineteenth century. Each patient admitted is submitted to a general examination, and no doubt has his height and weight measured, his temperature taken at intervals of time, and his urine tested for protein, glucose, etc. The extension of this principle to laboratory tests such as Dr. T. P. Whitehead and his colleagues have carried out so ably in Birmingham should not excite too much surprise. The advances in both analytical and data-processing technology are placing powerful tools

in our hands which are changing our traditional ways of investigating patients. In a semi-automated laboratory it is often simpler to perform a standard group of tests simultaneously than to perform any combination of these tests randomly selected by the clinician. It is the introduction of such machinery which has made the prospect of biochemical screening a practical one.

The selection of analytical methods by the manufacturers of large analytical machines has often been determined by the question: "How many of the most common biochemical or haematological tests can we perform at once on one sample?" As clinicians and pathologists I would suggest that we ask ourselves instead, "Which disease processes do we most commonly fail to identify early in hospital, and how can we best detect them?" Modest screening schemes such as the measurement of haemoglobin, plasma glucose, and urea would not be expensive to mount, and few patients with diabetes, anaemia, or renal failure who had been admitted to hospital for other reasons would remain undetected. (It may well be more effective and cheaper to detect diabetes among hospital admissions in this way than by using the time of a trained nurse in testing urines, possibly missing 10–20% of the mild cases.)

For the future we should remember that the number of tests which can be performed routinely on one sample (profile processing) is going to depend on the economics of laboratory organization. This is dependent on the relation of capital employed on buildings and apparatus to revenue expenditure on technical skill and materials.—I am, etc.,

M. G. RINSLER.

Group Pathological Laboratories,
St. Stephen's Hospital,
London S.W.10.

Aspirin and Gastric Bleeding

SIR,—Once more aspirin is under attack, and paracetamol is recommended as a better analgesic for occasional use in your leading article "Aspirin and Gastric Bleeding" (30 September, p. 810). The reason given for this is that aspirin may cause gastric bleeding, whereas paracetamol does not. But then no drug is totally without side-effects, and considering the quantities in which aspirin is taken (quantities which seem to take your leader writer by surprise) it must still be considered one of the safest drugs we have. If paracetamol were taken in equal quantities would we not start worrying about the blood dyscrasias it produced, or some other side-effect?

Moreover, paracetamol is not as good a drug as aspirin in several respects, as I

pointed out in your correspondence columns only last year (9 April 1966, p. 918). It is a weaker analgesic, and has not the satisfying sedative effect in children (even some adults find aspirin useful as a mild sleeping tablet). So far as cost is concerned, aspirin wins easily at 1s. 3d. for 100 tablets (300 mg.) against paracetamol at 3s. 8d. for 100 (250 mg.), these being the local over-the-counter prices. Even soluble aspirin (if it is considered better than the ordinary form) is only 2s. 3d. for 100 tablets.

But the side-effects of taking aspirin certainly can and should be reduced. Firstly, products containing it should never be advertised as being good for indigestion or stomach ache. (The last two cases of severe haematemesis I saw were both in people who had been taking

aspirin for recurrent indigestion.) Doctors have a responsibility for telling people with proved or suspected peptic ulcers to avoid the drug, and substitute paracetamol—a responsibility they often forget. They should also point out, of course, that even taking paracetamol is not the way to deal with their stomach ache, and give advice how best to do it. Finally, the public must slowly be educated to accept many of the minor, short-lived aches and pains of life, and not to depend on drugs (even relatively safe ones like aspirin) to overcome them.—I am, etc.,

T. C. DANN.

University College of Swansea,
Glam.

SIR,—Your leader-writer on the above subject (30 September, p. 810) wonders why the gastric mucosa has at times increased susceptibility to aspirin. In a fairly recent article,¹ based on a four-years observation, I suggested that the factor or factors for this increased susceptibility might be found by regarding the whole man and not by too narrow a consideration of the stomach in isolation. I had a strong impression that such factors as prolonged worry, emotional stress, infections, and chronic painful disorders—for example, arthritis of the spine—might well be factors of this type.

If I may again quote three writers² who came to a similar conclusion: "The gun must be loaded in order for an explosion to occur when salicylates pull the trigger." To me mental stress, prolonged fatigue, physical pain, and infection seemed to be effective "loaders," and with these sometimes went irregular meals, alcohol, and heavy smoking. Reference to the other many authors whose evidence has pointed the same way will be found in my paper.—I am, etc.,

G. H. JENNINGS.

Edgware General Hospital,
Edgware, Middlesex.

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- Jennings, G. H., *Gut*, 1965, 6, 1.
- Grossman, M. I., Matsumoto, K. K., and Lichter, R. J., *Gastroenterology*, 1961, 40, 387.

SIR,—The concluding sentence of a leading article (30 September, p. 810), "Surely the time has come to advise patients to keep this drug (paracetamol) rather than aspirin in the medicine cupboard," has been written without consideration of the wider implications of such advice. We do not doubt that the change would be advisable from the point of view of reducing the incidence of gastric bleeding.

Aspirin, however, is one of the drugs most commonly involved in self-poisoning in adults and accidental poisoning in children. Although the annual consumption of salicylate preparations in Great Britain is estimated at 4,000,000,000 tablets, in 1965 about 12,000 patients were admitted to hospital in England and Wales for treatment of salicylate poisoning, and only 264 died. This comparatively low mortality is largely due to awareness of the problem and a rapid

response to specific therapy, even when large numbers of tablets are consumed.

On the other hand, experience of paracetamol poisoning is very limited, but acute liver necrosis and death feature prominently in recorded cases.¹⁻³

Indeed, the manufacturers of one brand of paracetamol, very responsibly, give in their brochure information relating to a 13-year-old girl who died after taking 30 tablets. Post-mortem examination revealed massive diffuse toxic necrosis of the liver. The onset of liver disease in paracetamol poisoning may be delayed several days, and it is possible that survival from serious intoxication may be complicated by residual liver damage. The toxic effect of 50 aspirin tablets, a common overdose, is very much less than those that might arise from ingestion of a similar number of paracetamol tablets. Moreover, there is no adequate therapy for this type of poisoning.

Should the advice of your leader be accepted and paracetamol become as readily available as aspirin is at present, a greatly increased incidence of paracetamol overdose is inevitable. We consider that the resulting mortality and morbidity would be greater than that from aspirin poisoning, and certainly would not warrant acceptance of the change you have so strongly advocated.—We are, etc.,

HENRY MATTHEW.
A. T. PROUDFOOT.

Poisoning Treatment Centre,
Royal Infirmary,
Edinburgh.

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- Davidson, D. G. D., and Eastham, W. N., *Brit. med. J.*, 1966, **2**, 497.
- Thomson, Jean S., and Prescott, L. F., *ibid.*, 1966, **2**, 506.
- Jacobs, A., *Bull. Int. Ass. Forensic Toxicologists*, 1967, **4**, No. 1.

SIR,—It is to be hoped that your leading article "Aspirin and Gastric Bleeding" (30 September, p. 810) will inspire a change of heart in drug firms which advertise aspirin compounds for upset stomachs. There can be few better examples of inept therapy than treating alcoholic gastritis with aspirin.—I am, etc.,

J. C. BOWIE.

University Health Service,
The University of Birmingham,
Birmingham 15.

Treatment of Poisoning by Antidepressant Drugs

SIR,—In view of the increasing incidence I was pleased to see the article by Dr. C. M. Steel and others (9 September, p. 663) on the problem of the poisoning of children by antidepressant drugs.

There are two characteristics of this type of poisoning which I feel are not sufficiently well recognized, but which are of the utmost importance in the management and which deserve further emphasis. Firstly, that in children an extremely low dose (far less than the L.D.₅₀ in experimental animals) can be fatal; and, secondly, that recovery from the initial coma can be followed, after an interval, by a sudden and unheralded death. The necessity of appreciating these points fully is obvious.

My own experience is confined to opipramol, which is another, tricyclic compound closely re-

lated to imipramine and amitriptyline, and I have described a fatal case of overdose with this drug in a 14-months-old child (awaiting publication). The salient features of this case demonstrated the characteristics above. The dose taken was small—1,000 mg. in a 9-kg. child—that is, 110 mg./kg., which is less than one-third of the L.D.₅₀ for dogs (400 mg./kg.). There was an apparent recovery from the initial coma, and this was followed by a sudden and completely unexpected death about 18 hours after ingestion. The child was treated without the knowledge of the special features of antidepressant poisoning by curarization, intermittent positive pressure respiration, and forced diuresis. Consideration of the problem after this unsatisfactory outcome led us to much the same conclusion as Dr. Steel and colleagues for future management.

Of the 18 cases of opipramol overdose which have been reported six have been fatal, and four of these have been attributed to sudden cardiac arrest. At least three of the fatal cases had taken only very modest doses—much less than the L.D.₅₀ in dogs.¹ Only two of these cases, however, have been documented.^{2,3} In the case of opipramol poisoning the following additional information might also be useful. Less than 1% of the total dose is excreted unchanged in the urine; and serum levels remain extremely low even after intravenous administration (a dose of 10 mg./kg. produces peak levels of only 0.25–0.3 mg./100 ml.).⁴ This endorses the view that forced diuresis or other active measures are contraindicated. Also it has been shown that opipramol suppresses A.C.T.H. formation in experimental animals,⁵ and this suggests that in the event of collapse steroid cover might be appropriate.

It is hoped that these further observations might be helpful in deciding on the management of what must be among the most tragic of cases if fatal.—I am, etc.,

C. A. FUGE.

Department of Anaesthetics,
Southampton General Hospital,
Southampton.

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Psychotropic Drugs

SIR,—It is important that the Dunlop Committee and your other readers should not be given the impression that all psychiatrists are as enthusiastic as is Dr. William W. Sargent over the antidepressant drugs (30 September, p. 861). While one must acknowledge that Dr. Sargent has probably an unequalled experience of speaking and writing about the monoamine oxidase inhibitors, there are many clinicians "working whole-time at the bedside" who have used these drugs in thousands of cases during the past decade, and who have become increasingly doubtful of their value. On the other hand, there is no doubt whatever that they cause dangerous side-effects and no doubt whatever that they have killed patients. Dr. Sargent's letter adds another death to the growing list—that of a patient said to have tempted providence by eating cheese. She could equally well be said to have tempted providence by eating iproniazid.

The Medical Research Council is presumably well able itself to take care of the charge

that it has "already made rather a fool of itself" by carrying out a controlled trial of phenelzine on depressed inpatients which showed the drug to be somewhat less effective than a placebo. Those who know the details of this trial will know also that Dr. Sargent's description of it was not accurate. The M.R.C. trial performed a useful service in indicating that phenelzine was of no value in the treatment of cases of moderate or severe depression as defined in the terms of that trial; previously it had been widely prescribed for such patients. Of course, one must not generalize from this to say that it is of no value in any condition whatever.

But why is it so wrong to recommend that certain drugs should not be used for psychosomatic conditions unless proved to be valuable in controlled clinical trials? There is no good reason why psychiatry should continue to run on a lower level of scientific objectivity than other medical specialties. If physicians at St. Thomas's Hospital have found phenelzine and isocarboxazid to be so effective in so many psychosomatic states they should have little difficulty in carrying out a properly controlled trial to demonstrate this. The ethics of this suggestion are, as always, capable of being confused by someone who will say that we already know one particular treatment which is strikingly and uniquely effective. But such a trial, they could reassure themselves, may perhaps influence those of us who have used the same treatments in those same conditions and found them to be not only risky but also strikingly ineffective.—We are, etc.,

PETER LEYBURN.
A. O. A. WILSON.
PIERS C. ROBSON.
JOHN LE GASSICKE.

St. George's Hospital,
Morpeth, Northumberland.

Advantages of Health Centres

SIR,—Drs. E. Lace and H. I. Howard in their letter (7 October, p. 49) about their experience at the William Budd Health Centre are right to stress the many gains which accrue to the doctors and their patients working in such health centres. However, in their swipe at the so-called armchair critics and advisers have they not committed the same offence of which they accuse?

Their personal experience of privately owned centres must be limited. Thus their conclusions in that direction must not be allowed to discourage until proved correct. The many centres which are being developed up and down the country are not exactly the financial hare-brained undertakings which Drs. Lace and Howard infer. Further, I would like to remind your readers that almost all the pioneer attachments and use of ancillary help, whether seconded from local authority or as private ventures devolving around such privately owned centres, were published from such partnership or group practice centres or single-handed practices. The examples of general practice/local authority co-operation come from far and wide, and not necessarily from a health centre in the true sense. This of course is not synonymous with health centre development not being desirable. On the contrary. But the profession must not be left in any doubt that it can itself proceed to develop facilities

and centres, not to mention the help the finance corporation can give in this.

Quite correctly Drs. Lace and Howard advocate conferences on these subjects. One was held in 1965, and one earlier this year. Further such meetings are planned.—I am, etc.,

Edinburgh.

E. V. KUENSSBERG.

Intestinal Obstruction

SIR,—Your leading article "Intestinal Obstruction by Food" (24 June, p. 782), which comments on my paper "Intestinal Colic Caused by Food,"¹ is quite amusing and well taken. I would like to draw your attention, however, to a misinterpretation of my paper which, I believe, has some importance. Your article states that the condition is "a rare event in any surgeon's working life." While it is true to say that complete organic obstruction caused by food is in fact a rare event, I tried to give some evidence in the paper to show that incomplete and temporary episodes of food obstruction are probably not uncommon. Such episodes may be responsible for many otherwise undiagnosed bouts of intestinal colic which patients suffer not infrequently without ever attending a doctor's surgery.—I am, etc.,

F. O. STEPHENS.

Sydney Hospital,
Sydney, N.S.W., Australia.

REFERENCE

- ¹ Stephens, F. O., *Gut*, 1966, 7, 581.

Subcutaneous Atrophy After Local Corticosteroid Injection

SIR,—In the article by Dr. Ann Beardwell entitled "Subcutaneous Atrophy after Local Corticosteroid Injection" (2 September, p. 600) the author states that she could find no reports in the literature of this complication occurring in patients treated for arthritis. I would like to call her attention to an article by James T. Cassidy and Giles G. Bole.¹

In the same issue of the *B.M.J.*, under "Correspondence" (p. 614), Dr. Raymond Greene advocates the use of propranolol in myxoedema on the basis that thyroxine enhances beta-adrenergic activity. I would like to point out that the concept that thyroid hormone augments the actions of catecholamines on the cardiovascular system has been refuted both in man^{2,3} and in animals.^{4,5}—I am, etc.,

EDGAR GRUNWALDT.

Geigy Pharmaceuticals,
New York, U.S.A.

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- van der Schoot, J. B., and Moran, N. C., *J. Pharmacol. exp. Ther.*, 1965, 149, 336.
- Margolius, H. S., and Gaffney, T. E., *ibid.*, 1965, 149, 329.

SIR,—I read Dr. Ann Beardwell's paper (2 September, p. 600) with great interest, as I have noted this complication after steroid injections for "tennis-elbow," par-

ticularly when several injections have been given at the same site. The effect can occur with hydrocortisone acetate 25 mg. per ml. In my experience it has been more obvious in those with little subcutaneous fat to begin with, and subsequently, on clinical examination, there appears to be a total absence of subcutaneous tissue between the skin and the periosteum. The skin itself appears more transparent and very reminiscent of the "transparent skin" described in rheumatoid arthritis.

Two cases similar to Dr. Beardwell's were recorded by Iuel and Kryger.¹ They noted that in one case there was brown discoloration of the skin over the atrophic area, while in the other the atrophic skin failed to tan after exposure to sun. I have noted a similar disturbance of pigmentation.—I am, etc.,

London W.1.

E. N. GLICK.

REFERENCE

- ¹ Iuel, J., and Kryger, J., *Acta rheum. scand.*, 1965, 11, 137.

Cyst of Popliteal Artery

SIR,—We read with interest the article on cystic adventitial disease of the popliteal artery by Mr. G. J. T. Lewis and others (12 August, p. 411). We have recently encountered such a case in which we made some special studies.

Three months before admission the patient, a lighterman aged 32, experienced a severe pain in the right calf while climbing a ladder. Since

the swelling revealed a translucent wall with colourless contents shining through. Without applying clamps the cyst was opened and the jelly-like material sucked out. It was then seen that there was a small opening in the floor oozing the same material and leading to a second cavity projecting into the lumen and apparently the cause of the x-ray appearance. A probe inserted into this hole passed 1.5 cm. distally (Fig. 6). The outer cyst and roof of the deeper cyst were

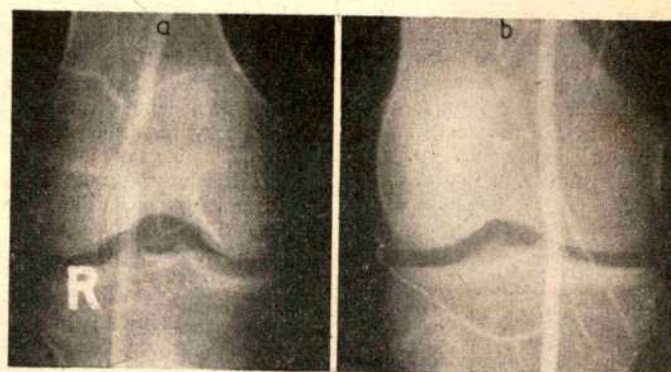
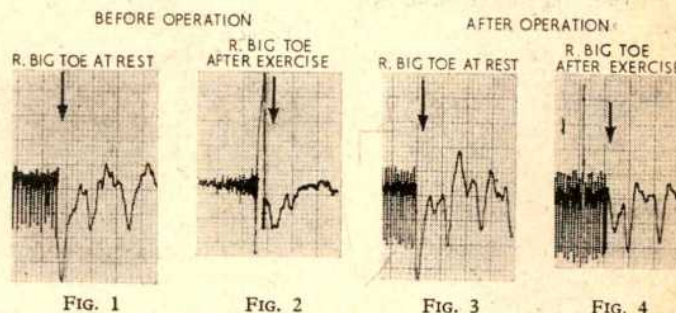


FIG. 5

then he had claudication at 25–30 yards (22–27 m.), and occasional rest pain in the right foot. On examination he was a well-built healthy man. At rest all peripheral pulses were present and equal. Following exercise, however, the right leg below the knee became white and cold and the dorsalis pedis and posterior tibial pulses disappeared, returning slowly after five minutes' rest.

The cutaneous pulses from the pulp of the toes measured with a photo-electric pulse meter (kindly loaned by Dr. R. H. Fox) showed corresponding changes (Figs. 1 and 2). An aortogram (Dr. L. Morris) showed an entirely normal arterial tree apart from a crescentic filling defect almost totally occluding the right popliteal artery (Fig. 5A), and a diagnosis of cystic degeneration was made.

At operation the popliteal artery presented a hemispherical swelling 3 cm. by 1.7 cm. situated on the p-stero-medial aspect. Apart from unusually dense adhesions the artery appeared otherwise normal. Full exposure of

excised and there immediately presented the normal shape of the artery, cylindrical, smooth, and of a light plum colour. The floor was presumed to be the intact medial coat. The adjacent tissue was then stitched over. Following this there was excellent pulsation in the artery.

Histologically the cyst wall was composed of fibrous tissue with occasional elastic fibres.

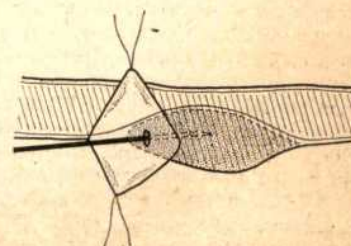


FIG. 6

The pulse meter recordings after operation show a return to normal of the amplitude and form of the pulse wave both before and after exercise (Figs. 3 and 4). Postoperative arteriography shows how completely the arterial lumen returned to normal.

The sudden onset of symptoms in our case may have been due to the floor of the superficial cyst giving way, resulting in the extrusion of the contents into the dissection plane of the vessel, so forming an internal projection which constricted the lumen. To postulate synovial cell rests in the arterial wall seems embryologically unlikely. The cystic fluid is identical in colour and consistency to that of a ganglion. We have always supposed a ganglion to be a degenerative cyst containing collagenous material and caused by trauma. We feel a *prima facie* case exists for postulating such an aetiology for the arterial cysts, although the mode and nature of the trauma is more difficult to visualize.

Dr. G. Leaf's comprehensive analysis of the cyst material has shown that it is not pure collagen. A similar analysis of ganglion contents might be illuminating, and significant differences would need to be shown before the similarity between the two types of cyst can be rejected.—We are, etc.,

HERMON TAYLOR.

R. S. TAYLOR.

C. A. RAMSAY.

London Hospital,
London E.1.

Elusive Popliteal Pulse

SIR,—Your comments on palpation of the popliteal pulse (5 August, p. 326) are well taken. However, I take exception to your statement that "a pulse that cannot be felt . . . is surely absent." Work with transcutaneous Doppler ultrasound was shown to be much more reliable than palpation, particularly in this elusive area. As reported in the literature,^{1,2} absence of the pulse does not necessarily mean absence of flow, even indeed of adequate flow. Obviously this is of particular importance in the evaluation of distal run-off following graft or bypass arterial surgery.—I am, etc.,

THOMAS G. DAVIS,

Medical Director,
Smith Kline Instrument Company,
Philadelphia, U.S.A.

REFERENCES

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Retinal Changes after Cardiac Arrest

SIR,—Sir Stewart Duke-Elder has kindly pointed out to me that my suggestion that observation of retinal changes after cardiac arrest is of grave prognostic significance (16 September, p. 722) is, alas, not as original as first thought. A fuller description of the changes that may be seen is given in his reference work.¹

It is of interest that the suggestion about the significance of retinal changes when considering resuscitation was originally made by Salsbury and Melvin more than 30 years ago as a result of experimental work.² Twenty years later Kevorkian³ confirmed this after observations made in two human subjects who

suffered cardiac arrest while at normal body temperatures (the retinal changes are different in hypothermic circulatory arrest). However, as Sir Stewart points out, quantitative confirmation about the usefulness of this physical sign in humans has been lacking, and I am grateful for having had the opportunity of providing these data.

In this connexion the number of cardiac arrests personally attended is now 95, of which 43 had the circulation initially restored. Retinal changes have now been observed on 20 occasions, and on these occasions there was failure in restoring the circulation with the exception of the decerebrate child described in my memorandum. This contrast speaks for itself.

It would thus appear that the suggestion that observation of retinal changes after cardiac arrest is of grave prognostic significance, proposed as a result of experimental studies by Salsbury and Melvin and confirmed qualitatively in man by Kevorkian, has now been confirmed quantitatively. Observation of these changes would provide an objective yardstick for deciding whether to attempt to resuscitate or not.—I am, etc.,

Queen Elizabeth Hospital,
Birmingham 15.

P. J. TOMLIN.

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Pernicious Anaemia and Intestinal Malabsorption

SIR,—We were interested to read Dr. C. G. Riley's report of a case of pernicious anaemia and intestinal malabsorption (9 September, p. 657).

There are several reports¹ in the literature of cases of jejunal diverticulosis associated with achlorhydria demonstrated by the augmented histamine test, and in none of them is there conclusive proof of the coexistence of Addisonian pernicious anaemia (P.A.). To establish this diagnosis in the presence of coexistent jejunal diverticulosis it would be necessary to demonstrate severe reduction of intrinsic factor (I.F.) production to the levels found in pernicious anaemia. The demonstration of intrinsic factor antibody in the serum is in itself insufficient proof.² Indirect evidence of inadequate intrinsic factor production may be obtained by the use of the Schilling test and its modifications. In uncomplicated P.A. the urinary excretion of ⁵⁷Co vitamin B₁₂ should be restored to normal levels by the addition of oral I.F.³ In jejunal diverticulosis a preceding course of antibiotics is usually sufficient to restore the urinary excretion values to normal without oral I.F. being given. In a few cases a combination of oral I.F. and antibiotics was necessary to restore urinary excretion to normal,⁴ suggesting inadequate endogenous I.F. production (i.e., coexistent P.A.). However, as there is evidence⁵ to suggest that even in the presence of adequate endogenous I.F. production additional oral I.F. may enhance vitamin-B₁₂ absorption in cases of jejunal diverticulosis, this conclusion may not be valid. Unfortunately Dr. Riley's case report fails to document severe depression of endogenous I.F. production. The complexities of interpreting in-

direct evidence in the situation of multiple pathology are such that direct measurement of gastric I.F. production is highly desirable. A report on such a case with this information is presently being prepared. We consider that the haematological and alimentary features of Dr. Riley's case could be attributed to jejunal diverticulosis alone with coexistent achlorhydria.

Cases of jejunal diverticulosis with progressive neurological damage occurring in the face of adequate vitamin-B₁₂ replacement such as he describes have been previously noted by Cooke and his colleagues¹ and by Badenoch *et al.*,² who also reported the post-mortem findings. Cooke and Smith³ have recently documented a similar sequence of events in cases of the sprue syndrome. Whether there is a disorder of vitamin-B₁₂ transport or utilization⁴ or malabsorption of some other nutrient awaits further elucidation.—We are, etc.,

IAIN M. MURRAY-LYON.

NIALL D. C. FINLAYSON.

Royal Infirmary,
Edinburgh.

REFERENCES

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- Badenoch, J., Bedford, P. D., and Evans, J. R., *Quart. J. Med.*, 1955, 24, 321.
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- Ellis, G. J., Breuer, R. I., Owen, E. E., and Laszlo, J., *Ann. intern. Med.*, 1966, 64, 654.

Alcohol and the Law

SIR,—The article of Professor J. P. Payne and his colleagues (30 September, p. 819) is clearly a useful contribution in the struggle to get physiological variability accepted by laymen and our legal colleagues. However, I think it should be emphasized that many of his data relate to the high blood levels which were commonly seen in prosecutions under the 1962 and previous Acts and not to those around 100 mg./100 ml. that we anticipate encountering under the 1967 Act.

In our own data (1 April, p. 49) and in some subsequent experiments we have studied subjects with levels up to a maximum of 114 mg./100 ml. in the blood. At these levels we found urine blood ratios to vary just as much as Professor Payne, but our range was from 0.31 to 2.0, with a mean of just 1.0. Our experience was therefore that at these what we may call new levels urine is marginally more helpful to the accused than blood. Our lower values are of course due to the presence of urine in the bladder at the time drinking began.—I am, etc.,

East Ham Memorial
Hospital,
London E.7.

J. ENTICKNAP.

SIR,—Your leading article (30 September, p. 809) seems to me to miss one very fundamental point in the question of road deaths. According to A. J. P. Taylor,¹ road deaths in 1934 were 7,343 when there were 1.3 million cars on the road, while in 1963 they had actually fallen to 6,922 when there were 7.3 million cars on the road.

While alcohol is no doubt a factor in increasing the number of road deaths, I

believe I am right in saying that the increase since 1963 has been very small, and, bearing in mind the large number of relatively inexperienced drivers who have taken to the road, the figures are really not as unsatisfactory as they are made to appear.

We generally like medically to assess the problem which we are trying to solve before advising solutions for it, and it might be as well if the Ministry of Transport followed this precept.—I am, etc.,

ALEC WINGFIELD.

Willesden General Hospital,
London N.W.10.

REFERENCE

- ¹ Taylor, A. J. P., *English History, 1914-1945*, 1965, vol. 15, p. 303. London.

Doctors for Industry

SIR,—I am very surprised that your leading article "Doctors in Industry" (16 September, p. 692) does not mention the fundamental difference in aim between the present appointed factory doctor system and the proposed new A doctor scheme.

The appointed factory doctor system was started in 1833, in the days of child labour in our factories. In its day it was one of the most forward-looking experiments in social medicine and social care. The Factory Inspectorate and the medical profession have allowed this unique opportunity for helping juveniles to make the very difficult transition from school to work to sink to the level of a perfunctory physical examination and the signing of a book for a derisory fee. The Chief Medical Inspector has on more than one occasion stated publicly that "neither in detail nor in principle has the examination by the appointed factory doctor altered since its inception." Could there be any greater indictment of both Government department and medical profession? Between us we have failed to give any thought to the youth of the country in their urgent need for help to meet and understand the severe demands, both physical and mental, which modern society makes. Now we could recognize the sins of omission in the past and could build a new service to youth in industry in collaboration with the school health service, the youth employment officer, and the general practitioner. Instead we are to have 100 A doctors orientated towards adults and physical hazards in modern industry. This is no doubt a worthwhile aim in its own right, but to replace a service directed towards that section of the population most in need and most neglected by all the social services—namely, juveniles in industry—by a service orientated towards adults seems to me to be taking a large step backwards into the Victorian era.—I am, etc.,

Chipping Ongar,
Essex.

F. E. S. HATFIELD.

SIR,—Your leading article (16 September, p. 692) states: "If the School Medical Service issues a certificate of fitness for most leavers and a small group receives a 'disabled' certificate it may . . . make it easy for an unscrupulous employer to refuse all but the healthy school-leavers." You omit to point out that many large employers already do just this. The British banks, for

example, refuse to accept anyone for permanent employment unless he is a first-class life in the insurance sense.

A few years ago I saw a 22-year-old man with a blood pressure of 180/105 mm./Hg (with no cardiac enlargement, albuminuria, or retinal changes) who applied in turn to four banks, was accepted by all at interview, but later rejected following a medical examination. I wrote letters on his behalf to two of the banks condemning their deplorable attitude, but with no effect.—I am, etc.,

Farnham, Surrey.

JOHN W. TODD.

Antinuclear Factor

SIR,—In the leading article "Antinuclear Factor" (10 June, p. 654) you mentioned the interesting study by Pitkeathly and Taylor¹ in which they avoided the difficulty of distinguishing borderline cases of rheumatoid arthritis and systemic lupus erythematosus by considering all the cases with connective disorders as one group, subdivided exclusively on the presence or absence of antinuclear factors in the serum. In this connexion we would like to draw your attention to the article by Hijmans *et al.*² concluding that discrepancies in the finding of antinuclear factors are due not only to quantitative differences in the sensitivity of the techniques used but also to the presence of apparently qualitative differences between the antinuclear factors in different patients.

Secondly, we feel that our discovery of a new factor, the so-called "antiperinuclear factor," in the serum of patients with rheumatoid arthritis is also of importance in this connexion. Our study has subsequently been confirmed by others.³⁻⁵ The antiperinuclear factor (A.P.F.) seems to be specific for rheumatoid arthritis, and has until now only incidentally been found in systemic lupus erythematosus (see Table), thus differentiating the two groups of patients suffering from in other aspects probably related diseases in a rather astonishing way.

	Year	Disease	No. of Cases	No. of Cases A.P.F. Positive	% A.P.F. Positive
Nienhuis and Mandema ³	1964	R.A. S.L.E.	105 12	51 1*	48.5 8.3
Visconti <i>et al.</i> ⁴	1964	R.A. S.L.E.	37 12	29 1†	78.4 8.3
Cava <i>et al.</i> ⁵	1965	R.A. other dis.	48 No. not specified	37	77.1 1.7
del Giacco and Mazzei ⁷	1965	R.A. S.L.E.	20 5	9 0	45.0 —
Marmont <i>et al.</i> ⁸	1966	R.A. S.L.E.	100 28	51 1‡	51.0 3.5

* This patient, an 18-year-old female, had serious joint involvement, besides a number of other symptoms, and is now classified as definite R.A.

† This patient had, besides symptoms of malignant dermatomyositis, a polyarthritis from the rheumatoid type, stage IV.

‡ No specific data provided.

Considering the well-known clinical and immunological overlap between rheumatoid arthritis and systemic lupus erythematosus, the rare occurrence of the antiperinuclear factor in systemic lupus erythematosus is indeed a strong point in favour of its

specificity for rheumatoid arthritis.—We are, etc.,

R. L. F. NIENHUIS.

Department of Internal Medicine,
University Hospital,
Groningen, Holland.

REFERENCES

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- ² Hijmans, W., Schuit, H. R. B., Mandema, E., Nienhuis, R. L. F., Feltkamp, T. B. W., Holborow, E. J., and Johnson, G. D., *ibid.*, 1964, 23, 73.
- ³ Nienhuis, R. L. F., and Mandema, E., *ibid.*, 1964, 23, 302.
- ⁴ Visconti, A., Cava, L., and Fontana, G., *Osped. maggiore*, 1964, 59, 1357.
- ⁵ Cava, L., Fontana, G., and Visconti, A., in *Simposio Internazionale su Recenti Acquisizioni nella Terapia antireumatica Non-steroides*, 1965, p. 326. Milan.
- ⁶ Nienhuis, R. L. F., Thesis, Rijksuniversiteit, Groningen, 1965.
- ⁷ Del Giacco, G. S., and Mazzei, D., *Reumatismo*, 1965, 17, 60.
- ⁸ Marmont, A. M., Damasio, E. E., Bertorello, C., and Rossi, F., *Arthr. & Rheum.*, 1967, 10, 117.

Warming Blood

SIR,—Dr. Patrick J. Bennett's apparatus for warming blood (23 September, p. 787) is very interesting, but we should like to point out that results as good are available with simpler apparatus.

We have investigated the Baxter Laboratories disposable Plexitron coil as a heat exchanger in conjunction with a standard Grant Laboratories (J.B.I) 3-litre waterbath. This combination of apparatus fulfils Dr. Bennett's requirements in that it is convenient to handle, simple, and cheap (under £15).

The Plexitron coil is preformed and therefore does not have to be wound on to a carrier. It is also shorter, with an internal volume of approximately 50 ml., which eliminates large priming volumes. The heat-exchange properties are much better than drip-extension tubing. We would like to stress the importance of using tubing designed to be heated, since substances used in the manufacture of tubing may be released into the lumen when heated. It would appear advisable to check with the manufacturer if any other form of tubing is used.

A 3-litre waterbath gives a greater heat reservoir and enables several bottles of cold fluid to be passed through rapidly without a drastic fall in bath temperature. When an efficient heat exchanger is used the limitations of a small waterbath may become apparent.

We have conducted several experiments with this coil and waterbath and found that 1 pint (0.6 l.) of blood could be transfused in five minutes and the temperature raised from 6° C. to 35.3° C. If two coils were used in series a pint of blood could be passed in under two minutes, with an increase in temperature from 4° C. to 35.7° C. A prolonged transfusion of six pints of cold fluid in 27 minutes was raised from an average starting temperature of 12° C. to 34.4° C.

We heartily agree with Dr. Bennett's safety devices. Grant Laboratories can supply a temperature cut-out and locked control device for a fixed temperature setting if these are desired. We think that the use of known laboratory apparatus seen to be satisfactory for many years is an added benefit.—We are, etc.,

Department of Anaesthesia,
Charing Cross Hospital,
London W.C.2.

B. PHILPOTT.

Department of Anaesthesia,
St. George's Hospital,
London S.W.1.

I. P. SLEE.

National Kidney Centre

SIR,—Your leading article (9 September, p. 631) on the closure of the National Kidney Centre does less than justice to the whole venture. It also shows a lack of appreciation of two facts. The first is that no patient is the property of one doctor, group of doctors, system of medicine, or, of course, the State. The second is that there is a basic defect in the N.H.S. plan for haemodialysis in that it is not home-orientated. It also seems that the author has insufficient experience of long-term home dialysis.

The National Kidney Centre has been of the highest significance for 30 patients in dire need, although obviously not for the Minister of Health (House of Commons, March 1967). The tragedy is that there would be no difficulty in dovetailing National Kidney Centre patients into the N.H.S. if the latter had initiated an expanding programme of home dialysis. It would have been better if instead of finding excuses for the actions and policy of the N.H.S. and poor reasons for the demise of the National Kidney Centre you had had some good word to say for a venture which, after all, has served to save the lives of some 30 people over the last nine months. This would have shown that you have the courage to speak up for advancement of thought rather than condone the conservatism and conventionality of the State machine.

We feel that you have overplayed the difficulties involved in treating intercurrent illness in patients on dialysis at home. Is it in fact certain that "complications [necessitating urgent admission to hospital is implied] [will occur] sooner or later"? For instance, the National Kidney Centre's experience (S. Shaldon personal communication) is that urgent hospitalization has been necessary on only two occasions in twenty patient-years of dialysis: an impressively low figure. Also it is often forgotten that when troubles do occur these patients have an advantage in that they have direct access to their systemic circulation, by way of shunts, for the administration of antibiotics (which it is quite possible for them or a relative to administer to themselves) and the collection of blood samples. Again shunt infection is not all that common in home dialysis and can usually be dealt with without hospitalization. If recannulation becomes necessary this is carried out as an outpatient procedure with no difficulty. Likewise, it is quite possible to deal with severe illness in the home, and one of us has experience of the successful cure of a classical lobar pneumonia at home while maintaining routine dialysis. This patient is now well and in steady employment.

If the N.H.S. had planned in time for home dialysis your criticism of such intercurrent illness prejudicing the treatment of an N.H.S. patient would in no way apply. We are not criticizing N.H.S. centres but the inexplicable reluctance of these centres to train their patients for home dialysis. Centre and home dialysis go hand in hand. A recent visit of one of us (M. H. F. C.) to British Columbia and the U.S.A. has shown that this is well recognized over there. It is the only way to treat the maximum number of patients with the available resources, and the rapid developments in renal transplantation make this policy more urgent, and the only humanitarian approach.

An equally strong argument in its favour, which would help your leader writer's problems, is of course that skilled hands (more rare and expensive than equipment) and equipment are freed to take on more patients in the centre. The National Kidney Centre could here have been of enormous help to the N.H.S., which could have used it to train its patients for home dialysis. Unfortunately the Ministry's decision has prevented this. Regional boards have had it within their power to refer patients to the

National Kidney Centre, but have unanimously decided not to make use of it.

One wonders what the personal decision of the members of these boards or even the Minister would have been if they had personally been confronted with a near relative dying of renal failure and unable to gain a place in the N.H.S. programme.

We believe that doctors exist to treat patients to the best of their ability from wherever they may come and however they may present. These patients are not the doctor's property. They cannot be blamed when treatment or a cure is not forthcoming from one source for seeking it from another, and we should applaud when private initiative provides an ethical and honest service where the N.H.S. has failed. We also believe with Mr. Medway (p. 680) that the closure of the National Kidney Centre would be a tragedy, and we strongly advocate the rapid development of an N.H.S. home dialysis programme and the more ready co-operation of all doctors in the treatment of their patients whether inside, outside, or half-way between any medical service or services.

Lastly, we would wish to put on record the thanks and admiration of ourselves and our patients with renal failure for the dedicated work done by the sponsors, staff, and the Director of the National Kidney Centre. We believe that this has been an inspired medical, scientific, and humanitarian venture.—We are, etc.,

M. H. F. COIGLEY.

I. R. McWHINNEY.

Stratford-on-Avon.

Use of Thorotrast

SIR,—Thorotrast is the subject of an approved new drug application under the provisions of the U.S. Food, Drug and Cosmetic Act. As you know, this means, in effect, that the Food and Drug Administration has approved the drug for use by the medical profession in the U.S.A. only under certain limited conditions, and that it is safe and effective only in those conditions. The label, labelling, and sales agreement which must accompany this product when sold in the United States set forth in precise detail the conditions of use which the Food and Drug Administration has approved for the drug. The authorized uses are closely restricted and the product may be administered only under the supervision of certified radiologists.

The article by Drs. A. O. Langlands and E. R. D. Williamson (22 July, p. 206) indicates that Thorotrast may be used for conditions other than those specified in the literature enclosed with each vial. This would be unwise, since not only is such use unauthorized in the U.S.A. but it could indeed seriously jeopardize the health and welfare of persons to whom it is administered. The drug must be used only in those conditions where the life expectancy is definitely short. Thorotrast is a valuable research item and is used in our most prominent research institutions to follow the effects of chemotherapeutic agents in malignant diseases of the liver and malignant cysts of the brain. Indeed, no other uses have been authorized.—I am, etc.,

GORDON A. GRANGER,
Medical Consultant,
Fellows—Testagar.

Fellows Medical Manufacturing
Company,
Detroit, Michigan, U.S.A.

Insulin Allergy

SIR,—We read with interest the case report by Drs. R. Cockel and Sheila Mann (16 September, p. 722) in which they described the value of the simultaneous administration of insulin and hydrocortisone in the management of insulin hypersensitivity phenomena, both local and systemic. One of us reported a series of similar observations with reference to local hypersensitivity phenomena at the Fourth International Diabetes Meeting in 1961,¹ and in subsequent publications we have investigated the immune mechanisms in such cases.^{2,3} The subject was also discussed at the 1963 meeting of the British Diabetic Association in Dublin.

The suggestion that the "allergic" response to insulin is due solely to impurities in the preparation seems unlikely in view of the abundant evidence now available of the development of antibodies to insulin using highly purified preparations.⁴ We have also demonstrated that the local weal and flare response to insulin, which is the local form of type I allergic reaction under discussion, is due to immune globulins which distinguish between highly purified recrystallized beef and pork insulins. The experience of Jorpes,⁵ who obtained his 300 cases of insulin hypersensitivity during the last war, when purified insulin preparations were not available, can hardly be compared with experience gained from current insulin preparations.—We are, etc.,

J. G. DEVLIN.

D. K. O'DONOVAN.

Department of Medicine,
University College,
Dublin 4.

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- 5 Jorpes, J. E., *Acta med. scand.*, 1950, 138, No. 239, p. 313.

Obstetric Complications and School Performance

SIR,—Perhaps I might be allowed to comment on the extremely interesting and valuable report by Drs. D. J. P. Barker and J. H. Edwards on obstetric complications and school performance (16 September, p. 695). It is said that the results obtained did not conform to my study,¹ and, although not referred to, a further study reported in 1967.² While this would appear to be fair comment in view of the comparatively large number of children available and detailed analysis of the Birmingham study, I would suggest that the two reports are not really comparable.

My report purported to relate intelligence in children who had had a normal antenatal and obstetric history. Intelligence was taken to be that quantum readily understood by the teacher who had had some years of experience with the child. That this is not related exactly to verbal reasoning scores assessed by the classic 11-plus examination method is, as the protagonists of the comprehensive school are only too ready to point out, now fully accepted—for example, in my own

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1. *J. Oral Surg. Anesth. and Hosp. D. Serv.*, 1961, 19, 30.

2. *Med. Times (N.Y.)*, 1963, Nov., 1063.

3. *Int. Rec. Med.*, 1959, 669.



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area a comprehensive school claims that last year the top third of the year examination results showed that 48% of them were 11-plus failures.

Our definition of "term" is in my submission significantly different; theirs being 38-41 weeks of gestation and mine being as near as possible to 40 weeks. My contention is that a higher intelligence is obtained in normal children born during weeks of gestation 37, 38, 39, than in those born during weeks of gestation 41, 42, 43, and Dr. Barker's Table IV, although it presumably includes children whom he shows to be at risk, would, I have thought, certainly not have failed to confirm my own results.

As regards his rather unexpected findings on forceps delivery, one wonders if the type of anaesthesia employed might not be a potent factor, as with the adoption of pudendal block as routine for forceps instead of inhalation anaesthesia it is most noticeable that the "shocked baby" has become something of a rarity and the "blue baby" even more so. While I would entirely agree with the comments on "sib control" in a series like the Birmingham one, I would suggest that this is not so important in so tight a controlled series as my own.

In conclusion may I say that investigations of this sort are still lamentably rare, on a subject as important as the possibility of raising the level of intelligence with the aid of fully considered obstetric manoeuvres, and Drs. Barker and Edwards will have done a real service in this respect if they have taught us that term is 38-41 weeks of gestation, and not 40 weeks or shortly after.—I am, etc.,

Walsall, Staffs.

M. H. DALE.

REFERENCES

- ¹ Dale, M. H., *Practitioner*, 1966, 196, 430.
- ² ——— *ibid.*, 1967, 198, 838.

Folate Deficiency in the Elderly

SIR,—I was interested in Dr. A. J. Gardner's comments concerning folate deficiency in the elderly (12 August, p. 436). When carrying out precise clinical investigations into folate deficiency states one should always aim at as large a degree of accuracy as possible, and it is particularly at the lower limits of "normal" serum folate levels in the elderly that I question that the test is accurate enough by itself for "practical purposes." I think that liver biopsies are only justified in exceptional circumstances as an aid to the diagnosis of folate deficiency in the elderly, and that red cell folate assays are, from the patient's point of view at least, a more satisfactory test.

Naturally there is a correlation between red cell folate levels and serum folate levels, but when one is dealing in clinical practice with individual patients it has been demonstrated that there is a very large range of red cell folate levels for any individual serum folate reading. Lowenstein *et al.*¹ showed that for a serum folate level of, say, 3.5 $\mu\text{g./100 ml.}$ the red cell folate range was between 100 and 400 $\mu\text{g./100 ml.}$ Cooper and Lowenstein² showed that for any serum folate level of 3.5 $\mu\text{g./100 ml.}$ the red cell folate range was between 50 and 400 $\mu\text{g./100 ml.}$, and Hoffbrand *et al.*³ showed that "at any given folate level in the borderline range there was a wide variation in the red cell folate level," varying from 100 $\mu\text{g./100 ml.}$ to

levels within the "normal range." Scatter diagrams in all three papers mentioned elaborate this point in detail. Moreover, Victor Herbert,⁴ in his classical work on experimental nutritional deficiency in man, showed that serum folate levels can rise transiently after folate replenishment within an hour or two following four and a half months of folate deprivation.

Folate levels in district hospitals are often difficult to obtain, but perhaps in the elderly at any rate, where serum folate levels below 6 $\mu\text{g./100 ml.}$ are relatively common, it would be a great aid to accurate diagnosis to be able to obtain red cell folate estimations in addition.—I am, etc.,

West Middlesex Hospital, JAMES ANDREWS.
Isleworth, Middx.

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- ³ Hoffbrand, A. V., Newcombe, B. F. A., and Mollin, D. L., *J. clin. Path.*, 1966, 19, 17.
- ⁴ Herbert, V., *Trans. Ass. Amer. Physns*, 1962, 75, 307.

Admirable Drug

SIR,—It appears likely that each civilization demands a drug. Tobacco is the most admirable of all. It soothes and composes, it makes for better temper, it keeps men in the chimney-corner, it stimulates thought.

If banned, whence should come the £1,000m. of lost revenue? It does not need an economist to point out that the release of this amount of spending power could not be allowed and that a similar amount would have to be claimed back by other taxes. If tobacco goes then drink and gambling must follow, for these two are home breakers and in anything but strict moderation can and do bring ruin. Not a single newspaper could survive the loss of advertising entailed. Is this of no interest to doctors?

As we get older nowadays we get more and more to fear the onset of helplessness and dependence—so here is a final beneficence of the divine weed. It clears us off before we begin to clutter up the earth.

It is the business of the B.M.J. to advertise as widely as possible the connexion between disease and tobacco. It has no business whatever to try to influence people's private decisions or to seek arbitrary extension of miserable old age by decree.—I am, etc.,

London N.W.4.

R. W. COCKSHUT.

Menace of Smoking

SIR,—In your informative leading article (23 September, p. 753) you say, "... it [smoking] is not, like the epidemics, a communicable disease—except by example." Of course it is. And it's not merely epidemic, it's pandemic. About half the adult population of western countries and vast numbers in eastern countries suffer from it. It is not communicated by the "old fashioned" method of micro-organisms but by something just as deadly—lies, and of course example, as you say—that is, "psychological infection." The basic lies are two:

(1) That tobacco is a luxury. In fact tobacco is a drug. Its pharmacological and toxic actions are described in all standard

textbooks on pharmacology. But it is sold in shops other than chemists. And it is heavily taxed—treated in fact like a luxury.

(2) That smoking is a habit. There is a habit factor in smoking, but essentially it is a means of taking nicotine—just as opium-smoking is a means of taking morphine.¹ Anyone who repeatedly takes a drug as strong as nicotine is addicted to that drug and is a drug addict. Most diseases are poisonings. All smokers suffer from nicotine poisoning—according to how heavily they smoke, and nicotine poisoning is a disease no less than lead poisoning, though the symptoms are more acceptable (to the smokers). The main symptoms are: recurrent sore throat and cough, and undue fatigability and depression (after depression). But smokers tend to repress or make light of the cause of their symptoms because of the strength of their craving for tobacco.

Your leading article also affirms that smoking "is surely the greatest menace to the public health of our time." Yet smoking is a curable and preventable disease. It is no more difficult to prevent than opium-smoking.

What is now needed is vigorous national health education: frequent talks, mainly short and sharp, with no punches pulled, on radio and television at peak times. We should press for this, and, should the Government veto or sabotage this campaign, we should go on-strike; deal with emergency cases only. How refreshing, a strike for something other than pay and conditions.—I am, etc.,

Malta.

LENNOX JOHNSTON.

REFERENCE

- ¹ Johnston, L. M., *Lancet*, 1942, 2, 742.

Headlight Glare

SIR,—The elimination of headlight glare by covering lights with polaroid film and drivers' eyes with film with its plane of polarization at right angles to the first, as recommended by Dr. S. J. Lines (30 September, p. 867), would almost certainly prevent a number of fatal and other accidents. However, his suggestion of setting the plane of polarization at 45° from the vertical is not necessarily the best solution.

Many motorists already possess polaroid spectacles with the transmission plane of polarization (direction of the electrical vector) set vertically so as to eliminate glare from the horizontally polarized light reflected from road surfaces, especially when wet. This advantage of existing polaroid spectacles, visors, or windscreens could be retained if headlights were all polarized horizontally.

The advantage of making the planes of polarization of a driver's own headlights and his glasses or visor compatible with one another is not as great as Dr. Lines assumes, since most of the light by which the driver views objects ahead would be depolarized by multiple reflections. The one important exception is "cat's eyes" and other reflecting signs, and the apparent intensity of these might be considerably reduced by the horizontal-vertical system. The problem is thus one of balancing advantages and disadvantages, and could easily be settled by simple practical trials. Polaroid film transmits a little unpolarized light at each end of the spectrum, and bright lights such as car headlights would possibly be sufficiently obvious

without any deliberate limitation of polarization, appearing as a deep reddish purple colour.

The question of cost would no doubt be raised. Most optical devices incorporating polaroid film are very expensive, but the film itself is relatively cheap and could probably become cheaper still if millions of mass-produced devices were needed—almost certainly much cheaper than many compulsory safety features already incorporated in cars.—I am, etc.,

A. E. MOURANT.

Serological Population Genetics
Laboratory,
St. Bartholomew's Hospital,
London E.C.1.

Court Lees School

SIR,—I would endorse Dr. J. H. Lancaster's plea (2 September, p. 619) for an elucidation of the points he raises, especially in regard to the accuracy of the colour photographs.

In a B.B.C. T.V. programme on 18 August, when this matter was discussed, a photograph which I believe was one of those used in evidence was shown briefly. It was in monochrome, but its appearance immediately roused my suspicions for two reasons. The first was that the marks were equally apparent on both right and left buttocks and the second that they were equally distributed across the buttocks from the top of the natal cleft to the upper part of the thighs.

Unless that boy was caned by an ambidextrous individual, operating first from his right side and then from his left, who had taken especial care to distribute the strokes at regular intervals from the sacral region to the upper part of the thighs, I would beg leave to doubt the authenticity of that picture.—I am, etc.,

Harrow, Middx. J. B. WRATHALL ROWE.

Portable Pharmacy

SIR,—I have a book of instructions sold with a portable pharmacy similar to those mentioned by Dr. P. W. Mathew (3 June, p. 641) and Dr. F. N. L. Poynter (24 June, p. 843), which is of added interest, as it contains a catalogue of these chests issued in 1814. They vary from the family dispensary at £20 8s. to the lady's dispensary at £5 10s. The country clergyman's dispensary at £9 5s. is "made on a very cheap plan, and supplied with black bottles," while the vestry medicine chest at £1 10s. 6d. "has been found very serviceable in cases of fainting or hysteric fits which often occur during divine service."

Chests are listed for the use of travellers on the Continent and in the tropics, and at £32 10s. the sea medicine chest is provided for Navy surgeons and captains of merchantmen. This latter chest, in addition to the usual formidable purges, contains a useful supply of mercury.—I am, etc.,

Southall, Middx.

R. J. RABETT.

Visible Alternatives

SIR,—I refer to your leading article (7 October, p. 6). Already 19 years have been futilely wasted on committees and reports. How much longer is the profession going to dither?

While the delusion exists that it is a health service there is no hope. Once it is recognized as an ill-health service the alternative of a health service is or should be obvious, and its organization reasonably clear. Being slow and dim-witted, it took me several years to fully recognize this.—I am, etc.,

Rochdale,
Lancs.

L. McASKIE.

Enticing the Emigrants Home Again

SIR,—We are told the Minister of Health is to launch a campaign to coax the emigrant doctors to return to the fold.¹

If this intention is genuine, and not just a gimmick for political window-dressing, then I suggest one of the first things he does is to rescind the wretched "break" clause in the seniority award regulations whereby any general practitioner who has a break of more than three months automatically forfeits his seniority awards.

Many of the general practitioners who have emigrated are in the 40–50 age group; contrary to popular opinion, they are by no means all young ex-hospital staff newly qualified. These older men would all qualify sooner or later for seniority awards if this pernicious "break" clause were to be removed. What better example of his good faith could the Minister make to these "erring" sheep than to restore their lost eligibility for seniority awards they rightly deserve?

I really cannot imagine how the older general practitioners are to be enticed back if they have to endure the insult (for that is what this idiotic clause really is) of going to the bottom of the queue again for their seniority awards. A large number of general practitioners have forfeited their awards because of this arbitrary and vicious penalty; and it astonishes me that more of a fuss has not been made about it.

I have a letter before me from one general practitioner who was foolish enough to go to Zambia under the scheme for secondment of doctors in the N.H.S. to underdeveloped territories. He was given to understand he would suffer no loss of pension rights. Now, after returning, he has been told that because of his absence he has forfeited any seniority award. What a cynical decision, and how very unfair and un-British this sort of political opportunism has become.

Never has a respectable profession been treated so cynically and so disgustingly. My advice to would-be returning doctors is to clear up this business of forfeited awards *before* they are persuaded to return home again. Otherwise they may find themselves in for an unpleasant surprise when it is too late to change their minds again.—I am, etc.,

C. C. M. WATSON,

Chairman,
North-West Wales Division, B.M.A.

Merioneth,
Wales.

REFERENCE

¹ *Brit. med. J.*, 1967, 3, 128.

Miserable Conditions

SIR,—As general practitioners are insidiously and relentlessly being cornered by the present Government into eventually having to accept a salaried service, we are rapidly approaching cross-roads. Some general

practitioners are so fed up that they themselves would opt for a salaried service as the least of the N.H.S. evils, so gaining regular hours and holidays, a supply of locums and staff, etc.

It continues to amaze me that we sit quietly by accepting new restrictions, regulations, and frustrations one after the other. Patients' signatures for immunizations, maternity care, and night visits are just three of these which come immediately to mind. Soon, no doubt, patients will have to sign that they have received the right and proper treatment and prescriptions as demanded.

One outstanding anomaly of this free N.H.S. is the example of specialist referral. I am not allowed to issue an E.C.10* to a private patient. Yet if a patient on my list elects to pay a consultant for certain privileges—for example, to save waiting time, to have a more lengthy consultation, or even to guarantee that he will be seen only by the consultant to whom he has been referred—he may then receive treatment on an E.C.10 via the general practitioner. This is quite ridiculous and most unjust. Of course, I may refuse to issue an E.C.10, but as long as I am being paid per caput as a basic income I will agree to do so or risk losing a substantial number of patients who are, in ever-increasing numbers, insuring themselves against private consultations.

Let us hope that in the foreseeable future either the general practitioners will unite against these miserable conditions of service or that the situation will change so that we can limit our lists (so giving a better service) and not toe the line, which we all at present do whether we like it or not.—I am, etc.,

Leeds.

G. R. ADDLESTONE.

How Many Old People?

SIR,—For pensioners over 65 on general practitioners' lists there is an extra capitation fee. Accordingly the executive council, which keeps the accounts, is able to state how many such persons there are in a given locality. In this area the executive council has kindly supplied the numbers of old people and just where they are situated. This is most helpful in planning hospital and geriatric services.

The object of this letter is to suggest to some of your readers this way of arriving at an accurate estimation of the number of old people.—I am, etc.,

St. Mary's Hospital,
Colchester, Essex.

K. HAZELL.

Points from Letters

Sales Promotion

Dr. W. M. E. TOPPING (Cheadle, Lancs) writes: I would like to assure Dr. J. R. Caldwell (16 September, p. 741) that he is not alone in noticing the great increase in numbers of representatives and also the frequency of their visits. So great was the interference with my work that I took the step that Dr. Caldwell contemplates about nine months ago. . . . The drug companies are their own worst enemies in this business, and I took the trouble to see each representative one last time to ask him to inform his company why I was doing this.

Until a great many more doctors take this step they will be increasingly pestered. It is like stopping smoking: it is infinitely easier to stop than to cut down.

Obituary Notices

J. B. McDougall, C.B.E., M.D., F.R.C.P.ED., F.R.C.P.GLASG., F.R.S.ED.

Dr. J. B. McDougall, a distinguished phthisiologist, for many years medical director of the British Legion Village Settlement at Preston Hall, Kent, and for some time chief medical adviser in tuberculosis to the World Health Organization, died in Athens on 30 September, aged 76.

John Bowes McDougall, son of Allan McDougall, of Greenock, was born on 5 December 1890. He was an able scholar at Greenock Academy, and carried off many prizes both at school and at Glasgow University, where he graduated M.B., Ch.B. in 1914. In 1916 he was awarded the M.D. with commendation, and was elected M.R.C.P.Ed. in 1919. In the same year he was elected Fellow of the Royal College (then Faculty) of Physicians and Surgeons of Glasgow. In 1928 he was elected to the Fellowship of the Royal College of Physicians of Edinburgh, and later in the same year to the Fellowship of the Royal Society of Edinburgh. In 1943 he was appointed C.B.E., and in 1964 the Royal College of Physicians and Surgeons of Glasgow elected him to the Fellowship of the College. These many academic achievements were accompanied by prowess in athletics and games, and he was one of the few who represented Scotland in international rugby, both before and after the first world war. He played for Scotland against France in 1914 and again in 1921, against Ireland in 1914, and against England in 1922.

From the earliest days of his professional career he was interested in tuberculosis, and soon after graduating he held appointments in tuberculosis hospitals and clinics in Manchester and Stoke-on-Trent. During the first world war he joined the R.A.M.C., attaining the rank of major and the command of No. 30 General Hospital at Calais. This administrative experience served him in good stead in his subsequent appointments. After demobilization he became medical superintendent of the Wooley Sanatorium, Northumberland, and it was here that he first showed his keen interest in the rehabilitation of tuberculous patients and the need to provide them with remunerative employment and eventually a career which would enable them to become again useful citizens. He became associated with Dr. (later Sir) Pendrill Varrier-Jones, who had by then established industries and a village settlement at Papworth. There were at that time many tuberculous ex-Servicemen, and the British Legion came to their help by sponsoring and financing a scheme for industries and a settlement at Preston Hall, near Maidstone. McDougall was the obvious choice for the post of medical director of this project. From 1925 he devoted himself unsparingly to the development of this institution, which by 1944 had grown into a great industrial concern, doing much Government work in the printing and woodwork departments, as well as providing a large number of houses and hostels for tuberculous ex-Service men and women, and their families. McDougall encouraged the British Legion to devote more attention and money to tuberculous ex-Service men and

women, and persuaded them to open Douglas House, Bournemouth, for the treatment and employment of elderly male patients; and Nayland Sanatorium, Colchester, for ex-Service women.

After studying tuberculosis in Canada, the U.S.A., France, and Germany, he introduced tomography in chest examinations, and installed the first of such units in this country at Preston Hall Hospital.

In 1944 he was asked by U.N.R.R.A. to advise on tuberculosis problems, and from this appointment he proceeded to be chief tuberculosis adviser to the World Health Organization. He travelled widely, and after leaving Geneva he went to Cairo, where he established a tuberculosis college for post-graduate tuition in all aspects of the disease. He contributed largely to tuberculosis literature, and was a prominent member of the then National Association for the Prevention of Tuberculosis (now the Chest and Heart Association) and the Joint Tuberculosis Council, of which he was secretary for many years.

On retirement he lived in Athens, where he derived much happiness from the good fellowship of the Greek people and the warm pleasant climate. He did not enjoy very good health in later years, and was much handicapped by having to have a leg amputated some five years ago. This was a great strain on a person with such unbounded energy, for McDougall never did anything by halves. While he was organizing and developing Preston Hall he studied music intensely, and obtained the A.R.C.M. and the L.R.A.M. In addition he wrote many books; some on tuberculosis, of which the *Global Study of Social Pathology* has become a standard work of reference. Other publications of his were about small livestock, in which he was always interested, and he became a leading authority on angora rabbits.

McDougall had a wide circle of friends, both in Scotland and in England, and his forthright, fearless, and valuable advice on the administrative and clinical problems of tuberculosis was widely sought and always willingly given. The passing of McDougall removes from the world one of the greatest veterans of tuberculosis medicine of this country, and all who knew him will have memories of his impressive personality for many years to come.

He leaves a widow and two sons, one of whom is a physician. We extend our deep sympathy to them in their great loss.—F. H.

S. B. RADLEY, M.B., B.S., F.R.C.S.

Dr. S. B. Radley, emeritus surgeon, Newark Hospital, died at his home in Newark-on-Trent, Nottinghamshire, on 13 September. He was 78.

Sidney Bertram Radley was born on 18 September 1888, and was educated at Manchester University and St. Bartholomew's

Hospital, London. He graduated M.B., B.S., with honours and distinction in medicine, from London University in 1911, and in the same year he graduated from Victoria University, Manchester, with second-class honours. After early house appointments in London and Manchester he took the Conjoint diploma in 1913 and the F.R.C.S. in the same year. During the first world war he joined the R.A.M.C., serving overseas as surgeon specialist. After demobilization he settled in Newark, and in addition to his appointment as honorary surgeon at Newark Hospital he was also in practice as a family doctor. In the second world war he was the senior surgeon at Newark Hospital, and spent many nights at the hospital operating on air raid and Bomber Command casualties.

A member of the British Medical Association, he was a representative at the Annual Meetings from 1942 to 1945, and again from 1948 to 1954, and was president of the Nottingham Branch in 1953-4. Among his hobbies were golf, archaeology, and ornithology. He retired in 1955.

From my first meeting with Sidney Radley in 1926, when I came to Newark as a young general practitioner, I felt that he was a man that I could trust and go to in any kind of trouble. This impression never altered, and must be shared by many of his colleagues and friends. He had a sense of humour all his own, and nearly always illustrated his points with some very appropriate anecdote fitting to the occasion. He was a fine man and a fine doctor.—A. M. D.

B. THOMAS, M.B., B.S., F.R.C.S.ED.

Dr. B. Thomas, formerly honorary surgeon at the General Hospital, Aberdare, died on 4 September. He was 72.

Benjamin Thomas, son of Dr. Ieuan Thomas, was born on 8 July 1895, and was educated at Epsom College and St. Mary's Hospital, London, qualifying with the Conjoint diploma in 1917. He served as a medical officer in the Royal Navy during the first world war, and after demobilization graduated M.B., B.S. in 1919. He held house appointments at St. Mary's Hospital and the Derbyshire Royal Infirmary before taking over his father's practice at Hirwaun, Glamorgan. Elected F.R.C.S.ED. in 1920, he became honorary surgeon at the General Hospital, Aberdare. He was the first chairman of the medical staff committee, and became senior hospital medical officer at Aberdare General Hospital when the National Health Service was introduced. He was also a member of the hospital management committee and a member of the local medical committees for Glamorgan and for Brecon. A member of the British Medical Association, he was chairman of the North Glamorgan and Brecknock Division in 1950-1. He retired some 10 years ago and made his home in the Penarth district.

As a general-practitioner surgeon he was held in high esteem by patients and colleagues, and will be remembered as a man

capable of wise decisions and sound judgement. These qualities were also much appreciated in his service to the community as deputy coroner for South Breconshire and as a justice of the peace for the county of Glamorgan.

We extend our sympathy to his widow and to his son, now an electrical engineer in Rhodesia.—J. E. T.

C. M. BARKER, M.A., M.B., B.CH.

Dr. C. M. Barker, a familiar figure to many generations of psychiatrists and psychotherapists, died on 11 September after a short illness. He was 76.

Culver Maynard Barker was born in England on 4 March 1891, but spent his early life in British Columbia. After working as an engineering apprentice for the building of the railway in the Klondike he returned to Britain during the first world war with the 1st Battalion of the Engineers of the Second Division and saw active service in France. After demobilization he decided to stay in Britain in order to train for one of the professions. He studied at Pembroke College, Cambridge, and at University College, London, qualifying in 1926 with the Conjoint diploma, after which he held house appointments at the Royal Northern Hospital and Manor House Hospital, London.

In 1927 Dr. Barker met C. G. Jung. It was a turning-point in his life. He arranged to study with Jung in Zurich throughout the following academic year. On returning to Britain he entered psychiatry by becoming medical officer to the observation ward at St. Peter's Hospital, Whitechapel, where Dr. E. Mapother, superintendent of the Maudsley Hospital, was the visiting psychiatrist. In those days no treatment or aftercare (other than referral to a mental hospital) was provided by observation wards. But Dr. Barker, inspired by Jung's work with psychotic and borderline psychotic cases in the Burghölzli Hospital, Zurich, introduced psychotherapy into what was then regarded as a most unpromising field. For several years he conducted an unofficial outpatient clinic, obtaining patients from among those who were discharged from the observation ward and from other departments of the hospital. The conditions were primitive and the work was often regarded with suspicion. But Dr. Barker persisted in it and in later years it was with some pleasure that he recounted how it had been in the East End of London that he first tested and proved the efficacy of Jung's method of psychotherapy. He received some official acknowledgement of this work when an account of it was included in a London County Council report in 1937. In the same year he completed the M.B., B.Ch., and left Whitechapel to take up a post at the Cassel Hospital; combining this with private practice and a clinical assistantship at University College Hospital. At the same time he was able to find expression for his interest in children by joining the staff of the Institute of Child Psychology, where he was consultant psychotherapist for many years.

During the second world war Dr. Barker, like many of his colleagues, became interested in the new physical methods of treatment which were being introduced into our mental hospitals at that time. Having learned the technique of administering E.C.T. in a large

hospital, he became one of the first psychiatrists to acquire his own apparatus and use it in his private practice, where he often combined it with psychotherapy. After the war he returned to a more exclusively psychotherapeutic practice. He was able to renew his contact with Jung and with his many other colleagues and friends in Zurich. He became a frequent visitor to that city, and he gave many lectures in the C. G. Jung Institute. Dr. Barker was an indefatigable worker up to the time of his death; and he was a keen participant in the affairs of various societies concerned with psychotherapy, in particular the Society of Analytical Psychology, of which he was a founder member.

Barker was, at one and the same time, a most ordinary and a most unusual person. Many would count him as a familiar friend and colleague, but few knew him at all intimately: he hardly ever spoke of himself. He was dedicated to his work, for which he had exceptional gifts, though he did not always do himself justice in this respect in his public utterances. He seemed almost totally uninterested in power and prestige; and, although not without shrewdness, he had a most kindly and philosophical outlook on life. Culver Barker occupied a unique place in the lives of many of us and he will be very much missed. He is survived by his widow.—R. L. M.

C. B. C. writes: Dr. Culver M. Barker was one of my closest friends for 40 years. He was kind, wise, and enthusiastic. He referred everything to its roots. He was a real lover of nature, and keen on getting back to nature. He was always talking about his consciousness as part of the universal consciousness of all living things. Thus he was able to act as guide and father to a large circle of people who were lonely and found life too much for them. He will be sadly missed.

F. O. WALKER, M.R.C.S., L.R.C.P. D.P.M., D.O.

Mr. F. O. Walker, who was formerly consultant ophthalmic surgeon to the Dartford Group of Hospitals and Queen Mary's Hospital, Sidcup, died in Joyce Green Hospital on 21 September. He was 73.

Frederick Oliver Walker was born in London on 10 November 1893. Throughout the first world war he served in the ranks in the R.A.M.C. at casualty clearing stations in France. During his service, assisted by a young medical officer and encouraged by his commanding officer, he matriculated. After demobilization in 1919 he entered the Middlesex Hospital Medical School, and qualified with the Conjoint diploma in 1924. He entered the mental hospital service, working at Colney Hatch, Horton, Hanwell, and eventually at Bexley. He took the D.P.M. in 1928. It was at Bexley that he developed his interest in ophthalmology and began studying at the Royal Ophthalmic Hospital, taking in 1933 the diploma in ophthalmology. About 1929 opportunities for engaging in ophthalmic surgery developed in Dartford, and so Mr. Walker resigned from the mental hospital service and devoted himself to this specialty. During this time his services were utilized by the local hospitals—

West Hill, Joyce Green, and the Southern Hospital at Dartford, and Queen Mary's Hospital at Sidcup; and he also became ophthalmic surgeon to the Battersea General Hospital.

During the second world war Mr. Walker's services were in great demand, and he was unsparing in his efforts on behalf of the injured. In 1948 he was appointed consultant ophthalmic surgeon to Queen Mary's Hospital, Sidcup, and to the Dartford group of hospitals, and he maintained his private practice, centred on Dartford, where he lived. He retired in 1958, and was appointed honorary consultant surgeon to the hospitals he had served. He continued his own consultative work, however, up to the time of his death.

A member of the British Medical Association, he was representative at the Annual Meeting in 1953, and chairman of the Dartford Division in 1953-4. He was not intimately known by many, but he gained the good will, the loyalty, and confidence of his patients and colleagues. He lived among those for whom and with whom he worked, and was well known in his professional and private capacity, and was trusted in both.

He leaves a widow and three sons.—T. S. C.

W. L. WINSLOW SMITH, M.C., M.B. B.CH., B.A.O.

Dr. W. L. Winslow Smith, a well known general practitioner of East Horsley, Surrey, died on 14 September while on holiday at Kirkcudbright. He was 71.

William Leslie Winslow Smith was born at Blackrock, County Dublin, on 10 February 1896. He was educated at Mountjoy School, Dublin, and entered Trinity College, Dublin, in 1912. He studied mathematics and was elected Scholar of the House in 1914. He volunteered soon after the outbreak of the first world war, and served with the Royal Artillery in France, being awarded the Military Cross, and was twice mentioned in dispatches. During the latter part of his service he was captain and adjutant. After demobilization he returned to Dublin University in 1919, taking his B.A. in 1920 and qualifying M.B., B.Ch., B.A.O. in 1923. He was captain of the Dublin University Rugby Club for two years after the war, and was also an outstanding athlete, creating a record at Trinity College, Dublin, for throwing the discus. He went to Ceylon in 1924, where he spent six years as medical officer of the Dickoya District planters' association. On returning to England he served as house-surgeon at the Royal Victoria and West Hants Hospital, Bournemouth. He came to East Horsley in 1931, and very soon became a successful general practitioner. He was appointed district medical officer and vaccination officer for the Horsley and Clandon districts.

Dr. Winslow Smith was a family doctor who took a very personal interest in all his patients. In the days before the comprehensive National Health Service, he attended less fortunate patients for nominal fees, and as often as not for love, in the highest tradition of the medical profession. He was an active member of the British Medical Association, serving for many years on the executive

committee of the Guildford Division, also on the Surrey Branch Council, and was chairman of the Guildford Division in 1950-1.

After a life of strenuous service he had a serious illness in 1961, and was obliged to retire from National Health Service practice to live a quiet life. During these last years those who visited him either socially or for medical advice were invariably struck by his cheerfulness, his patience, and his concern for others. No one ever heard him complain of his own pains or disabilities.

In 1933 he married Marjorie Florence, daughter of the late Mr. J. H. Cleland, of Richmond. She was a tremendous support to him, particularly in recent years of suffering and relative inactivity. Their many friends in the profession will offer her their deep sympathy.—C. P. W.

M. G. GARRY, L.R.C.P.&S.I., L.M.

Dr. M. G. Garry, medical officer of health for Formby, Lancashire, died in hospital on 17 September after a short illness. He was 80.

Michael Gerald Garry was born in Ennis in 1887, and qualified with the Conjoint diploma of the Royal College of Surgeons in Ireland in 1912. He later became assistant master at the Coombe Lying-in Hospital, Dublin. After several hospital appointments he took up general practice in Co. Clare. In 1926, however, after the death of his infant son, he came to England and joined the late Dr. A. C. Wilson and Dr. E. L. Roberts in practice at Formby, Lancashire, where he later became medical officer of health, an appointment he held until his death.

Michael Garry had great personality and clinical flair, reinforced by deep sympathy and unlimited patience. He was by nature a rebel, always prepared to cut the red tape of officialdom if by so doing he could benefit a patient, and there are very many who will mourn his death. But it was as a sportsman that he was known to a much wider public. Between 1908 and 1911 he was capped for Ireland seven times against England, Scotland, Wales, and France, and it was seldom that he missed seeing the England-Ireland rugby international. He had the Irishman's love of racing, and for years was medical officer to Aintree racecourse, where many of the leading National Hunt jockeys came under his care. Golf took up much of his spare time, and he was an ex-captain of the Formby golf club.

He was married twice, and to his widow, Cynthia, and his three daughters we extend deep sympathy in their loss.—E. L. R.

LEONARD COLEBROOK, D.S.C.

M.B., B.S., F.R.C.S., F.R.C.O.G., F.R.S.

B. W. writes: As one who worked as a resident at Queen Charlotte's Hospital in the days of the Isolation Block, and who had much help from him in one of the early trials of the sulphonamides, I should like to pay my tribute to the memory of this great man, known affectionately to all as "Coli" (obituary, 7 October, p. 59). Although always very modest about his success, his results came from a prepared mind which had studied deeply the problem of infection, and from his training with Almoth Wright, whose biographer he was. Wright's main claim to fame may well rest on the work

of his great disciples, Fleming and Colebrook. No aspect of obstetrics escaped Colebrook's attention. He would spend time and effort instructing a house-surgeon in cross-matching, when this was a "do it yourself" procedure. But his vision ranged far beyond the laboratory. His experience with burns led him into his successful campaign for non-inflammable clothing. His principle was, "If preventable, why not prevented," and present-day obstetricians who have never seen puerperal sepsis in full flood should remember that the long experience of this great worker with infection in peace and two wars never made him subscribe to the easy but dangerous view that the age of infection is past.

F. H. K. G. writes: I was privileged, as secretary of the M.R.C. War Wounds Committee, to see much of Dr. Colebrook (obituary, 7 October, p. 59) during the second world war, and I should like to pay tribute to his industry, his humanity, and his modesty. A pioneer in the clinical trial of sulphonamides against streptococcal infections, he played an important part in establishing the role of these drugs, and later of penicillin in the control of infection in wounds and burns, as well as in devising other methods to prevent hospital cross-infection of injured surfaces. Although he had no children himself he was devoted to children, and the high incidence of burns due to domestic accidents among children admitted to his units at Glasgow and Birmingham caused him great distress. After his retirement he devoted much of his energy to a successful campaign for the improvement of safety standards for gas and electric fires and to encouragement of the use of fireproof clothing for children.

G. S. W. writes: Leonard Colebrook's friends will be saddened by his sudden, though not unexpected, death (obituary, 7 October, p. 59). He was one of those happy mortals who command both respect and affection. He had a most endearing nature. Modest in the extreme about his scientific attainments, loyal and devoted to his chief, lively, humorous, and entertaining as a companion, brave and uncomplaining in face of the adversities that finally overcame him, he will long be remembered by his numerous and varied colleagues. To his wife, Vera, who tended him so faithfully during the latter years of his life, all who knew her will extend their sympathy.

Sir JAMES LEARMONTH, K.C.V.O.

C.B.E., LL.D., M.D., CH.M., F.R.C.S.

F.R.C.S.ED., F.R.A.C.S., F.A.C.S.

F.R.F.P.S.GLASG.

R. L. R. writes: As a teacher James Learmonth (obituary, 7 October, p. 58) was superb, and the students soon learned that the high standards which he expected of them were a reflection of his own approach to the practice of surgery. Technically also he was a fine craftsman, and while not normally a fast operator he could act swiftly when the occasion demanded. Although a trained neurosurgeon, he soon showed that he was a master of all branches of the craft of surgery, and when in Aberdeen he was looked upon as a skilled abdominal and urological surgeon. At that time the chair was not a full-time one, and, in addition to his teach-

ing and the establishment of a department of surgery which produced much original work, he had a considerable private practice, and many general practitioners and patients were grateful for his surgical help. Personally his years in Aberdeen for him and his family were happy ones. In the difficult years in Edinburgh during and after the second world war he was at times heard to say that he had his application all ready if the opportunity to return to Aberdeen should arise.

During the war years he worked extremely hard. He succeeded to the chair of systematic surgery in Edinburgh just as war was declared. In spite of all the difficulties of wartime, he maintained the high standard and the volume of work from the department which had been established by Sir David Wilkie, and made it a Mecca for the many Commonwealth and American surgeons whom the war brought to this country. He carried on the clinical, administrative, and teaching duties of the chair with a depleted staff. If this was not enough for one man, he was also surgical director for South-east Scotland, ran the unit for peripheral nerve and blood vessel injuries at Gogarburn Hospital, and for a time also was in charge of a surgical unit at the Western General Hospital. In addition to these activities in Edinburgh he served on the Medical Research Council and on several of its committees, and was also a member of the Goodenough Committee on medical education. These commitments meant many weary nights in blacked-out trains held up by air raids.

When peace came he seemed to be busier than ever. In 1946 he took on the additional duties of the chair of clinical surgery, and for a further ten years he led the life of a busy surgeon, teacher, and administrator. He also travelled extensively, being in great demand as a lecturer and medical ambassador. These were difficult years, and it came as no surprise to those who knew him well that he decided the pace was too fast and that he should retire from both chairs. In his retirement it was a source of great pleasure to him that his Alma Mater, which had been unable to find a suitable place for him in his youth, should make amends by electing him an assessor on the University Court, and in recent years Glasgow University has benefited greatly from his wise counsel.

TERENCE EAST, M.A., D.M., F.R.C.P.

T. K. L. writes: In the various accounts that have been written about this scholar-physician (obituary, 9 September, p. 684) I do not think sufficient emphasis has been put on the fact that not only was he a remarkably able teacher but he thoroughly enjoyed teaching. Admittedly it was necessary to listen carefully to his remarks, because he always spoke quietly and rarely repeated himself, but to attend his ward rounds was of great educational value and an unforgettable pleasure. By careful analysis and an assessment of the merits of every symptom and physical sign he had a remarkable facility for making the most difficult clinical problem appear perfectly simple. I consider that to have served as one of his house-physicians was the greatest privilege, for at that stage one appreciated his teaching all the more and, in addition, one found that in Terence East one had a staunch friend and a sound adviser.

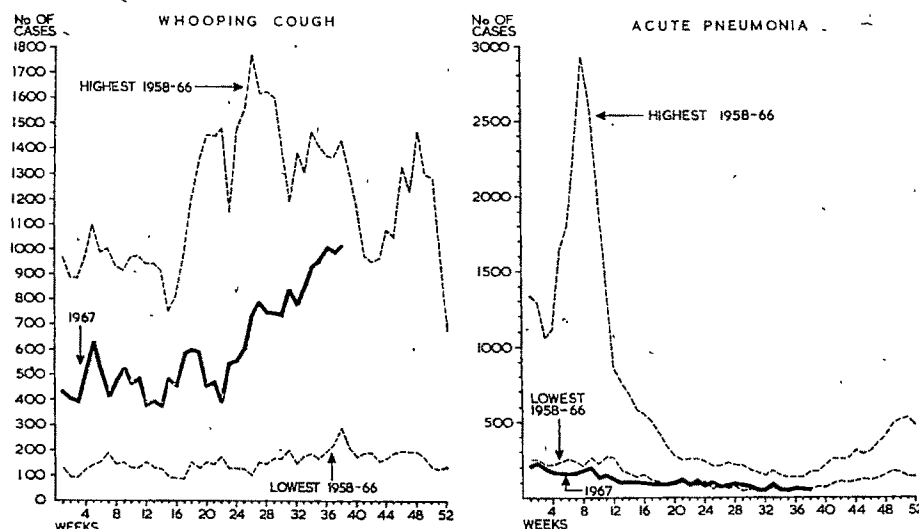
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of whooping-cough and acute pneumonia in England and Wales.

Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending	
	22 Sept.	29 Sept.
Paratyphoid Fever		
Greater London ...	1	6
Typhoid Fever		
Stockton-on-Tees (M.B.)	0	1
Bristol C.B.	0	1
Haringey (London)	0	1
Poulton-le-Fylde (Lancs)	0	2
Birmingham C.B.	0	1
Dysentery		
Greater London ...	51	45
Lancashire ...	33	44
Warwickshire ...	17	21
Coventry C.B.	1	9
Glasgow ...	63	38
Edinburgh ...	15	8
Food-poisoning		
E. Sussex ...	45	68
Brighton C.B.	43	60

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 23 September (No. 38) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included). Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	0	0	
Dysentery ..	214	51	115	4	5	279	55	88	13	4
Encephalitis, acute..	7	1		0		0	0		0	
Enteric fever: Typhoid	6	1	1	0	1	6	4	0	0	
Paratyphoid..	7	1	0	0	0	3	3	3(B)	0	
Food-poisoning	186	32	12	2		261	34	2	4	
Infective enteritis or diarrhoea under 2 years				27	36				22	87
Measles*	650	49	5	18	9	2,791	340	86	73	32
Meningococcal infection ..	1	0	2	0		5	0	3	0	
Ophthalmia neonatorum..	7	2	0	0		15	0	0	0	
Pneumonia†	59	9	51	4		53	9	43	0	1
Poliomyelitis, acute: Paralytic	0	0	1	0		0	0	0	0	
Non-paralytic	0	0	0	0		0	0	0	0	
Puerperal fever‡	60	17	1	0		84	29	1	0	
Scarlet fever ..	172	23	18	7	5	208	22	22	6	8
Tuberculosis: Respiratory ..	188	38	10	4		227	51	30	11	
Non-respiratory ..	41	9	4	3		43	9	4	2	
Whooping-cough	1,020	137	61	6	22	627	101	31	12	10

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	8	0		1	4	4	0	0	0	1
Influenza ..	0	0	0	0	0	3	1	0	0	0
Measles ..	0		0	0		0		0	0	0
Meningococcal infection ..			1					0		
Pneumonia ..	545	103	20	11	8	495	76	21	16	8
Poliomyelitis, acute..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	32	5	3	2	0	21	2	5	1	1
Non-respiratory ..				0	0				0	0
Whooping-cough	2	1	0	0	0	0	0	0	0	0
Deaths 0-1 year	277	59	12	2	17	293	51	30	11	5
Deaths (excluding stillbirths)	9,251	1513	490	98	171	8,920	1463	512	102	130
LIVE BIRTHS	15,649	2566	819	277	456	16,786	2774	936	279	300
STILLBIRTHS	258	40	21			259	44	16		

* Measles not notifiable in Scotland whence returns are approximate.

† Includes primary and influenzal pneumonia.

‡ Includes puerperal pyrexia.

MOTORING

Progress Towards Safer Night Driving

[FROM OUR MOTORING CORRESPONDENT]

Autumn is traditionally the time of year for criticism and reappraisal of car headlamp systems and the ways in which they are used (and misused). The exercise is of more than ordinary interest on this present occasion for two reasons—the new ideas which are to be found in some of the 1968 models and the probable intention of the Ministry of Transport to take a decision, before long, on the vexed question of the extent to which headlamps should be used when driving in cities and their suburbs.

It is a sad commentary on the way in which we deal with traffic problems that there is still no legal obligation to fit headlamps to cars used in the United Kingdom, though if they are fitted certain specific conditions must be met. Consequently no legal ruling about the use of headlamps by drivers can be given until the fitting of headlamps is itself made obligatory. This first step is now said to be "imminent."

For several winters past the City of Birmingham has sponsored a full-scale experiment in which large numbers of drivers have voluntarily used dipped headlamps continuously at night, no matter what the level of street lighting might be in any particular area. Accident statistics appear to show that greater safety has resulted as compared with the more general practice (in the U.K.) of using sidelamps alone in built-up areas. The driving public does not seem to have been particularly bothered by glare from either approaching or following cars, which suggests that more than ordinary care was taken to have the lamps properly adjusted.

We are so insular in these matters that little notice is taken of the fact that the use of headlamps has always been obligatory, whenever a car is on the move at night, in large areas of the United States and in Europe. I have myself had much driving experience under these conditions in large American cities and can vouch for the fact that, apart from giving better driving vision, dipped headlamps identify an approaching car more positively than sidelights, the use of the latter being confined to parked cars. It is interesting to recall that over a year ago British automobile engineers (through the Society of Motor Manufacturers and Traders) pronounced themselves in favour of the obligatory use of headlamps on all moving vehicles at night.

Dim-dip Lamps

The Road Research Laboratory has strongly advocated an alternative scheme as being more likely to find ready acceptance from British drivers, many of whom show an extraordinary disinclination to use their headlamps—or even their sidelamps for that matter. The R.R.L. plan involves complicating the electrical system to provide a "dim-dip" stage. No extra switch position is needed because (provided the sidelamps are switched on), the dimmed and dipped head-

lamps light up automatically with the use of the ignition switch and consequently remain in action whenever the car is on the move. The usual switches provide for the alternative use of fully illuminated headlamps, both dipped and undipped.

In my view a serious disadvantage of this plan (which has been tried experimentally on a number of London taxis) is that the driver has a discretionary option on whether to use "dim-dip" or "normal-dip" headlamps. He can therefore deprive himself of a safe driving light in a badly lit suburban street by forgetfully (or deliberately) leaving the lamps in the dim-dip condition. We should be moving towards fewer alternatives and simpler driving conditions rather than adding to our difficulties. However, the R.R.L. has taken a firm stand versus the motor industry (and the City of Birmingham), and the decision now rests with the Ministry of Transport.

To make the general use of dipped headlamps tolerable it is certainly essential that car-lighting systems should be serviced more frequently and more efficiently than at present. Comparatively few garages can give an immediate check of headlamp alignment using quick and accurate equipment. Every time the R.A.C. (or some similar body) offers special local testing facilities on a "free trial" basis a high proportion of the cars tested are found to have maladjusted lamps.

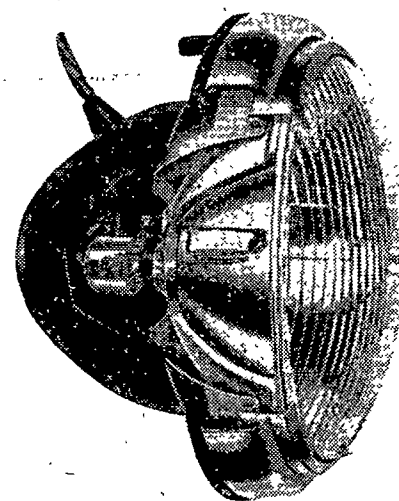
The adjustment is fairly critical and should be done with the car loaded to represent normal conditions of use. It is a serious disadvantage of the softer and more comfortable suspension systems now in vogue (even in smallish cars) that the addition of rear-seat passengers or luggage can tilt the vehicle sufficiently to dazzle oncoming drivers even though the beams are dipped. For example, if the additional load depresses the rear springs by an extra inch (2.5 cm.), leaving the front springs unaffected, the fore-and-aft trim of a typical medium-sized car will alter to an extent sufficient to lift the beam by about 12 in. (30 cm.) at a distance of 100 ft. (30 m.).

There are two ways of overcoming the difficulty. The first requires the use of an elaborate self-levelling suspension system which automatically compensates for changes of load. This is so far found only on a few relatively costly cars (such as the Rolls-Royce and some Mercedes models) but will probably become more widely used in the future. The second plan is to link the headlamps to the suspension system in such a way that their alignment relative to the road is preserved when the load changes or even when the car pitches on an undulating surface. This latter method is used in the 1968 version of the D-type Citroën Pallas model.

Pattern of Beam

The distribution of light—or pattern of the beam—depends on the spatial relation-

ship between the filament and the reflector in addition to the precise shape given to the latter part of the lamp. Consequently it is most important that reflectors and bulbs should be made and assembled with a high degree of accuracy. A bold solution to this problem is represented by the "sealed beam" unit in which a glass envelope forms both a reflecting surface and a vacuum container for the filament (Fig.). There is no separate bulb, so that the relative positions of the filament and the reflecting surface can be



A Lucas "sealed beam" headlamp in section, showing how the filament is fixed within the glass container.

closely controlled in manufacture and will remain unaltered in use. The reflecting surface is also well protected from deterioration. Unfortunately, the sealed-beam principle has not yet been applied to the rectangular type of headlamp which has latterly become a popular competitor to the circular lamp.

Four-headlamp systems have the advantage that one pair can be expressly designed to provide dipped beams and the other pair to provide driving beams. This leads to greater functional efficiency and consistency in manufacture than with normal dual-purpose lamps which use bulbs with two filaments. In the new Citroën system already mentioned the inner pair of long-range driving lamps are of the powerful quartz-iodine type and are coupled to the steering so as to turn with the vehicle. It is the outer pair of dipped lights which are self-levelling in relation to springing movements.

Earlier attempts to use steerable and self-levelling devices were unsuccessful because they did not continue to work with sufficient precision after normal wear and tear on the road. It will be interesting to see whether the resourceful Citroën engineers have surmounted this difficulty, but so far no details of the design have been released. On some American cars "seeing round corners" at night is made possible by providing two additional fixed lamps, set obliquely. These

light up automatically as a supplement to the headlamps when the steering is moved away from the straight-ahead position.

The pop-up headlamp, becoming popular for streamlined sports cars, has the slender

advantages of keeping clean when not in use and contributing to a sleek, streamlined appearance. One hopes that the mechanism is fully reliable, because under present driving conditions the transition from sidelamps to

headlamps is often an urgently important matter. If headlamps must be concealed, it seems a better plan to cover them with hinged doors, or sections of grille, so that the lamp itself remains fixed.

MEDICAL NEWS

Bicentenary of Leeds General Infirmary

On 2 October the Leeds General Infirmary celebrated the bicentenary of its foundation. The first annual report recorded that 89 in-patients and 272 outpatients were treated in the first year at a cost of £469. In 1966, more than 20,000 inpatients and nearly 700,000 outpatients were treated. The foundation stone of the present infirmary was laid in 1864, the building being completed in 1868. Now, 100 years later, a new teaching hospital and medical centre is to be built on the site of the infirmary and its satellite hospitals. With a total of 1,400 beds the new infirmary will be one of the largest hospitals in Europe. Among the events marking the bicentenary was a commemorative service in Leeds Parish Church and the opening of a new eye ward and theatre by Sir DONALD KABERRY, M.P., chairman of the board of governors.

Postgraduate Medical Education

The Central Committee on Postgraduate Medical Education (Great Britain) met on 29 September, when there was a discussion between the committee and representatives of the Ministry of Health and the Scottish Home and Health Department on the staffing structure in the hospital service in relation to service and to education and training.

Early Detection of Disease

A project to ascertain the benefits of early diagnosis and treatment of disease is being organized by the department of social medicine at St. Thomas's Hospital Medical School in collaboration with the South-east Metropolitan Regional Hospital Board and the health department of the London Borough of Bromley. It is sponsored by the Ministry of Health. Announcing the project, the Ministry says it will be carried out in a group general practice with a list of about 12,000. Initially, persons between the ages of 40 and 64 will be examined. They will be invited to undergo a series of tests and to answer a simple questionnaire. After the examination they will see their own doctor, who will have the results of the tests before him. By comparing the experience of tested and untested groups an assessment will be made of how much the medical services are used by each group and how much benefit can be derived from early diagnosis and treatment. Another aim of the project is to study ways in which the general practitioner can be given help to relieve him, as far as possible, of work other than clinical work.

Smoking Habits of Medical Students

Attitudes to smoking among medical students are not greatly influenced by their training, according to the findings of a survey conducted by the Government Social Survey for the Ministry of Health. The smoking habits of medical and non-medical students

were found to be similar, except that the incidence of smoking was lower among female medical students than among the others, and that pipe-smoking was more popular among medical students. Attempts to stop smoking, or to cut it down, were most frequent during the first year of clinical training. At this stage the proportion of smokers who thought that doctors should set an example to their patients and to the public rose to a peak. Thereafter the reaction against smoking declined. Only about half of the third-year clinical students thought that doctors should advise their patients not to smoke. The report concludes that if the antismoking campaign is to succeed more needs to be done in medical schools to discourage students from smoking. (*Medical Students' Attitudes Towards Smoking*, H.M.S.O., 25s.)

Mining Deaths Lowest Recorded

Last year 160 people were killed in mining accidents and 1,061 seriously injured. This represented an overall reduction of 11.2% on the figures for 1965. There was, however, a reduction of about 7% in the number of man-shifts worked. The accident rate—that is, the number of accidents per 100,000 man-shifts—fell from 1.31 to 1.26. Over the past four years it has fallen by about 12%. For the first time the number of men killed in haulage and transport accidents (67) exceeded those from falls of ground (60). In his report (H.M.S.O., 6s.) the Chief Inspector of Mines and Quarries notes that the number of new cases of pneumoconiosis diagnosed by the Pneumoconiosis Medical Boards has fallen considerably in recent years. "The comparison of the results obtained in 1966 [937 cases] with those five years earlier [2,768 cases] indicates that there is every reason to hope that dust suppression measures are beginning to have their effect."

Progress in Smoke Control

Premises in smoke control areas in Great Britain now number more than 3 million. The Greater London region continues to lead, with over 61% of its premises covered by orders. Next come Yorkshire and Humberside (35%) and the North-West (34%). A table in the new year book of the National Council for Clean Air, which gives these figures, shows that domestic fires were responsible for the emission of 900,000 tons of the 1,100,000 tons of smoke that polluted the atmosphere in 1965.

Chelmsford Medical Society

At the annual general meeting of the Chelmsford Medical Society the following officers were elected: *president*, Dr. K. A. D. TURK; *treasurer*, Dr. K. R. ABERDOUR; *secretaries*, Dr. K. H. NICKOL and Mr. G. L. S. RANKIN.

People in the News

► Professor K. W. DONALD has been appointed a physician to the Queen in Scotland in place of Professor Sir EDWARD J. WAYNE, who has resigned.

► Professor MARTIN ROTH has been elected to the Mayne Guest Professorship in the University of Queensland, Australia. He will be attached to the department of psychological medicine and will take up his duties at the end of March 1968.

► Major-General J. A. D. JOHNSTON has been appointed honorary physician to the Queen.

► Colonel CAMERON WEYMES has been appointed honorary surgeon to the Queen.

► Professor A. L. D'ABREU has been appointed a deputy lieutenant for the County of Warwick.

► Sir JOHN ECCLES, F.R.S., is to join the faculty of health sciences at the State University of New York at Buffalo in July 1968.

News in Brief

PRINCESS ALEXANDRA has agreed to become the patron of the National Kidney Research Fund.

The Medical Research Council has set up a powered limbs research unit at West Hendon Hospital, London, under the direction of Dr. A. B. KINNIER WILSON.

Grants and Awards

Dr. WINIFRED M. WATKINS, Ph.D., and Professor W. T. J. MORGAN, F.R.S., of the Lister Institute of Preventive Medicine, London, will share the 1967 Karl Landsteiner memorial award of the American Association of Blood Banks.

Among the recipients of the third annual Barraquer Award is Mr. PETER CHOYCE, F.R.C.S.

Recent Publications

Scottish Health Service Studies: *Cancer Registration, 1959-61*, issued by the Scottish Home and Health Department. A review of the organization of cancer registration in Scotland is being undertaken.

The Mental Hospital Library, by Mr. D. Boorer, R.M.N., deputy editor of the *British Hospital Journal and Social Service Review*, is based on nearly two years' experience of working as librarian at Moorhaven Hospital, Ivybridge, Devon. The pamphlet is published by the Library Association, 7 Ridgmount Street, Store Street, London W.C.1, price 10s. (7s. 6d. to members of the Library Association).

Coming Events

Cambridge University School of Clinical Research and Postgraduate Medical Teaching.—Postgraduate courses for general practitioners, 1 October 1967 to 31 July 1968. Details from Secretary, Cambridge University Medical School, Tennis Court Road, Cambridge.

Oxford Seminar on Designing for the Disabled.—20 October, College of Technology, Oxford. Details from Mr. J. R. REGAN, Assistant Regional Architect of the Oxford Regional Hospital Board (Oxford 64861).

Ipswich Postgraduate Medical Centre.—Official opening by Sir GEORGE PICKERING at the Ipswich and East Suffolk Hospital, Anglesea Road Wing, 24 October, 2.15 p.m.

Medical Society for the Study of Venereal Diseases.—Meeting, "Recruitment to the Speciality of Venereology," 27 October, 7 p.m. for 7.30 p.m., 11 Chandos Street, London W.1.

Association of Clinical Biochemists: Southern Region.—Symposium, "Chemical Pathology in Relation to Neuropathology," 28 October, 10 a.m., National Hospital, Queen Square, London W.C.1. Details from Dr. V. MARKS, Area Laboratory, West Park Hospital, Epsom, Surrey.

Medical Practitioners Union.—Medical World conference, "The Future of the National Health Service," 29 October, 10 a.m. to 4.30 p.m., Queen Mary College, Mile End Road, London E.1. The chairman will be Sir MAX ROSENHEIM. Admission is free, but tickets for luncheon (16s.) must be obtained from the Conference Secretary, M.P.U., 55-56 Russell Square, London W.C.1.

Peripheral Circulation Group.—Symposium, "Peripheral Circulatory Assessment in Human Arterial Disease," 31 October, 8 p.m., Royal Infirmary, Glasgow.

Institution of Mechanical Engineers.—Symposium on basic problems of artificial prehension, movement, and control of artificial limbs, 31 October to 1 November 1968. Details from Mr. E. P. DAVIES, Groups Department, Institution of Mechanical Engineers, 1 Birdcage Walk, Westminster, London S.W.1.

Queen's Institute of District Nursing: Welsh Federation.—Conference, "Care and Rehabilitation of the Elderly," 1-2 November, Sherman Conference Hall, Ty Maeth, King George V, Drive East, Cardiff. Fee £1 15s. Details from General Secretary, Q.I.D.N., 57 Lower Belgrave Street, London S.W.1.

King Edward's Hospital Fund for London.—Conference, "Damage in Hospitals," 2 November, Hospital Centre, 24 Nutford Place, London W.1. Details from the Hospital Centre.

Share-Jones Lecture in Veterinary Anatomy.—"Adventures in Neuroendocrinology," by Professor B. A. CROSS, 2 November, 6.30 p.m., Royal Veterinary College, Royal College Street, Camden Town, London N.W.1. Those wishing to attend should notify the secretary of the college.

Institute of Ophthalmology.—Open day 2 November. Admission by ticket, obtainable from the Secretary, Institute of Ophthalmology, Judd Street, London W.C.1.

Glasgow Postgraduate Medical Board.—Conference, "Ischaemic Heart Disease," 9-10 November, Royal College of Physicians and Surgeons of Glasgow. For details see advertisement on p. xxxix.

Society for Psychosomatic Research.—Conference, "Disorders of Sex and Reproduction—Psychosomatic Aspects," 10-11 November, Royal College of Physicians,

London. Details from Conference Secretary, Dr. C. J. LUCAS, 17 Gordon Street, London W.C.1.

Society for Medical and Dental Hypnosis: Midlands Branch.—Intermediate course in "Techniques and Applications of Hypnosis," 11-12 November, Grand Hotel, Colemore Row, Birmingham. The course registration fee is £10 10s. and applications should be made to Mrs. S. NEWBERRY, 1 White House Green, Solihull, Warwicks.

Royal Northern Hospital.—Symposium on clinical immunology for general practitioners, 16-17 November, Royal Northern Hospital, London N.7.

London University.—Course of four Heath Clark lectures, "Perspectives in Health Planning," by Dr. A. ENGEL (Sweden), 14, 16, 20, and 21 November, 5.30 p.m., London School of Hygiene and Tropical Medicine, Keppel Street, London W.C.1. Admission free, without ticket.

Queen's Institute of District Nursing: Home Counties Federation.—Conference, "The Changing Scene in Domiciliary Nursing," 17 November, Assembly Hall, Royal Commonwealth Society, Northumberland Avenue, London W.C.2. Fee £1 12s. 6d. (including refreshments). Details from General Secretary, Q.I.D.N., 57 Lower Belgrave Street, London S.W.1.

Institute of Child Health.—Seventh course on "Problems of Developmental Neurophysiology and E.E.G. in Paediatrics," 16, 17, 18 November, Hospital for Sick Children, Great Ormond Street, London W.C. Details from the Dean, Institute of Child Health, 30 Guilford Street, London W.C.1.

Sussex Postgraduate Medical Centre.—Symposium on chronic renal disease, 18 November. For programme and admission ticket apply to Secretary of Centre, Brighton General Hospital, Elm Grove, Brighton 7.

Royal College of General Practitioners.—James Mackenzie lecture by Dr. RONALD GIBSON, "Lucerna Pedibus Meis," 18 November, 11 a.m., followed at 2 p.m. by annual general meeting, B.M.A. House, London W.C.1. Annual symposium, "Combined Operations—Medicine, Science, and Humanism," 19 November, 9.15 a.m., Wellcome Building, Euston Road, London N.W.1.

University of the West Indies.—Fourth annual workshop in otolaryngology, 14-20 January 1968. Applications to Dr. K. A. MCNEILL, University of West Indies, Kingston, Jamaica.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 16 October

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.
HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, 7 p.m., presidential address by Dr. C. C. Chesterman: Tropical Trail.
INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Dr. J. W. Pierce: The Oesophagus.
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., combined staff consultation clinical meeting.
INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 11.15 a.m., discussion: Contracted Pelvis. Speakers, Mr. J. M. Brudenell, Mr. J. M. Holmes.●

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. J. M. Talbot: Pathology of Trauma—Wound Infection; 6.30 p.m., Dr. G. B. Hill: Design of Clinical Trials.●
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Dr. O. H. Belam: Some Hazards of Surgery and Anaesthesia in Patients under Treatment with Modern Drugs. (2) 6.30 p.m., Mr. R. B. Zachary: Obstructive Lesions of the Alimentary Tract in the Newborn.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. M. Turner-Warwick: Rheumatoid Factors and Lung Disease.

Tuesday, 17 October

DOLTON AND DISTRICT MEDICAL SOCIETY.—At Gymnasium, Bolton Royal Infirmary, 8.15 p.m., clinical meeting.
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Beveridge Hall, Senate House, London University, 5.30 p.m., Lord Florey, O.M., F.R.S.: Elements of the Vascular System.
CAMBRIDGE MEDICAL SOCIETY.—At Blue Room, Dorothy Restaurant, 8.30 p.m., jointly with University Medical Society, debate by Dr. M. H. Pappworth (for) and Professor I. H. Mills (against): This House Believes that Experimentation in Patients has Reached an Unacceptable Level.
HORDER MEMORIAL TRUST.—At Physiology Lecture Theatre, St. Bartholomew's Hospital Medical College, 5 p.m., Horder memorial lecture by Professor D. A. K. Black: Chronic Renal Failure.
NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., Dr. R. Isaac: The Happy Puppet Syndrome (case and film).
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Mr. H. Shaw: Diagnosis and Management of Tumours of the Larynx and Pharynx. (2) 6.30 p.m., Dr. Deborah Doniach: Auto-immune Disorders in relation to Surgery.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. A. G. Cox: Surgery in Peptic Ulcer.
WHIPPS CROSS HOSPITAL.—At Medical Education Centre, 1 p.m., clinical meeting.

Wednesday, 18 October

B.B.C. 1 TELEVISION.—11.15 p.m. (approx.), medicine today: Rheumatoid Arthritis. (Sponsored by A.S.M.E.)
CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. L. Szur: Principles of Dermatological Radiotherapy—I.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. Lloyd Rusby: Extrapulmonary Manifestations of Carcinoma of the Bronchus.
INSTITUTE OF UROLOGY.—5 p.m., Mr. J. P. Williams: Surgery of the Ureter.
KENNEDY INSTITUTE OF RHEUMATOLOGY.—At rear of West London Hospital, 5 p.m., Dr. J. Hobbs: Immunoglobulins.
MANCHESTER MEDICAL SOCIETY: Section of Paediatrics.—At Large Anatomy Theatre, Manchester University Medical School, 5 p.m., Dr. M. C. Joseph: The Facies in Down's Syndrome—A Study by Measurement.
OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Dr. J. Last: Career Aspirations and Training of Young British Doctors.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Professor R. Barnes: Injuries of the Cervical Spine. (2) 6.30 p.m., Mr. V. Logue: Neurosurgical Relief of Pain.
ROYAL FREE HOSPITAL.—5.15 p.m., Dr. I. Chanarin: Vitamin B₁₂ and Folate Metabolism in Man.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conferences by Dr. G. Neale: Steatorrhoea; Dr. D. J. Evans: Liver Failure. (2) 2 p.m., Dr. T. R. E. Pilkington: Ketosis.
STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. Margaret Walshe: Awful Warnings. (2) 6 p.m., Dr. B. G. Dooley: Industrial Poisons.
WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Professor A. W. Woodruff: Some Problems Concerning Tropical Disease in Britain.
WHIPPS CROSS HOSPITAL.—At Medical Education Centre, (1) course for general practitioners, 2 p.m., Mr. J. S. Conway: Causes of Blindness; 3 p.m., Dr. A. A. G. Lewis: Recent Developments in the Diagnosis and Management of Diabetes. (2) 8.30 p.m., Dr. R. M. Mason: Gout and Pseudo-gout.
WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY.—At Staff Recreation Hall, 8.30 p.m., clinical quiz by Dr. D. Geraint James.

Thursday, 19 October

ABERDEEN UNIVERSITY FACULTY OF MEDICINE.—At Large Lecture Theatre, University Medical Buildings, Foresterhill, 5 p.m., Dr. J. Williamson: Old Age—a Positive Approach.
ADDENBROOKE'S HOSPITAL.—At M.R.C. Lecture Theatre, New Addenbrooke's Hospital, 8.30 p.m., Dr. J. V. Farman: Circulatory Effects of Atropine and Gallamine.
BRITISH INSTITUTE OF RADIOLOGY.—6 p.m., discussion group; 8 p.m., presidential address by Dr. R. D. Hoare.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Professor E. Jean Hanson, F.R.S.: Molecular Structure of Muscles in Relation to Mechanism of Contraction.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—Queen Charlotte's Hospital, 2 p.m., Professor J. K. Russell: Diagnosis of Placenta Praevia.

LEEDS UNIVERSITY FACULTY OF MEDICINE.—At Rupert Beckett Lecture Theatre, the University, 3.15 p.m., inaugural lecture by Sir Geoffrey Vickers, V.C.: What to Expect of a Doctor.

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University Medical School, 4.30 p.m., presidential address by Mr. D. S. Poole Wilson: Urology—the Past, the Present, and the Future.

MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Theatre B, Roscoe Building, Brunswick Street, 8 p.m., presidential address by Dr. J. Raventos: Anaesthetics and Research.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Mr. D. S. M. Barlow: Management of Chest Injuries. (2) 6.30 p.m., Mr. J. Tulloch Brown: Fractures of the Upper End of the Femur.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. W. H. Stephenson: Post-irradiation Fractures.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., presidential address by Professor P. C. C. Garnham, F.R.S.: Reflections on Laveran, Marchiafava, Golgi, Koch, and Danilewsky after 60 years.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Mr. F. E. Loeffler: Induction of Ovulation.

Friday, 20 October

BIOLOGICAL ENGINEERING SOCIETY.—At Botany Theatre, University College, Gower Street, London W.C.1, 6 p.m., Woolmer memorial lecture by Professor A. R. Huxley, F.R.S.: Forgetting and Rediscovery in Physiology.

BRITISH INSTITUTE OF RADIOLOGY.—2 p.m., radiobiology meeting.

INSTITUTE OF CHILD HEALTH.—At Kennedy Lecture Theatre, 5.30 p.m., Professor J. Tizard: Problems of Education of Handicapped Children.

KENT POSTGRADUATE MEDICAL CENTRE AT CANTERBURY.—At Kent and Canterbury Hospital, 8.30 p.m., Dr. P. J. Lawther: Air Pollution and Health.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—8.15 p.m., Dr. L. C. Payne: Automation in Medicine.

LONDON SOCIETY OF FAMILY PLANNING DOCTORS.—At West Hall, Royal Society of Medicine, 8.15 p.m., Mr. P. L. C. Digory: Complications of I.U.D.s.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5.15 p.m., Mr. L. Kessel: Management of Fractures and Dislocations in the region of the Shoulder Joint. (2) 6.30 p.m., Mr. S. R. Mawson: Management of Infections of the Mastoid Process.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Dr. J. A. Dossett: A Simplified Nomenclature of Breast Disease. (2) 11.30 a.m., Mr. J. I.

Burn: clinicopathological conference (Breasts). (3) 4 p.m., Dr. Wilfrid Oakley: Some Complications of Diabetes and their Treatment.

Saturday, 21 October

ABORTION LAW REFORM ASSOCIATION.—At Kensington Central Public Library, Phillimore Walk, 7 p.m., annual public meeting: Abortion Bill—Will it Work?

Appointments

BIRMINGHAM REGIONAL HOSPITAL BOARD.—J. W. H. Foy, M.R.C.S., D.M.R.E. (whole-time consultant radiologist to the St. George's and Stafford groups); I. S. Chatha, M.B., F.R.C.S., D.O. (part-time consultant ophthalmologist to the Wolverhampton and Lichfield, Sutton Coldfield, and Tamworth groups); W. M. Park, M.B., D.M.R.D. (whole-time consultant radiologist to the Shrewsbury group and the Robert Jones and Agnes Hunt Orthopaedic Hospital).

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—R. D. Jones, M.B., M.R.C.P.Ed., D.C.H. (consultant in paediatrics, Norfolk and Norwich area); R. G. Gibbs, M.B., M.R.C.P. (consultant physician, Norwich, Lowestoft, and Great Yarmouth Hospital group).

MANCHESTER REGIONAL HOSPITAL BOARD.—J. S. S. Stewart, M.B., F.R.C.S. (whole-time or maximum part-time consultant surgeon, Wigan and Leigh group of hospitals); D. H. G. Cowie, M.B., M.R.C.O.G. (whole-time or maximum part-time consultant obstetrician and gynaecologist, West Manchester group of hospitals); K. J. Rees, M.B., M.R.C.O.G. (whole-time or maximum part-time consultant obstetrician and gynaecologist, Stockport and Buxton group of hospitals); Edith M. Varley, B.M., F.F.A.R.C.S. (whole-time or maximum part-time consultant anaesthetist, South Manchester group of hospitals).

MINISTRY OF DEFENCE.—R. A. Kemp Harper, M.D., F.R.C.P., F.F.R. (consulting radiologist to the Royal Navy).

MINISTRY OF OVERSEAS DEVELOPMENT.—Catherine A. Ryan, M.B., F.F.A.R.C.S., D.A. (anaesthetist with the British Paediatric Unit of the Children's Hospital in Saigon).

NEWCASTLE REGIONAL HOSPITAL BOARD.—J. G. Crumney, F.R.C.S. (consultant in orthopaedic surgery, West Cumberland); C. H. McCulloch, M.B., F.F.A.R.C.S. (consultant in anaesthetics, Gateshead); F. Clark, M.B., M.R.C.P. (consultant in general medicine, Newcastle); D. Smith, M.B., M.C.Path. (consultant in pathology, West Cumberland); R. G. Gold, M.B., M.R.C.P., M.R.A.C.P. (consultant in cardiology, Newcastle); E. Holmes, M.B., D.A. (consultant in anaesthetics, Sunderland); F. Fleming, M.B., F.R.C.S., D.L.O. (consultant in otolaryngology, South Tyneside); J. C. Linn, M.B., D.M.R.D. (consultant in radiology, Sunderland).

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—J. Q. Mathias, M.D., M.R.C.P. (part-time

consultant physician in general medicine to Tottenham group of hospitals).

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—P. M. Jackson, M.B., D.P.M. (consultant psychiatrist, Devon and Exeter clinical area (Royal Western Counties)); D. E. P. Jones, B.M., F.R.C.S., D.O. (consultant ophthalmologist, Bath clinical area); N. Seymour, M.B., F.R.C.S. (consultant orthopaedic surgeon, Plymouth clinical area); P. D. Mulcahy, M.D., M.R.C.P. (consultant physician, Plymouth clinical area); N. M. C. Mayne, M.D., M.R.C.P. (consultant general physician, North Gloucestershire clinical area).

Universities and Colleges

LONDON

M.D.—E. H. Burgess, Lorna I. M. MacLay.
M.S.—O. H. Shaheen, M.R. H. Ashken.
M.Phil.—In the Faculty of Medicine: Margaret D. Walker.
Ph.D.—In the Faculty of Medicine: R. J. Anderson, D. K. Brooks, M. N. Cauchi, G. G. S. Collins, J. W. Freston, Francesco B. Giannelli, S. A. H. Khalil.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

Appointment.—L. J. Bruce Chwatt, M.D., M.P.H., D.T.M.&H. (senior lecturer (technical assistance) in the Ross Institute of Tropical Hygiene).

BIRMINGHAM

Appointments.—Dr. A. S. Abraham (research fellow in the Department of Medicine); Dr. R. A. Thompson (temporary lecturer in the Department of Experimental Pathology), Dr. M. J. McCulloch (lecturer in child psychiatry, Department of Psychiatry).

LIVERPOOL

Appointments.—Dr. R. F. Roos (lecturer in obstetrics); Dr. J. T. Quinn and Dr. J. Price (lecturers in psychiatry).

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

On 29 September the following were admitted Fellows *qua* Surgeon: A. F. A. Fattah, T. Bhaduri, J. Dudgeon, J. N. Gangopadhyay, E. S. Glen, S. E. P. Miller, J. C. Mustardé; Members *qua* Physician: A. H. Barlas, W. B. Doig, T. Fyfe, M. A. Halim, M. H. Husain, A. F. M. A. Islam, Ida J. McFadyen, T. Myint, R. L. Willing.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council of the College held on 30 September the following lecturers were appointed for 1967: Dr. R. W. Barter (Green-Armytage Anglo-American lecture); Mr. F. E. Stabler (William Meredith Fletcher Shaw lecture); Dr. W. G. Cosbie (J. Y. Simpson Orator).

The following were admitted to the Membership *in absentia*:

I. A. W. Hamdy, F. S. Lynes, R. G. Selvanayagam.

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Treatment of Lead Poisoning: A Comparison Between the Effects of Sodium Calciumedetate and Penicillamine Administered Orally and Intravenously. Stig Selander.

Control of Lead Workers by Determination of Urinary δ -Aminolaevulinic Acid. Kim Cramér and Stig Selander.

A Dry Ashing Method for the Determination of Blood Lead Using Cathode Ray Polarography: Comparison with a Wet Ashing Technique. A. A. Cernik.

A Simplified Procedure for the Determination of Urinary δ -Aminolaevulinic Acid. M. K. Williams and J. D. Few.

Auditory and Subjective Effects of Airborne Noise from Industrial Ultrasonic Sources. W. I. Acton and M. B. Carson.

Incorporation of Uranium. I. Distribution of Intravenously and Intraperitoneally Injected Uranium. G. Walinder, L. Hammarström, and U. Billadelle.

Incorporation of Uranium. II. Distribution of Uranium Absorbed Through the Lungs and the Skin. G. Walinder, B. Fries, and U. Billadelle.

Metabolism of Ethylene Glycol Dinitrate and its Influence on the Blood Pressure of the Rat. D. G. Clark and M. H. Litchfield.

Tryptophan Content of the Serum Albumin of Normal and of Cadmium-poisoned Monkeys. J. E. Kench and Elizabeth M. Sutherland.

A Study of the Skin Absorption of Ethylbenzene in Man. Tadeusz Dutkiewicz and Halina Tyras.

Miscellanea:

Lead Poisoning in Jewellery Enamellers. R. Fothergill, M. D. Kipling, and A. B. Weber.

Book Reviews. Index.

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ABSTRACTS OF WORLD MEDICINE

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 21 OCTOBER 1967

Pointers

Hazards of Therapy: Carcinogenic action of new therapeutic agents cannot be predicted from their chemical structure, and co-operation between laboratory workers and clinicians is of paramount importance in avoiding this potential danger (p. 129).

Acrylamide Poisoning: Six cases in Britain. Clinically characterized by peripheral neuropathy and a midbrain disturbance. Prevention is relatively easy (p. 134). Leader at p. 125.

Fructose Intolerance: Genetically determined metabolic disorder which may present in infancy, childhood, or adult life. It is prevented by excluding fructose from the diet (p. 138).

Pulmonary Valve Closure: Delay, causing splitting of second heart sound, observed in eight patients with renal failure. Splitting disappeared after correction of oedema. It seems a useful sign of fluid overload (p. 141).

Role of Glucagon: Blood glucose levels affected more by its glycogenolytic action than by its insulin release action (p. 145).

Coronary Occlusion and the Thyroid: Blood fibrinolytic enzyme system is probably influenced by thyroid hormones (p. 147).

Fat Embolism: Lipaemia found in series of patients followed after trauma, one-third of whom had fat embolism. Use of clofibrate in a second series reduced lipaemia, suggesting that the cause of embolism may be metabolic rather than traumatic (p. 149).

Behçet's Syndrome: Occurrence of aortic aneurysms emphasizes the general nature of this syndrome (p. 152).

Case Reports: Hepatic murmurs and anaemia (p. 154). Jaundice after carbamazepine (p. 155). Myelomatosis diagnosed by electrophoresis of C.S.F. (p. 156).

Spare-part Surgery: Recent advances in the use of inert, dead, or living foreign materials to replace or repair diseased or missing organs (p. 157).

Paediatric Neurology: Management of children with progressive neurological handicap (p. 162).

L.S.D.: Risk of foetal abnormality (p. 124).

Gastritis: Description of the two distinct and probably unrelated types and their clinical significance (p. 164).

Scottish Council: Meeting (*Supplement*, p. 17).

"Better Medical Care": Edinburgh Conference (*Supplement*, p. 18).

Overseas Affairs: Service overseas discussed (*Supplement*, p. 20).

Consultant Merit Awards: Results of ballot (*Supplement*, p. 22). Leader at p. 128.

Medical Management Services: B.M.A. Council's resolutions (*Supplement*, p. 23).

Teaching the Behavioural Sciences

One of the most persistent criticisms of the medical curriculum has been that it paid too little attention to the teaching of psychiatry and of the psychological aspects of health and disease. As late as 1960 an international survey submitted to the World Health Organization could state that "in the United Kingdom and British Commonwealth psychiatric teaching in general is still hardly a legitimate part of the medical curriculum, in spite of the repeated requests for improvement, which have come from both faculty and undergraduates."¹

There has been no lack of proposals how to incorporate into medical education the great advances in the study of normal and abnormal behaviour as well as in the treatment of mental disorders. The memoranda submitted to the General Medical Council by the Royal Medico-Psychological Association² in 1965 and the British Medical Association³ in 1966 both emphasized the need for the teaching of behavioural sciences in the preclinical curriculum side by side with anatomy and physiology. A W.H.O. Expert Committee had made similar recommendations in 1961.⁴ Possibly the first teaching programme in Britain based on these principles was the "Sheffield Plan,"⁵ introduced from 1956 onwards. Psychiatric teaching in the clinical curriculum there was said to have two tasks: to bring home to the student the ubiquity of psychiatric problems, and to enable him to acquire some familiarity with psychiatric illness comparable to his knowledge of physical illness.

The objectives of psychiatric education and students' interest in psychiatry were discussed in a series of articles in an educational number of the *B.M.J.* four years ago⁶⁻⁹ as well as elsewhere. Has anything come of this campaign? Surprisingly, more than might be expected from the usually slow pace of change in medical education. Several new chairs of psychiatry have been established in this country during the last few years, and in the 1967 Recommendations as to Basic Medical Education of the General Medical Council¹⁰ psychiatry has for the first time been given the status of a major clinical subject. The need for the study of human structure and function being combined with the study of human behaviour has been stated more explicitly than before. A clinical clerkship in psychiatry with obligatory residence in hospital has been declared essential. The total period of clinical clerkships recommended is "not less than 18 months," an extension by three months over the 1967 Recommendations. In some medical schools a three-months clerkship in psychiatry is being introduced.

The incorporation of a new major subject into both the preclinical and the clinical course will require more than minor readjustments here and there. The General Medical Council Recommendations cannot be implemented without substantial changes in the curriculum. The Advisory Committee of the new Nottingham Medical School¹¹ has wholeheartedly adopted the new policies and recommended that the teaching of the behavioural sciences should run as a thread throughout the

preclinical and clinical courses. It should be the responsibility of a subcommittee of the curriculum committee chaired by the professor of psychiatry, with representatives from the departments of psychology, physiology, the social sciences, and community health. It will be interesting to watch how Nottingham, unfettered by established traditions and vested interests, will tackle this task. Here is a rare opportunity for starting something new and exciting.

Now that an official policy on the teaching of the behavioural sciences and psychiatry has been laid down, the problem of what to teach and how to teach it is in the forefront of discussions. Deeply established attitudes in the teachers, as in anyone, tend to influence their predilections. Psychiatrists are, like other doctors, the products of their medical education, which taught them mainly to recognize and to treat physical diseases. H. J. Walton and J. Drewery¹² have shown that there are several distinct types of psychiatric teachers differing in their preferences for the subjects to be emphasized in the teaching of medical students. A. C. Woodmansey,¹³ for instance, wants the teaching to be focused on child and family psychiatry because it looms large in general practice and is fundamental to prevention. Such teaching, he argues, requires the student to have first-hand experience in diagnostic-therapeutic interviews and to be taught the principles of psychotherapeutic management. Similar views were expressed by M. Balint¹⁴ and R. F. Tredgold¹⁵ some years ago. Other teachers emphasize the descriptive aspects of mental disorders. Such diversity of approaches is inevitable and can be stimulating for the student provided no one approach monopolizes the whole of the teaching programme.

Differences in teachers' and students' attitudes to the organic and psychological aspects and causes of behaviour are unlikely to be due to their medical education only. Personality factors play an important part. This has been shown by Walton, Drewery, and G. M. Carstairs⁹ in a study of students' interests in social and emotional factors of illness. Walton¹⁶ has also studied the effects of different teaching methods. He set out to test experimentally the relative merits of teaching by lecture and seminar as methods of psychiatric instruction. Contrary to expectation, students taught by lectures did not gain more factual knowledge than students taught in seminar groups. In all other respects which mattered educationally, seminar group teaching proved superior. So students will in future be able to support their demands for fewer lectures and more seminars with experimental evidence—unless something is done about the quality of lecturing which should change students' attitudes towards

it. Psychiatric lectures came out with credit in another Scottish medical school when a multiple-choice examination was used as the measuring instrument.¹⁷ In a recent American study¹⁸ the response of newly graduated doctors to their psychiatric training received in medical school was assessed with the help of a questionnaire, but only 110 of 329 interns and residents replied. Of these, 20% considered psychiatry the poorest taught subject and 19% the least learned subject. Only surgery had a poorer rating. Though the results of this study are difficult to interpret, if only because of the poor response to the inquiry, they at least show that psychiatry was in good company.

L.S.D. and Chromosomes

Despite the use of lysergic acid diethylamide (L.S.D.) both for therapy and for illicit self-administration our knowledge of its toxic effects is incomplete. In addition to the drug's acute and unpredictable hallucinogenic actions¹—leading in some instances to permanent mental damage—it has now been suggested that L.S.D. has powerful cytogenetic effects. The great majority of people who take the drug are young, so that information on this action is needed with special urgency. Is L.S.D. as dangerous as thalidomide, and, if so, what is the evidence?

The first reports of genetic effects appeared earlier this year in *Science*. M. M. Cohen and his co-workers² in Buffalo added L.S.D. to cultured human lymphocytes in doses varying from 100 µg./ml. to as little as 0.001 µg./ml. for periods varying from 4 to 48 hours. The doses of 100 and 50 µg./ml. killed the cells and arrested mitoses. All other treatments (with the exception of that with 0.001 µg./ml. for four hours) resulted in at least a twofold increase in chromosome breakage compared with controls. The types of chromosome aberrations seen included dicentric and acentric fragments, chromatid exchanges, and chromatid breaks. Cohen's team showed similar damage to chromosomes in a patient who had been given L.S.D. 15 times between 1960 and 1966 in doses varying from 80 to 200 µg. The study was carried out eight months after the last treatment.

More recently workers from Oregon³ have found similar chromosome damage in eight users of L.S.D. who had received between 4 and 200 doses with a mean estimated dose of between 200 and 600 µg. Again, chromosome and chromatid breaks and exchanges were seen. In two users there were repeated findings of a chromosome resembling the Philadelphia (Ph¹) chromosome seen in cells of patients with chronic myeloid leukaemia.⁴ L.S.D. has also been shown to cause abortion, stillbirth, congenital malformation, and reduced litter size in rats injected with the drug early in pregnancy.⁵ The same study showed that some of the surviving progeny developed less well than did controls.

Much more work is needed to study the effects of L.S.D. on the chromosomes and on mutations, as well as to assess its teratogenic danger. At this stage, however, it can be stated with certainty that L.S.D., as well as being a potential risk

¹ Wld Hlth Org. Publ. Hlth Pap., No. 9, 1961.

² Royal Medico-Psychological Association. Memorandum on Medical Education submitted to the General Medical Council, 1965. London.

³ *Brit. med. J. Suppl.*, 1966, 1, 116.

⁴ *Wld Hlth Org. techn. Rep. Ser.*, No. 208, 1961.

⁵ Stengel, E., *Lancet*, 1961, 2, 418.

⁶ *Brit. med. J.*, 1963, 2, 575.

⁷ Hill, D., *ibid.*, 1963, 2, 581.

⁸ Ellis, J., *ibid.*, 1963, 2, 585.

⁹ Walton, H. J., Drewery, J., and Carstairs, G. M., *ibid.*, 1963, 2, 588.

¹⁰ General Medical Council. Recommendations as to Basic Medical Education. 1967.

¹¹ University of Nottingham. Report of the Medical School Advisory Committee. 1965. Nottingham.

¹² Walton, H. J., and Drewery, J., *Brit. J. Psychiat.*, 1966, 112, 839.

¹³ Woodmansey, A. C., *Brit. J. med. Educ.*, 1967, 1, 183.

¹⁴ Balint, M., *Lancet*, 1961, 2, 1051.

¹⁵ Tredgold, R. F., *ibid.*, 1962, 1, 1344.

¹⁶ Walton, H. J., An experimental study of effects on medical students of three methods of teaching psychiatry. Ph.D. thesis, 1966. Edinburgh.

¹⁷ Ingram, I. M., Mowbray, R. M., and Drewery, J., *Lancet*, 1961, 2, 358.

¹⁸ Castelnuevo-Tedesco, P., *Arch. gen. Psychiat.*, 1967, 16, 668.

¹ *Brit. med. J.*, 1966, 1, 1495.

² Cohen, M. M., Marinello, M. J., and Back, N., *Science*, 1967, 155, 1417.

³ Irwin, S., and Egozcue, J., *ibid.*, 1967, 157, 313.

⁴ *Brit. med. J.*, 1966, 2, 719.

⁵ Alexander, G. J., Miles, B. E., Gold, G. M., and Alexander, R. B., *Science*, 1967, 157, 459.

to the mind of the user, may also cause chromosomal abnormalities, foetal malformations, and possibly leukaemia.

These reports raise the question whether the screening of drugs introduced therapeutically or illegally is yet adequate. Is sufficient care being taken with a new drug to determine not only its teratogenic potential but also its potentialities as a chromosome-breaking agent and mutagen? In-vitro techniques are now sufficiently developed for these tests to be carried out. How many drugs in use today have similar effects to L.S.D. and how many have been tested?

Getting on Their Nerves

It has recently been pointed out that about half of the cases of peripheral neuritis seen by the neurologist are of unknown aetiology.¹ Drugs and poisons that may give rise to a neuropathy range from isoniazid prescribed by doctors to podophyllin (American mandrake) sold by herbalists to young women suffering from amenorrhoea.² Lead and arsenic are well known as occasional causes of peripheral neuritis. Now an article by Drs. T. O. Garland and M. W. H. Patterson in the *B.M.J.* this week at page 134 draws attention to another cause of peripheral neuropathy with probable signs of central disturbances.

Acrylamide is a white crystalline solid with no significant volatility. As a biologically harmless polymer it is familiar to engineers and biochemists. The former waterproof soils with it so that tunnels may be constructed under rivers and mines sunk through water tables; biochemists use small quantities to separate proteins. In another form the polymer is used to flocculate particles so that, for example, the same water may wash successive heaps of coal. The users of the polymer are safe and so are those who make the polymer from acrylamide under reasonably good hygienic conditions. However, when the men handling the white acrylamide powder in large bags work under poor conditions where they cannot carry out simple measures of personal hygiene, an insidious condition can develop which neither they nor their family doctors may recognize as being a result of the work they are doing. Indeed, one case of acrylamide poisoning was recognized by Garland and Patterson only in a work-place as they watched the man trying to open a bag with his knife.

That work with acrylamide might produce a neuropathy had been suggested by the first scientific study of the compound by A. S. Kuperman.³ He drew attention to its extraordinary cumulative action, for in cats it could produce a similar condition whether it was given as a single dose of 50 mg./kg. body weight or 50 daily doses of 1 mg./kg. This chronic cumulative effect has since been shown to occur in other species.^{4, 5} Detailed studies of poisoned rats have shown the lesion to be a "dying back" process similar to that discussed by J. B. Cavanagh,⁶ and it is the large-diameter motor fibres that appear to be the most sensitive to the toxic effect of acrylamide.⁵ In rats doses spread over days or even weeks could eventually produce clinical evidence of neurological

damage.⁵ Fortunately in man, as in animals, the condition is slowly reversible after exposure ceases, but it is not yet possible to say whether recovery will be complete in severely affected patients. While there is no information yet on the biochemical disturbances which this relatively simple compound produces in the nervous system, it seems likely that its mode of action will be studied in the hope that more will be learnt about the metabolic processes essential to the maintenance of healthy neurones.

If ever there was good experimental evidence to warn users that a substance might be a chronic cumulative poison, the case of acrylamide seems outstanding. Perhaps the principal manufacturers believed that everyone would use it with the care they had exercised in making it after they had encountered a few cases among their workers. Yet, notoriously with chemical poisoning, it is the user and not the maker who is liable to meet trouble. Garland and Patterson conclude that acrylamide poisoning "is a relatively easy hazard to contain." Not only have some users failed to contain the hazard but neither do they seem to have appreciated that the disability suffered by some of their employees handling the substance had resulted from exposure to it.

The immediate lesson of Garland and Patterson's report is that doctors should never fail to make detailed inquiries into the occupation of their patients who present with unusual illnesses, though clearly many cases of illness (for example, neuritis or leukaemia) that may be related to a man's work are not necessarily so. The point about acrylamide poisoning is that the clinical course is unusual compared, for instance, with the Guillain-Barré type of peripheral neuropathy.

Acrylamide poisoning has been seen in the U.S.A., and published accounts, referred to by Garland and Patterson, are available from Japan and Canada as well as Great Britain now. The main lesson to be learnt is that simple hygiene is essential in every chemical plant. In most cases this is all that is needed to prevent poisoning. When so much attention is paid to the establishment of magical figures known as M.A.C.s (maximum allowable concentrations) for atmospheric contaminants, surely employers in this country, which led the Industrial Revolution, might pioneer the Industrial Safety Revolution by providing the means and encouraging the discipline necessary for the protection of employees from injury.⁷

Dysmenorrhoea

Few women menstruate without some degree of discomfort, but it is only when this discomfort becomes sufficiently severe to warrant treatment that the diagnosis of dysmenorrhoea is made. Primary dysmenorrhoea—also called congenital or essential—affects the young girl, occasionally as soon as she starts menstruating, but usually within a year or two of starting. Secondary, congestive, or acquired dysmenorrhoea describes painful periods which are the result of local disease such as infections, fibroids, or endometriosis. The condition arises in later life and the treatment is of the underlying cause. Where no underlying cause can be found, then treatment should be given on the empirical lines which are used for primary dysmenorrhoea.

In the primary or spasmodic type of dysmenorrhoea there is apparently no underlying pathological condition, though in some cases hypoplasia of the uterus or stenosis of the cervix

¹ Miller, H., *Brit. med. J.*, 1966, 2, 1219.

² Clark, A. N. G., and Parsonage, M. J., *ibid.*, 1957, 2, 1155.

³ Kuperman, A. S., *J. Pharmacol. exp. Ther.*, 1958, 123, 180.

⁴ McCollister, D. D., Oyen, F., and Rowe, V. K., *Toxicol. appl. Pharmacol.*, 1964, 6, 172.

⁵ Fullerton, P. M., and Barnes, J. M., *Brit. J. industr. Med.*, 1966, 23, 210.

⁶ Cavanagh, J. B., *Int. Rev. exp. Path.*, 1964, 3, 219.

⁷ *Brit. med. J.*, 1967, 3, 507.

is blamed. In some cases of primary dysmenorrhoea there may be psychogenic overlay or a low threshold of pain,¹ but this is probably not the whole explanation. J. Chassar Moir² found that patients with dysmenorrhoea felt pain when the intrauterine pressure exceeded their own blood pressure. This ischaemic type of pain would be expected to last for longer than the duration of the single contraction of the uterus, and indeed the pain of dysmenorrhoea has two components: the colicky part due to contraction and the prolonged part due to ischaemia.

Other theories of causation for primary dysmenorrhoea have been advanced. On the basis of histological studies of the endometrium the condition has been attributed to an imbalance in the oestrogen-progesterone equilibrium, but this has not been confirmed when assays of these hormones in the blood and urine of women with dysmenorrhoea have been done. It has also been postulated that an excess of progesterone could cause overdevelopment of the endometrium and also that progesterone causes high tone in the isthmus and upper part of the cervix. The belief that progesterone can cause dysmenorrhoea is strengthened by the fact that anovulatory cycles are painless. However, a progestational agent, dydrogesterone, has been shown³ to be effective in the relief of dysmenorrhoea, though it does not suppress ovulation.

A measure of our continuing inability to understand the mechanisms underlying primary dysmenorrhoea is reflected in the form of treatment in use. Among the many suggestions made recently by G. C. Schauffler⁴ in a symposium on paediatric and adolescent gynaecology are physiotherapy, hot Sitz baths, and diathermy. He found exercise relatively valueless and hypnosis surprisingly effective. Schauffler scorns the use of hormone therapy but still advocates dilatation of the cervix without mentioning the possible risk of causing incompetence of the cervix.

Another approach to the problem has been made by N. L. Warren and R. W. Hawker,⁵ who found that blood obtained from girls suffering from dysmenorrhoea contained less oxytocin than normal. They postulate that oxytocin has a regulatory function in the control of menstrual uterine contractions and that a low level of oxytocin could give rise to contractions associated with dysmenorrhoea. Certainly intramuscular injections of oxytocin have been shown to relieve dysmenorrhoea.⁷

The underlying cause of dysmenorrhoea remains obscure and treatment is variable. In the past it was believed that all that was required to prevent dysmenorrhoea was a "healthy outlook," plenty of exercise, and fresh air; and though this view has died out a healthy psychological outlook and attention to exercise and hygiene are nevertheless still important. When treatment with drugs is required it is usual first to try the effect of a simple analgesic such as aspirin, possibly combined with an antispasmodic, phenobarbitone, meprobamate, or amphetamine. If these relatively simple procedures are unsuccessful then recourse to hormone therapy is the next step. This can be done either by giving dydrogesterone 5 mg. b.d. from the fifth to the twenty-fifth

day of the cycle or by using one of the contraceptive pills to suppress ovulation. Dilatation of the cervix is less commonly performed nowadays and the drastic approach of presacral neurectomy is fortunately very seldom if ever required now. It is important to avoid drugs with a potential for addiction. Each practitioner acquires his favourite forms of therapy and rings the changes as and when required, but the simplest and safest is best.

Westward Ho!

Nobody who reads last week's report¹ on the "brain drain" can doubt the validity of its conclusion: "This is now increasing to such an extent that it constitutes a threat to the interests of this country." A report by the Royal Society² on the emigration of Ph.D.s evoked much the same comment in these columns³ four years ago, but in the interval more evidence has accumulated—and the emigration accelerated.

Though the present report excludes the medical and allied professions, it may be pertinent in several ways to the emigration of doctors, and the scientists whose departure it does discuss doubtless include among their numbers some whose work has a bearing on medicine. In round figures the numbers of engineers, technologists, and scientists emigrating for at least a year from the United Kingdom rose from 3,200 in 1961 to 6,200 in 1966. Some will return, but the report holds out little hope that many will, for it goes so far as to state that "this trend could have disastrous consequences for British industry and the economy within ten to twenty years if it were to continue at the present rate." Though the emigration of scientists might be less disturbing in the short term than that of engineers and technologists, the report considers that in the long term "it throws light on attitudes which are developing and whose consequences could be serious for our capacity as a nation to hold our own in the advance of science-based industries." It is not difficult to foresee that the development and practice of medicine must likewise suffer great harm if the emigration of the profession's energetic and able younger men continues in the way it has done for some years.

Most of the emigrants go between the ages of 25 and 35, and since the report rightly excludes any idea of imposing restrictions to stop them it looks for reasons why these highly qualified people, exceptionally favoured to compete for professional advancement in their own country, make their career elsewhere (mostly in North America). But since the motives for emigration are often complex and sometimes only half recognized by the emigrant himself any information obtained by questioning is apt to be difficult to interpret. According to the report North America is thought of as a "young man's country" where ability counts more than age, experience, or seniority. The standard of living is attractive, and though British taxation as such is not believed to be a prime motive for leaving the country it is thought to have more influence in deterring emigrants from coming back. What is believed to be a "cause of much malaise" is the

¹ Haman, J. O., *Amer. J. Obstet. Gynec.*, 1944, 47, 686.

² Moir, J. C., *Trans. Edinb. Obstet. Soc.*, 1933-34, 54, 93.

³ Bishop, P. M. F., *Proc. roy. Soc. Med.*, 1961, 54, 752.

⁴ Fairweather, D. V. I., *J. Obstet. Gynaec. Brit. Cweth.*, 1965, 72, 193.

⁵ Schauffler, G. C., *Ann. N.Y. Acad. Sci.*, 1967, 142, 794.

⁶ Warren, N. L., and Hawker, R. W., *Aust. N.Z. J. Obstet. Gynaec.*, 1967, 7, 78.

⁷ Woodbury, R. A., *Menstruation and its Disorders*, ed. by E. T. Engle, 1950, p. 290.

¹ *The Brain Drain*, Report of the Working Group on Migration, Committee on Manpower Resources for Science and Technology, Cmd. 3417, 1967. H.M.S.O.

² *Brit. med. J.*, 1963, 1, 490.

³ *Emigration of Scientists from the United Kingdom*, Report of Committee appointed by the Council of the Royal Society, 1963. London.

⁴ Gibson, T. C., *Brit. med. J.*, 1967, 1, 688.

extreme difficulty confronting the salary earner in Britain of accumulating any capital. Both entrenched privilege and economic egalitarianism are believed to be aspects of the British scene that emigrants dislike. The views of British physicians who had emigrated to North America were analysed recently by T. C. Gibson,⁴ and though expressed in somewhat different terms they have many points of resemblance with those recorded in last week's report. The three main factors influencing their decision to emigrate were dissatisfaction with opportunities for promotion, the lure of better economic conditions, and dissatisfaction with conditions of work in the United Kingdom. On a specific question whether the decision to emigrate was influenced by conditions in the National Health Service Gibson found that the replies were evenly divided between yes and no.

The report's approach to halting the brain drain is, through a number of recommendations both to the Government and to industry, to try to make prospects in Britain so attractive that young people will prefer to remain here than to seek their fortune overseas. This surely is the right way, for medicine as well as for the non-medical occupations now reported upon. As much the largest employer of doctors, the Government has a special responsibility to make conditions of employment attractive if the present damaging flow of talent abroad is to be reduced to healthier proportions. And senior members of the medical profession too, especially those in a position to mould the future course of medical practice, have a responsibility to see that their juniors have decent prospects and opportunities.

Surgery in Pulmonary Tuberculosis

There are two main reasons for the recent decline in the necessity for surgical treatment of pulmonary tuberculosis. Firstly, the development of effective antituberculous chemotherapy has undoubtedly played the major part, and, secondly, there has been a notable improvement in general living conditions. Nevertheless, there is still a small but definite place for surgery in the treatment of pulmonary tuberculosis,¹ and this is likely to remain so as long as the disease is present.

The few patients who still require surgical treatment to complete their recovery fall roughly into six groups. The first of these are those patients with cavitated disease who after six months of adequate chemotherapy are still producing positive bacillary tests, particularly where the original organism showed an appreciable degree of resistance to the standard antituberculous drugs. After a period of unsuccessful treatment the risk of the development of resistance increases steadily, while the patient's acceptance of his treatment—as well as the doctor's enthusiasm—may be sorely tried. Resection while antituberculous drugs are still effectual should therefore be carried out in these cases after the chest physician and thoracic surgeon have discussed all the factors concerned. The drugs should be continued after operation for three months to one year according to the severity of the disease.

The second group comprises those patients who have an undiagnosed nodular lesion on the chest radiograph, particularly those over the age of 40. Frequently it is possible to make a differential diagnosis only of tuberculosis, carcinoma, or a lesion such as hamartoma, and hence resection should be carried out. If the lesion is found to be tuberculous the

patient's antituberculous chemotherapy should be continued, and he should be allowed to return to his normal activities fairly rapidly.

The third group contains those patients who are left with troublesome residual damage from earlier pneumothorax therapy, or from other forms of collapse therapy such as plombage. Here the problem is usually that of an empyema, and often even many years later tubercle bacilli can be recovered from the fluid. Hence these lesions should be removed, and total pleurectomy may well be needed. The fourth group of patients who may need operation are those who suffer from repeated or severe haemoptysis. This usually originates from bronchiectatic lesions, though the actual tuberculous process is frequently quiescent or healed. Similarly a few patients with "healed cavities" which have become secondarily infected with *aspergillus* fungus may also need surgery.

There is also the rare occurrence of the patient who gets recurrent attacks of pneumonitis and pleurisy secondary to a localized bronchostenosis, which can be treated only surgically. Temporary antituberculous chemotherapeutic cover during, and a few weeks after, operation (which is usually a conservative resection) is advisable.

Sometimes the thoracic surgeon may be asked to consider early resection of a tuberculous lesion for what is said to be a social or occupational reason. This fifth group may include patients, such as alcoholics or those with mental illness, whose attendance at hospital is likely to be irregular, and occasionally patients such as seamen, who, if unwilling to submit to treatment, are apt to cause cross-infection in enclosed communities. Nevertheless, this indication should be accepted only with considerable reserve, as modern chemotherapy is adequate to deal with these lesions, and the patient should be pressed to co-operate for the necessary time. This indication varies widely from unit to unit and is probably a commoner indication for surgery in the United States, as H. T. Langston and his colleagues² have pointed out.

Lastly, there is a small group of patients who have tuberculous disease of the lungs in association with other diseases—such as cancer or congenital heart disease—and its treatment may present special problems and require early operation.

The standard methods of diagnosis and investigation of patients with pulmonary tuberculosis have been unaffected by the decline in the amount of surgical treatment. Nevertheless, bronchoscopy is still an important investigation in any patient who requires surgery. The number of cases of endobronchial lesions reported is now extremely small owing to efficient drug therapy, but it is still important that these should be looked for before surgery is carried out. The commonest operations used are still lobectomy or segmental resection of the lung for localized tuberculous foci, and occasionally pneumonectomy is needed for widespread tuberculosis, and—particularly if the pleura is involved—pleuro-pneumonectomy is required as well. Nevertheless, thoracoplasty still has a place, particularly in patients who are left with upper lobe cavitation, a positive sputum and possibly an organism resistant to several of the available agents, and, last—but most important—a limited lung reserve. A combination of resection and a limited thoracoplasty is sometimes valuable in the treatment of upper lobe lesions, either performed at the same time or more usually with the resection first and the thoracoplasty second. The indication for this procedure is

¹ Langston, H. T., Barker, W. L., and Pyle, M. M., *Ann. Surg.*, 1966, 164, 567.

² Chesterman, J. T., *Thorax*, 1957, 12, 159.

usually a persistent air space or the risk of emphysema developing in the residual lobe of the lung, or an exacerbation of the disease in the lobe.

A rare but associated problem to that of pulmonary tuberculosis, which arises particularly in children, is the treatment of tuberculous mediastinal glands. These can enlarge and press on or ulcerate into the bronchus. Repeated piecemeal bronchoscopic debridement is often required to restore the bronchial lumen and maintain normal lung function beyond it. If bronchoscopic aspiration is unsuccessful with a florid primary tuberculous infection of this type, thoracotomy and excision or evacuation of the glands may be required. This procedure is particularly valuable in preventing irreversible damage in the peripheral bronchi beyond the narrowed area.²

Langston and his colleagues have drawn attention to the recent increase in the study of atypical mycobacteria, which has resulted largely because of the greatly increased use and refinement of cultures for studying sputa. These organisms present varying problems of sensitivity, and in their view surgical intervention may have to be accepted earlier in patients infected by atypical organisms than in ordinary cases of infection with *Mycobacterium tuberculosis*.

The aim of surgery in pulmonary tuberculosis is still to be as conservative as possible; and careful preoperative investigation and proper surgical technique should enable the minimal amount of lung to be removed to achieve a satisfactory end result.

No Change

In these times of opinion polls and "random" surveys there is something refreshingly solid and reliable about a ballot. At the Annual Representative Meeting in 1966 the principle of merit awards was under discussion and it was resolved¹ "that a postal ballot should be undertaken of all consultants and senior hospital staff and senior registrars to ascertain their views in respect of merit awards for consultants." The results are published at p. 22 of this week's *Supplement*.

The overall impression given by the response to the questions asked is that senior hospital staff are satisfied with the present system of merit awards. Despite considerable publicity in the *B.M.J.* and the *Lancet* only half the doctors concerned took part in the investigation. Not surprisingly, 95% of those with awards who replied were in favour of their continuation, though nearly half of them thought some changes were needed in the system. Even of those without awards 65% favoured their retention; but 80% of this group thought changes should be made in the system of distribution. The ballot papers asked what changes in the system were desirable. Though many comments were made there was little agreement on what features needed reform. Secrecy was the most popular subject for comment—but even here only a fifth of those replying mentioned it. The form of the questions may have caused doctors some difficulty, and the 50% poll detracts from the results, but nevertheless most hospital doctors in the senior grades seem happy with the system of merit awards, and no feature is widely disliked. The constructive comments should not be ignored: but if democratic principles mean anything this ballot has produced a mandate for "no change."

¹ *Brit. med. J. Suppl.*, 1966, 2, 60.

Stanley Morison and the B.M.J.

Mr. Stanley Morison, who died last week at the age of 78, was a typographer of world-wide renown; designer of the type-face known as Times New Roman, now used extensively in the printing of books, periodicals, and newspapers throughout the civilized world; at one time editor of *The Times Literary Supplement*; and the principal architect and author of the monumental five-volume *History of The Times*—"the solid historical and political foundations on which the whole structure rests were due to his astonishing (because it seemed to be effortless) power for research," to quote from the obituary in the newspaper whose history he helped to mould as well as record. Stanley Morison was a great scholar and a great man who profoundly influenced those fortunate to know him. His contributions and distinctions were recorded in the biography published in *The Times* last week. What may be not well enough known is the part he played in the history of the *British Medical Journal* when his advice as a typographer was sought in 1935. It is therefore fitting that we should report at this time some of the facts of his beneficent intervention in the affairs of a periodical which thirty years ago looked—to use the description he then gave to the Journal Committee—more like the boiler-makers' magazine than the weekly journal of a learned profession. The rich overtones of his laughter as he passed this apt judgement removed all possible offence from it.

The scene on which Morison appeared in 1935 was one of some concern about the affairs of the *B.M.J.*: about its contents, its circulation, its physical appearance, and about the method of printing it and methods of management. It was not long before Morison had persuaded the Journal Committee that in the approaching reform the sham Gothic of the title on the cover should go. From that as a starting-point he went in detail through the whole of the *B.M.J.*, relating the changes he proposed to the significance of its different sections. He was soon invited to turn his attention to the various operations of producing the journal, and increasingly his advice on them was taken. A turning-point in this investigation was his recommendation that the composing-room immediately above the editorial offices should be abolished. The Council of the B.M.A. finally, after much debate and some close voting, accepted the Journal Committee's recommendation that this should be done, and accepted the consequences that flowed from it. And so when the *B.M.J.* made its first appearance in its new dress in 1937 the composing-room on the fourth floor of the north side of B.M.A. House was being dismantled, and the new journal was then composed and machine-printed for the first time by one and the same printer. This inevitably led to changes in managerial structure. The sum total of these changes altered the fortunes of the *B.M.J.* to the great financial advantage of the B.M.A. Many experts were consulted on the way to this radical reform. But if there is one man to whom in retrospect we may turn for special praise and thanks it is Mr. Stanley Morison. He gave the Journal Committee unstintingly of his unique experience, his wisdom, his practical sense, and his fearless integrity. This he continued to do for many years after the grand climax of the *B.M.J.*'s revolution had passed. It would, we believe, have pleased him to have in this brief commemorative tribute a few notes about a bypath in the history of journalism, one of many subjects he made his own and thereby made the world so much better informed and the richer for it.

Papers and Originals

Cancer Hazards of the Pharmacy*

GEORGIANA M. BONSER, M.D., F.R.C.P.

Brit. med. J., 1967, 4, 129-134

New therapeutic agents are constantly being synthesized and then scrutinized from the viewpoint both of their value in the treatment of disease and of their possible undesirable effects. One such effect is the induction of cancer, and I shall recount the steps which are being taken at the present time to ensure that cancer-producing chemicals are not used in the treatment of human beings. This is far more difficult than appears at first sight, for the following six reasons.

(1) The chemical structure of a compound rarely allows prediction of its carcinogenic properties. Though ideas have been suggested for a connexion between structure and activity, important exceptions to all such correlations have been found. Minor variations in molecular structure can lead to enhancement or abolition of carcinogenic activity. None the less, as new carcinogens are discovered the field of relation of chemical structure to carcinogenesis will be widened so that at least some compounds may be detected by structure alone. This argument provides a strong justification for the pursuit of studies which elicit carcinogenic activity from compounds hitherto untested.

(2) As little help can be got from chemical structure, theoretically it becomes necessary to test every proposed synthetic drug by well-planned and prolonged animal experiments. This is quite impracticable, and therefore a selection of compounds has to be made. Great efforts are in train to devise shorter screening tests for carcinogenicity, such as the use of newborn rodents or the detection of reliable precancerous changes.

(3) The time between the first administration of a carcinogen and the appearance of the tumour is a long one. In the human being it ranges from about 5 to 40 years (longer in exceptional cases); in the rat from nine months to two years. This is known as the latent or induction period.

(4) There is no need for the carcinogen to be present during the whole of the latent period. For example, Case, Hosker, McDonald, and Pearson (1954) recorded that 6 out of 281 men exposed to carcinogens in industry for six months to one year developed tumours of the bladder 10 to 25 years after leaving the industry. There are numerous examples in animals where a single dose of a carcinogen may be followed months later by the development of a tumour. Limited doses are, however, unlikely to be effective unless a subsequent latent period is allowed to elapse.

(5) Species differences in response to the administration of chemicals are very great, and therefore tumours induced in animals may not reflect what is likely to happen in man. But it is a fact that with one important exception all the *known* chemicals causing tumours in man cause tumours also in the experimental animal. The importance of species variations in response to drug administration is emphasized by Roe (1966).

(6) Little is known about the relation between the dose of chemicals and tumour induction in various species. Therapeutic doses may never attain to those required to induce tumours in animals; but we do know that small doses can induce tumours in human beings. For example, there was 0.2% of 2-naphthylamine in rubber, which could be the cause of bladder cancer in an exposed tire-maker.

In January 1964 the Ministry of Health set up a Committee on Safety of Drugs. The scheme is voluntary and the terms of reference are wide. The two which concern us are: (1) to invite from the manufacturer or other person developing or proposing to market a drug in the U.K. any reports they may think fit on the toxicity tests carried out on it; to consider whether any further test should be made, and whether the drug should be submitted to clinical trial; and (2) taking into account the safety and efficiency of each drug, and the purpose for which it is to be used, to consider whether it will be released for marketing, with or without precautions or restrictions on its use.

It is thus clear that the manufacturer is guided by the committee in the selection of drugs for carcinogenic testing. The sole means of judging carcinogenic potentiality, apart from unfortunate unwitting occurrences in man, is by tests in animals. The difficulty which arises is in the interpretation of the results of animal tests in relation to man. This is recognized as needing an expert Panel on Carcinogenesis to advise the Minister of Health.

I propose now to consider carcinogenic therapeutic agents under two headings (Table I). (1) Those of which the cancer-inducing properties were first demonstrated in man; some of these were later confirmed in animals and some not. (2) Those of which the cancer-inducing properties were first demonstrated in animals; some of these later induced tumours in man and some have not done so until the present time. Added to these are the drugs which aroused suspicion on toxicity testing and were therefore not administered to man.

TABLE I.—Classification of Carcinogenic Therapeutic Agents

- | |
|--|
| 1. Carcinogenic activity first seen in man |
| Arsenic |
| Chlornaphazin |
| X-radiation (confirmed in animals) |
| 2. Carcinogenic activity first seen in animals |
| Thorotrast (confirmed in man) |
| Iron-dextran |
| Isoniazid |
| Trypan blue |
| Griseofulvin |
| Urethane |
| Goitrogens |
| Oestrogens |
| HPA* (not given to man) |
| SADA† (not given to man) |

* 4-Ethylsulphonylnaphthalene-1-sulphonamide (anticonvulsant and diuretic).
† 2-p-Methoxybenzenesulphonamido-5-isobutyl-1,3,4-thiadiazole (hypoglycaemic agent).

Group 1

Arsenic

Neubauer (1947) collected from the literature 143 cases of skin cancer attributed to the medicinal use of arsenic, and Hueper (1957) recorded a further 37 cases. In Neubauer's

* Stewart Memorial Lecture delivered at the University of Leeds on 19 May 1967.

series the disease for which the arsenic was given was known in 125 cases. In 89 (71%) there was an underlying skin condition, psoriasis being the commonest (54%), so that in the subsequent development of the skin tumours another factor, apart from the arsenic, might have been operating as well. In only 2 of the 125 cases had arsenical treatment been given for syphilis. This is surprising, as it was the usual treatment for that disease before the advent of antibiotics. No attempt has been made to relate arsenical skin cancer in man to the size of population from which the cases were drawn. For these reasons a valid statistical evaluation of the carcinogenic properties of arsenic in man is still awaited. Many attempts have been made over the past 40 years to induce tumours experimentally in animals with arsenic and none has been successful (Baroni, van Esch, and Saffiotti, 1963). This may be due to the toxic nature of arsenic and its derivatives, which effectively precludes the administration of sufficiently large doses to animals and also shortens the life of the animals.

Chlornaphazin

Chlornaphazin (*N,N*-bis(2-chloroethyl)-2-naphthylamine) has been used, especially in Scandinavia (Thiede, Chievitz, and Christensen, 1964) for the treatment of polycythaemia vera. This compound is a mustard derivative of 2-naphthylamine, which is an important industrial bladder carcinogen, and it might be expected to yield 2-naphthylamine or its metabolites when introduced into the human body. Or the compound might act in virtue of the mustard moiety, or in both ways. The effect of the drug was favourable to the original disease in 75% of patients. Of the 61 treated patients, seven developed tumours of the bladder (five carcinomas and two papillomas), all of these having received a dose greater than 100 g. and having been treated for 2 to 11 years. Some of these patients also received treatment with ^{32}P , but it seems clear that the chlornaphazin was responsible for the induction of the bladder tumours. No more recent report has been published, but it seems probable that further cases will have emerged in the time intervening since 1964.

This drug has also been used in the treatment of Hodgkin's disease, where survival is likely to be much shorter than in polycythaemia, and at least two cases of bladder cancer have been recorded after five and six years of treatment respectively (Videbæk, 1964). Thus chlornaphazin is carcinogenic to man when given in adequate dosage for an adequate period of time. No animal experiments have been reported, but when tested this drug is certain to be carcinogenic.

X-radiation

X-radiation was first used for diagnostic purposes and occasionally for therapy at the end of the last century (Schuster, 1962). Such use caused squamous carcinomas of the skin of the exposed areas in those who worked with the rays unless rigid precautions were taken. During the years 1935-54, of 14,554 patients treated in Great Britain for ankylosing spondylitis by means of ionizing radiations (Court-Brown and Doll, 1965), a highly significant increase in mortality from leukaemia and aplastic anaemia was observed—52 actual deaths from

leukaemia (0.36%) against 5.48 deaths expected (Table II). The proportion of the myeloid over the lymphatic type was also increased.

In 1955 Simpson, Hempelmann, and Fuller showed that children who had received local irradiation for "thymic enlargement" were more likely to develop thyroid tumours than non-irradiated children. Among 1,722 irradiated children there were six thyroid cancers and nine thyroid adenomas compared with none and one respectively in 1,795 related non-irradiated children. The mechanism of this occurrence is presumably radiation damage to the thyroid gland causing the blocking of thyroxine secretion followed by excess thyroid-stimulating hormone secretion by the pituitary gland. The latter causes the remaining thyroid cells to undergo excessive growth and finally neoplasia.

Both these findings, but especially the first, demonstrate that the association between administration of a carcinogen and the subsequent development of a neoplastic condition need not be an obvious one and may need patient research in order to uncover it and advanced statistical methods to elucidate it. The chances that any single practitioner will encounter a case are remote indeed.

Group 2

Thorotrast

Thorotrast (colloidal thorium dioxide) is not strictly a drug but has been widely used in man as a contrast medium for diagnostic purposes. It was shown to induce subcutaneous sarcomas in rats and mice (Selbie, 1938) and in guinea-pigs (Foulds, 1939) following injection, the tumours being attributable to its radioactivity. Much later it was realized that tumours were occurring in man, and in 1961 Dahlgren (Table III) collected some 60 cases from the literature of which I have selected the following examples. In all, 24 tumours occurred where thorotrast had been placed in hollow organs, seven being situated in the maxillary sinus. Twenty-seven were due to the compound injected systemically, taken up in the reticulo-endothelial system and deposited chiefly in the liver, spleen, and bone marrow. Though the compound was administered at sites distant to those of the tumours, the latter must be regarded as due to the local presence of the radioactive material in the affected organs. The variety of induced tumour was very great, the commonest being in the liver—hepatomas, bile-duct carcinomas, or haemangioendotheliomas. The induction period was 6 to 35 years. In many cases this could be calculated exactly, as only one dose was given. No tumours were recorded in bone. An unusual tumour was a carcinoma of the kidney occurring after cerebral angiography. No estimate can be made of the total number of thorotrast-treated patients from whom these cases were drawn, and to establish cause and effect with certainty this information is necessary. However, it was possible to demonstrate radioactive material in the vicinity of the tumours in many cases.

TABLE III.—*Examples of Tumours in Man Induced by Thorotrast (Dahlgren, 1961)*

Mode of Origin	Procedure	Nature and Site of Tumours	Range of Latent Period (Years)
At site of injection	Cerebral angiography (1)	Sarcoma	6
After deposition in pre-formed cavities	Pyelography (7)	Sarcoma } Kidney	16-25
	Maxillary visualization (7)	Carcinoma sinus	10-21
	Dacryocystography (1)	Carcinoma eyelid	35
	Hepatolienography (9)	Sarcoma } Liver	12-24
After systemic injection	Arteriography (13)	Sarcoma } Liver	12-24
	Cerebral angiography (1)	Carcinoma } Liver	20
		Carcinoma kidney	

TABLE II.—*Two Examples of Post-irradiation Tumours in Man*

Disease Treated	Irradiated Patients		Non-irradiated Patients	Tumour Deaths		Latent Period (Years)
	Years	No.		Treated	Control	
Ankylosing spondylitis	1935-54	14,554		52 leukaemias	5.48 (expected)	5-25
Thymic enlargement	1925-51	1,722	1,795	6 thyroid carcinomas 9 thyroid adenomas	0 1	5-15

Iron-dextran

Iron-dextran (Imferon) has wide use in man as a means of supplying parenteral iron. It is a complex of colloidal ferric chloride and a dextran of low molecular weight. It has been found to induce sarcomas on intramuscular and subcutaneous injection into rats, mice, and hamsters (Richmond, 1960; Haddow and Horning, 1960) and rabbits (Haddow, Roe, and Mitchley, 1964). The latent period was 12 months or more in rodents and three to four years in rabbits.

The experimental doses were large in relation to the size of the animals, but Roe, Haddow, Dukes, and Mitchley (1964) argued that "since the size of body cells is similar in man and laboratory animals, the actual dose, and not the body weight, may be the critical factor in determining the induction of tumours . . . a particular volume of material will come into contact with approximately the same number of body cells in the rat as it does in man." They then conducted an experiment directed to finding out "whether the incidence and time of appearance of tumours in rats given a fixed number of injections of iron-dextran would be affected by distributing the injections between 2, 4, or 6 sites, instead of giving them, as in previous experiments, all into the same site." This is important from the viewpoint of clinical use.

Twenty-four subcutaneous injections of 0.5 ml. were given to each rat, all in the same site in group 1 and distributed among six sites in group 4 (Table IV). It is seen that increasing the number of injection sites does reduce, but does not abolish, the chance of tumour development at any one site and does delay the date of their appearance. It also decreases their malignancy. However, it is to be noted that as little as 2 ml. of iron-dextran induced 12% of tumours at 75 weeks.

TABLE IV.—Iron-dextran Tumour Incidence After Subcutaneous Injection at One or More Sites (Rat)

Group:	1	2	3	4	5
No. of rats	24	24	24	24	24
No. of injection sites per rat	1	2	4	6	0
Total amount injected at each site (ml.)	12	6	3	2	0
Time of appearance of first malignant tumour (weeks)	47	66	64	75	—
Injection sites with tumours	14/22 64%	11/46 24%	29/96 30%	17/138 12%	0

It is suggested that in order to exert a carcinogenic effect an excess of heavy metal must be present, and this could lead to oxidation of sulphhydryl groups and in turn to gross disturbance of enzyme systems in adjacent cells. Whatever the mechanism, the local excess of iron seems to be important. The role of dextran may be to aid penetration of iron into the cell.

No tumours have yet been reported in man, but patients will need to be followed for 15 to 40 years before they can be regarded as safe. The accumulation of iron in human tissues has been suggested as carrying a carcinogenic risk—for example, the hepatomas found in haemochromatosis and the carcinomas of the bronchus in iron-ore miners (Faulds and Stewart, 1956). Stewart (1931) could not satisfy himself that the former was the case, though other authors have been more positive, but he accepted the association between iron-ore mining and lung carcinoma.

Isoniazid

As a most useful therapeutic adjunct to streptomycin in the treatment of tuberculosis isoniazid has proved its worth. Since 1957 it has become increasingly clear that this drug is carcinogenic in the experimental animal (Biancifiore and Severi, 1966). Pulmonary adenomas and carcinomas have been induced by oral and other administration to mice (Table V). Furthermore, hydrazine (a hydrolysis product of isoniazid) caused pulmonary tumours and hepatomas in mice, but isonicotinic acid was

much less effective. A derivative of hydrazine (Natulan) caused mammary tumours in male and female rats; hydrazine sulphate caused lung tumours in rats (Biancifiore, Giornelli-Santilli, Milia, and Severi, 1966). It is suggested that isoniazid acts by virtue of its hydrazine component.

TABLE V.—Induction of Tumours by Isoniazid and Derivatives in Mouse and Rat

Compound	Species	Sites of Tumours
Isoniazid	Mouse	Lung. Lymph nodes Lung. Liver Lung (a few)
Hydrazine sulphate		
Isonicotinic acid		
Natulan	Rat	Breast (male and female) Lung
Hydrazine sulphate		

No tumours have been reported in man following the prophylactic or therapeutic use of isoniazid, and it will be unusually difficult to demonstrate such an association because virtually all tuberculous patients receive the drug and so there is no comparable untreated population to evaluate. Hammond, Selikoff, and Robitzek (1967) have attempted an evaluation of the effects of isoniazid in the 16 years since the introduction of therapy with this drug in 1951. In a series of several thousands of tuberculous males and females, some of whom may have been given isoniazid, there was a slight excess of lung cancer compared with the general population in males but not of a magnitude to be regarded as significant. Of a much smaller series of tuberculous patients treated with isoniazid there was no excess of lung cancer in the few who have died, nor was there any suggestion of a dose-response relationship. Of a series of pregnant women treated prophylactically, together with a scrutiny of their offspring (some of whom had attained an age of 13 years) there was again no evidence of an increase in lung cancer. This investigation is still in progress, and though the results are reassuring so far they cannot be expected to give the complete answer regarding the carcinogenic effects of isoniazid in the human being.

Ferebee (1965) has been undertaking since 1955 an investigation of the carcinogenic effects of isoniazid used prophylactically in 70,000 persons ranging in age from 2 months to 100 years. This author argues that a comparison of lung cancer incidence in treated tuberculous patients with that of the general population would not be valid because (1) tuberculosis may predispose to lung cancer; (2) tuberculous patients receive extra radiation for diagnostic and therapeutic purposes; and (3) tuberculous patients may smoke more and they usually belong to selected poorer social groups. Therefore the control population for this investigation is derived from a group of subjects given a placebo in place of isoniazid. The results are not yet available.

An additional difficulty in assessing the effects of the drug is that only a small number of patients treated with isoniazid, with or without tuberculosis, come to necropsy, and in those that do the past history is often not known. None the less, the starting-point of all the work which has been done on these compounds was the observation of Berencsi, Entz, and Vajkoczy (1952) that in a patient being treated with isoniazid presumptively for tuberculosis, but actually suffering from carcinoma of the lung, the clinical course was extremely rapid owing to precocious, numerous, and voluminous metastases due, it is suggested, to the enhancing effect of the isoniazid.

Trypan Blue

Trypan-blue has been used in man, by intravenous injection, for the estimation of blood volume and also to demonstrate the lymphatic pathways in block dissection of lymph nodes. Gillman, Gillman, and Gilbert (1949) gave intravenous injections of 10 mg. of trypan blue in water to pregnant rats and induced malformations in the offspring resembling those caused by rubella in the human being. They then continued the experiments in the same mothers, and in new females and males,

giving a total of 100–200 mg. of the chemical to each animal. They obtained a high yield of reticulum-cell sarcomas in the liver, smaller numbers of spindle-cell sarcomas, and many lymphomas and proliferations resembling Hodgkin's sarcomas in nodes. The latent period was less than a year. They found that the dye was bound to plasma albumin and then taken up by reticuloendothelial cells throughout the body, but especially in the liver. They were able to demonstrate spindle-cell sarcomas in the liver after a single injection in as short a period as 19 weeks. They found also that Evans blue had a similar action in causing liver tumours. They made the very interesting observation that although trypan red and Congo red do not cause proliferation of the reticuloendothelial cells in treated mothers, Congo red causes malformations in the offspring. Thus trypan blue is carcinogenic and teratogenic, and Congo red is teratogenic but not carcinogenic, and trypan red has neither action. Obviously much more information about the effects of these compounds is needed.

Griseofulvin

Griseofulvin is an antibiotic derived from three types of *Penicillium* (*P. patulum*, *P. griseofulvum*, and *P. janczewski*) and is extensively used in the systemic treatment of superficial fungal infections in man and animals. When it is administered orally and continuously to mice (Weston Hurst and Paget, 1963) this drug causes derangement of the porphyrin mechanism so that protoporphyrin is deposited in large quantities in the liver. Consequent on this, liver-cell necrosis, bile-duct proliferation, and cirrhosis occur, followed by the induction of multiple hepatomas. If the conditions of the experiment are such that the protoporphyrin can be eliminated from the liver—for example, if the dose is small or discontinuous—the liver damage and tumours do not occur. It could be postulated that continuous absorption could take place in treated patients, but the amount absorbed would be unlikely to reach a sufficient dimension to cause the damage seen under experimental conditions. No tumours have been reported in man or in the veterinary field. It is of significance that other mould products, such as aflatoxin derived from *Aspergillus flavus*, are potent liver carcinogens.

Urethane

Urethane, which induces lung tumours in rodents, has the property of initiating tumour formation in mouse skin even when administered orally, but requires the topical administration of a co-carcinogen to render the tumours manifest. It has been virtually abandoned for therapeutic use as more efficient tumour chemotherapeutic agents have been found.

Goitrogens

Goitrogens act by a feedback mechanism similar to that described in thymic irradiation. When given orally they cause carcinomas of the thyroid gland in rodents. The incidence can be increased and the malignancy enhanced by combining the short-term administration of a known chemical carcinogen with subsequent administration of the goitrogen (Bielschowsky, 1945).

Oestrogens

Oestrogens, by whatever route administered, cause mammary carcinomas in mice, but only if other factors such as a virus or progesterone are also present.

The work of Court-Brown and Doll (1965) has emphasized how advantageous is a large population in demonstrating a

carcinogenic risk in treated patients. This would apply also to those treated with goitrogens and oestrogens, but so far no large series has been analysed from the point of view of cancer induction. The small amount of evidence available does not suggest that these compounds have induced tumours in man. Another factor is present, however, in the use of synthetic and semisynthetic hormones. Apart from their cancer-inducing potentialities due to their hormonal action they may induce tumours, especially of the liver, by virtue of their chemical structure. A large-scale trial of the long-term effects of synthetic oestrogens and progestins has been initiated in the introduction of the contraceptive pill, and information will certainly eventually become available in regard to the presence or absence of tumour-inducing properties in these compounds in man. Meanwhile straws are blowing in the wind. Poel (1966) found an enhanced incidence, earlier onset, and more rapid development of pituitary tumours in female mice treated with progestins than in virgin controls (Table VI). But old breeding mice of this strain in another laboratory developed many pituitary tumours, so that the meaning of this experiment is far from clear. He also found 10 hepatomas in 96 treated mice and none in the controls, but unfortunately gave no further details.

TABLE VI.—Pituitary Tumours in Mice Treated with Progestins (after Poel, 1966)

Compound	Daily Dose	Tumours in Survivors to 85 Weeks or More	Approximate Size (mm.)
50 parts norethynodrel and 1 part mestranol	70 µg.	7/7	2–7
	7 "	6/11	1–5
50 parts norethindrone and 1 part ethinyloestradiol	70 "	5/8	2–4
	7 "	7/15	2–6
Control	None	2/15*	<1–1

* Killed at 90 weeks.

Cahal (1966) referred to experiments by manufacturers of oral contraceptives and concluded that "mestranol, when administered in high doses and for prolonged periods to rats, causes liver damage which is sometimes severe, including on occasion the development of hepatomas. Adequate experiments have not been carried out on other species of animals."

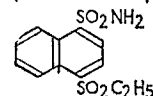
Stoll (1967) used Lyndiol (a contraceptive pill containing ethinyloestrenol as progestin and mestranol as oestrogen) in the treatment of breast cancer in postmenopausal women. He found disordered liver function, jaundice, or hepatic necrosis on biopsy in 15 of 38 patients, apparent at the contraceptive dose of one tablet a day but more marked when the dose was increased to six tablets.

It would be very reassuring to learn of negative results in well-conducted long-term experiments in animals before the human experiment has assumed too great a dimension.

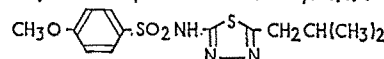
HPA

Brimelow and Vasey (1958), in a British patent, described the chemical synthesis of a new class of sulphonamides which held promise as anticonvulsants and diuretics. Walpole (personal communication) and Paget (1958) observed hyperplasia of urinary tract epithelium in rats fed relatively large amounts

HPA
4-Ethylsulphonylnaphthalene-1-sulphonamide



SADA
2-p-Methoxybenzenesulphonamido-5-isobutyl-1,3,4-thiadiazole



of one of these compounds, 4-ethylsulphonylnaphthalene-1-sulphonamide, or HPA (see Formula). The incorporation of as little as 0.01% in the diet of rats—that is, one part in 10,000—induced focal hyperplasia of urinary tract epithelium. For this reason the drug was not introduced for human therapy. This is an excellent example of the piercing scrutiny which is applied during toxicity-testing of new drugs.

My colleagues and I decided that this was an unusual compound, worthy of further investigation, because we knew of no other chemical which had been demonstrated to cause hyperplasia of renal tract epithelium on short-term testing. We therefore gave this compound to mice in the diet at a level of 0.01% for up to 65 weeks (Clayson and Bonser, 1965) and obtained five transitional-cell papillomas and 23 carcinomas of the bladder in 73 effective mice, but no tumours in any other organ. This was also unusual as all the other members of the small group of mouse-bladder carcinogens had induced tumours in other organs as well (Table VII).

TABLE VII.—Bladder Tumours Induced by Oral HPA (Mouse)

Dose	Sex	No. Surviving 30–69 Weeks	Papillomas	Carcinomas	
				No.	%
0.01% in diet	M	34	2	5	15
	F	39	3	18	46

Paget and Walpole's observation was thus very astute, as the hyperplastic action of the drug proved to be the first stage in the carcinogenic action. Clayson, Lawson, Santana, and Bonser (1965) have extended this observation in an attempt to devise a short-term test which could be used to pick out compounds carcinogenic to the bladder by means of their hyperplastic action and thus reduce the testing time to six weeks or less.

SADA

This compound was being investigated for use as a hypoglycaemic agent when it was discovered that it caused bladder tumours when given in the diet to rats, and it was therefore discarded. The chemical structure bore no resemblance to that of any other known carcinogen, which emphasizes how impossible it is, at present, to foretell carcinogenic activity from chemical structure (see Formula).

In Table VIII the results of tests in rats by the oral route are shown. This was a large experiment, adequately controlled. No tumours were obtained until one year of experiment had elapsed, and then only when the drug was given at a concentration of 0.6% or over in the diet, which is much more than is needed relatively in the mouse treated with HPA. Again no tumours were observed in organs other than the bladder.

TABLE VIII.—Induction of Bladder Papillomas and Carcinomas by SADA (Rat)

Dose (% in Diet)	No. of Rats at Start		Bladder Tumours				3 Years	
			1 Year		1½ Years			
	M	F	M	F	M	F	M	F
Control 1 ..	20	20					0	0
0.05-0.4 ..	80	80					0	0
Control 2 ..	10	10						
0.6 ..	10	10		0/4		0/5		
0.8 ..	10	10		1/5		1/5		
				2/4		1/4		
Control 3 ..	20	20						
0.8 ..	30	30			0/15	0/15		
					9/22	4/22		

Although we have no information about the way in which HPA and SADA would act in the human being, no one would dream of permitting their clinical use, because of the extreme potency in man of several other known experimental bladder carcinogens.

Discussion

I have brought to your attention some known or suspected carcinogenic properties of certain therapeutic agents in use or discarded before use in the human being. A more complete list may be found in Roe's (1966) paper.

We are now in a position to discuss the more philosophical problems raised by the facts that I have described to you.

We would all agree that therapeutic compounds which have been proved to induce tumours in man should not be administered for any but the most exceptional clinical purposes—for example, where the expectation of life is short and no other suitable drug is available. It might be suggested also that if a drug is still in the trial stage and is found to be carcinogenic to animals it should be withheld from human use. If we adopt this policy we shall have to realize that we may be withholding a drug which would be of inestimable value in the treatment of a disease or a group of diseases. But what attitude are we to take in regard to a drug which has already proved its worth in the treatment of human disease and has subsequently been shown to cause tumours in animals? The examples I would quote are iron-dextran and isoniazid. In the former case we know that one factor in the development of the experimental tumours is the local accumulation of iron at the site of injection. Therefore I should reserve the use of iron-dextran for patients in the older age groups who do not require large doses continuously or for the acute emergency. I consider that its routine use in pregnant women is unjustified. To vary the injection site might be useful. In regard to isoniazid I should use it as required in the treatment of tuberculosis, though there seems to be recent evidence of bacillary resistance to this compound, but I should not give it prophylactically to young contacts of tuberculous patients, as is the practice in some boroughs in the United Kingdom and elsewhere. It has to be remembered that the duration of the latent period is the most important factor in the quantitative assessment of the causes of cancer and that the longest latent period occurs when exposure starts in childhood.

We now come to the problem of whether all new drugs should be tested for carcinogenic activity before they are marketed. If it were possible to predict this property from chemical structure then such tedious biological work would be avoided. Only occasionally can carcinogenicity be predicted from chemical structure (as I think could now be done in the case of chlor-naphazin). No one could have predicted that HPA and SADA would have this property. I suggest that a commonsense view must be taken of this matter. If a drug is to be used only to treat degenerative disease in old age there is less need for testing than if it is to be used for chronic disease in the young. Any new compound should be tested if a related compound (whether near or distant) is known to be carcinogenic. The strongest argument against testing all new compounds is that it is an expensive task which consumes much skilled scientific labour that could be put to more constructive use, such as the synthesis and preliminary trials of new compounds.

As carcinogenesis is dependent upon the interaction between chemicals and enzyme systems, it is not surprising that species and even strains within a species react in different ways. For example, when the industrial carcinogen 2-naphthylamine is administered to man and the dog, tumours occur in the bladder (and nowhere else), but when administered to the mouse the tumours are in the liver, and in the rat no tumours occur at all. Thus if, on testing a compound in the experimental animal, tumours are induced in the liver, it may be necessary to look for them in the exposed human being in the intestine or bladder. If it happens that the site of election is an organ, such as the intestine, where so-called spontaneous tumours are frequent, any association between the drug and subsequent cancer will not be evident and will require diligent search to uncover it. Linked to this aspect is the gap between the discoveries of the experimentalist and the appreciation by the

clinician of the significance to him and his patient of what has been discovered in the laboratory. Means must be found to bridge this gap.

Summary

The synthesis and exploitation of new therapeutic agents bring hazards as well as benefits to the patient. One hazard is actual or potential carcinogenic action. It is often not realized that the chemical structure of a compound rarely allows prediction of its carcinogenic properties, though it is to be hoped that such a relation will eventually be discovered. At present the only method of demonstrating carcinogenic activity is by laborious tests in animals, and even then the relevance of the results to man is uncertain.

The latent period of tumour induction is long, ranging in the human being from 5 to 40 years. There is no need for the carcinogen to be present during the whole of the latent period, so that a limited exposure in childhood may declare itself later in adult life. Little is known about the relation between the dose and tumour induction.

Carcinogenic therapeutic agents are here discussed as: (1) those of which the cancer-inducing properties were first demonstrated in man; (2) those of which the carcinogenic activity was first seen in animals but the compound had already been given to man; and (3) those which were withheld from man because their tumour-producing potential was discovered by animal experiment.

It is emphasized that laborious statistical investigation may be needed to uncover a relation between therapy and subsequent tumour induction, the treatment of ankylosing spondylitis by x-irradiation being cited as an example.

I hold the view that compounds which have been proved to induce tumours in man should not be administered to patients for any but the most exceptional clinical needs—for example, where the expectation of life is short and no other suitable drug is available. Drugs shown in the trial stage to be carcinogenic in animals should normally be withheld from man, in the knowledge that thereby valuable therapeutic agents may be lost. Drugs which have already proved their worth in therapy and which have subsequently been shown to induce tumours in

animals should be regarded with much suspicion and should in general be withheld from the young and from use as prophylactics. Thus an assessment must be made of the risks and of the benefits in each individual patient. This will be greatly helped by improved communication between the laboratory worker and the clinician.

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Six Cases of Acrylamide Poisoning

T. O. GARLAND,* M.D., D.P.H.; M. W. H. PATTERSON,* M.B., CH.B., B.SC.

Brit. med. J., 1967, **4**, 134-138

Early in February 1967 a 19-year-old youth (Case 1) was admitted to the Central Middlesex Hospital with severe peripheral neuropathy and dermatitis of the hands. The occupational health unit was asked to report on any toxic material that he might have contacted at work.

A director of the small factory where he was employed said that they had carefully reviewed all the materials he had handled and none of them could have poisoned him. He was held to be a rather dull lad, who virtually did only labouring work. He lodged with a local farmer, was a poor time-keeper, and by way of recreation spent much time in a local dance hall, which was under suspicion as a place where drugs were peddled.

In appearance the patient bore out this story. His ataxic walk and tendency to fall over almost emphasized it. His

mother had died when he was a child, and life had not been easy for him. He agreed that he was a bad time-keeper, especially lately. However, he denied that he had ever taken drugs, though he had been offered them at the dance hall, and added that lately he had given up smoking and drinking. He knew that he had been working with acrylamide, some of which came from the Cyanamid Co. of New Jersey, and some from Japan, and he told us that the bags from the U.S.A. had a warning label on them.

A further call was made to the factory chemist. He thought that acrylamide could be toxic and remembered having read in a booklet, issued by Cyanamid International, that it poisoned small mammals. The London headquarters of the Cyanamid Co. produced a paper on the toxicology of acrylamide by D. D. McCollister, F. Oyen, and V. K. Rowe, but assured us emphatically that they had no knowledge of any humans having suffered from it. McCollister's description of poisoned

* Central Middlesex Hospital, London N.W.10.

monkeys, however, made us feel fairly sure that the youth had been similarly poisoned.

The managing directors of two other firms making flocculators from acrylamide gave us names of employees whom they thought might have been further cases, and we visited seven factories where acrylamide was used. The cases described occurred in three of the four making flocculators.

A flocculator aids the separation of suspended solids from aqueous systems, which may be useful in mining, soil stabilization, the disposal of industrial wastes, and on any filtration or centrifugal process. There is a use for smaller quantities of acrylamide in the dyeing, photographic, plastic, paper, textile, ceramic, and paint industries.

Acrylamide

Acrylamide ($\text{CH}_2=\text{CHCONH}_2$), a white crystalline powder, is a vinyl monomer which exhibits the usual reactions of the amide group and will readily undergo polymerization and copolymerization. The polymer is non-toxic. It is when handling the monomer or during the process of polymerization that there is a hazard.

It should be noted, in passing, that a small paragraph in the Cyanamid booklet on the chemistry of acrylamide states: "Solutions of acrylamide can be stabilized when necessary by incorporation of cupric and ferrous salts or by organic inhibitors such as hydroquinone and *N*-phenyl- β -naphthylamine." This is a pointer to further care needed if these organic inhibitors are used.

Manufacturing a Flocculator.—The bare outline of the process is as follows: The bags of acrylamide powder are slit along the top with a knife and then emptied manually into a reactor vessel, either through the wide-open top or through a hopper. A catalyst, water, and other chemicals are added. As polymerization proceeds the mixture thickens, finally coming to the state of a gelatinous solid. At this point it is decanted into other vessels and subsequently washed and dried, cut up, and ground. When the polymer is ground up considerable fine dust is produced, but the heavier crystalline monomer does not appear to fly and cause a serious dust hazard. The finished product, sold as a flocculator, is in the form of a granulated solid.

Case Notes

We present these cases under some difficulties. Only one of them has been a patient in this hospital; the others live and work far from London. We have heard of them only through the assistance of their employers, and in regard to their clinical details have been helped by a number of doctors. We have ourselves examined all but one, Case 3, who was away on the Continent. Two are back at work quite well; two have returned—one with serious and the other with mild residual signs and symptoms; one we found still at work though severely poisoned; and one is still off work after eight months.

The situation clearly calls for a great deal more study and trailing, but the wide and growing use of acrylamide justifies an early warning of its dangers.

Case 1. Factory A

A 19-year-old labourer in a very small plant making flocculators first handled acrylamide in December 1966. He was seen in February 1967 complaining of severe muscular aching in the calves and buttocks and with a story of becoming increasingly unsteady on his legs. There was a weakness of his hands, noticed when controlling a bicycle, and finally his legs gave way abruptly on several occasions. The climax arrived in a dance hall, when, having collapsed on the floor, he could not get up again and an ambulance was called for.

The first sign he noticed was in January 1967, when his hands became excessively moist and the skin peeled off, about four weeks after the first contact with acrylamide. Shortly afterwards he was excessively tired and difficult to arouse in the morning, and then the presenting symptoms of weakness and loss of balance appeared. He had lost 7 lb. (3.2 kg.) since December 1966, but had had no diarrhoea.

On examination his palms were moist and peeling. He had a generalized coarse tremor, which had troubled him on two or three occasions in the previous few days. There was also a noticeable slurring of speech.

Neurological examination revealed normal cranial nerves, sluggish reflexes in the arms, and loss of knee and ankle jerks with absent plantar responses. Weakness and wasting of the small muscles of the hands was obvious, together with weakness of the wrist extensors (3/5 M.R.C. scale). Weakness of the dorsi and plantar flexors of the ankles was pronounced. Vibration sense was lost at the wrist and ankle, but there was no other sensory loss, and position sense was not impaired. There was marked truncal ataxia and a positive Romberg sign. C.S.F.: protein 40 mg./100 ml., 4 lymphocytes.

While in hospital his hands healed but the tendon reflexes in the arms disappeared. Otherwise there was little change in his condition, and he was discharged on 9 March.

On 29 April, three months after stopping work, he was still severely disabled and had lost a further 5 lb. (2.3 kg.). He had experienced further episodes of generalized uncontrollable shaking, worse in the upper half of the body. He had no diarrhoea or urinary symptoms. There was muscle-wasting, most pronounced in the anterior tibial compartment, and no return of power, but vibration sense was now intact. Tendon reflexes were absent and Romberg's sign was positive. By June he was much better, but still severely ataxic.

Case 2. Factory B

This man, aged 23, had been working with acrylamide for three months before the skin of his hands peeled. Two weeks later his finger-tips became numb and this numbness gradually crept up his hands. His grip became weak, he found shaving difficult, and he could not appreciate the temperature of his baby's bottle. Six weeks after the onset of symptoms his toes also became numb and his legs progressively weaker, until it became difficult to climb stairs and impossible to run. He stumbled frequently. He had no difficulty with his speech, no tingling, no impotence, no disturbance of micturition, no loss of appetite, and no disturbance of sleep. He worked until admission to hospital three months after his symptoms began.

On admission to hospital on 8 September 1965 there was an absence of tendon reflexes in arms and legs, loss of power in the small muscles of hands and feet, and anaesthesia of the fingers and toes to light touch and pinprick. Vibration sense was intact. C.S.F.: protein 29 mg./100 ml., cells nil.

He was discharged from hospital on 21 September and returned to work at the beginning of November, though there was still weakness of certain hand muscles. By March 1966 tendon reflexes had reappeared, and when we examined him on 17 April 1967, after he had been back working with acrylamide for some months, we found no abnormality whatever.

Case 3. Factory B

This man, aged 30, had been closely concerned with the previous patient (Case 2) developing the process for manufacturing flocculators. He knew his colleague's story and had had similar symptoms, but seems to have put up with them for four or five months before he consulted a neurologist on 10 March 1966.

He felt unbalanced at times when dancing, he had lost his sense of touch, and tended to drop cigarettes. These symptoms were more noticeable after taking alcohol. Generally he was very tired. The neurologist found arm and ankle jerks to be absent. Knee jerks were present though sluggish. There was slight loss of vibration and joint sense in the toes but no other sensory loss. The neurologist had also seen Case 2 and found the present patient much less seriously affected. Recovery was fairly quick and uneventful.

months. With regard to the more severely poisoned, we are still in doubt whether complete recovery ever takes place.

It is a relatively easy hazard to contain. Awareness of the severely toxic nature of the substance on the part of the management and workers is the principal factor in prevention of acrylamide poisoning.

We wish first to thank the managements of the seven factories who allowed us to study their methods of using acrylamide. In particular we are grateful to those directors of factories making flocculators who unearthed cases among their own staff. They could so easily have behaved very much less helpfully.

We thank Dr. J. C. Phemister for his permission to publish Case 1 and for his advice throughout on the neurological aspects. We

thank also the following doctors for answering our letters promptly and giving every assistance they could to our understanding: C. L. Davidson, P. Knight, B. O. Porchetta, J. A. Price, J. V. Reuben, L. W. Smith, and T. Thorburn.

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Fructose Intolerance

J. A. BLACK,* M.D., F.R.C.P.; K. SIMPSON,† M.D., M.R.C.P.

Brit. med. J., 1967, 4, 138-141

Fructose intolerance is a genetically determined disorder in which the giving of fructose or fructose-containing sugars such as sucrose causes severe hypoglycaemia, while the continued absorption of small amounts of fructose results in fatty infiltration and fibrosis of the liver. The condition was first described by Chambers and Pratt (1956), and Froesch *et al.* (1957) in Zürich demonstrated the biochemical response in affected individuals to a dose of fructose or sucrose. Since then more than 40 cases have been described, and it is probable that fructose intolerance is at least as common as is galactose intolerance. In all except one family (Wolf *et al.*, 1959) the condition seems to have been inherited as an autosomal recessive.

This is a potentially fatal condition in infancy if untreated; in those infants who survive, hypoglycaemic symptoms may continue throughout childhood and even into adult life, and it is therefore equally important that the family doctor, the paediatrician, and the general physician should be aware of this easily treated disorder.

Case 1

The patient, a girl born on 19 March 1962, was the fourth child of healthy unrelated parents; birth weight 6 lb. 8 oz. (2.95 kg.). She was breast-fed for three days and later fed on various dried milks with the conventional additions of sucrose. On return home from the maternity hospital she began to vomit, lost weight, and became jaundiced. At the age of 1 month she was admitted to hospital. She was a pale, jaundiced baby with a blotchy face and a blood-stained nasal discharge. The abdomen was distended by ascites and by a moderately enlarged liver (two fingerbreadths below the costal margin).

Investigations.—Haemoglobin 8.8 g./100 ml. (61%); W.B.C. 27,000/cu. mm. (neutrophils 71%). Serum bilirubin 5.5 mg./100 ml. Serum alkaline phosphatase 22 units/100 ml.; thymol turbidity 1 unit; S.G.O.T. 140 units/100 ml.; S.G.P.T. 100 units/100 ml. Serum proteins 3.5%, with a lowering of albumin and β -globulin, and an elevated α_1 - and γ -globulin. Urine normal to routine examination.

One week after admission a laparotomy was done (Mr. H. H. Nixon). There was much ascitic fluid and the liver was greenish brown with a finely granular appearance. A piece of liver was removed; part of this was sent for routine histological examination and the rest was kept in a deep freeze. The histological report on the liver (Dr. Barbara Ockenden) was as follows: "There is intra-

lobular bile retention in the canaliculi, with widespread but patchy giant-cell transformation. There is a variable degree of sublobular cirrhosis. A little glycogen is present but there is no fatty change." A provisional diagnosis of giant-cell hepatitis was made, though galactosaemia was also considered, but was excluded by finding a normal activity of galactose-1-phosphate uridyl transferase in the infant's red cells.

After the laparotomy she improved. The urine at this time showed a gross amino-aciduria on two occasions with small quantities of galactose (50 and 12 mg./100 ml.) and traces (less than 5 mg./100 ml.) of glucose, sucrose, fructose, and lactose.

She was discharged at the age of 7 weeks weighing 8 lb. 5 oz. (3.77 kg.) but improvement was not maintained. At the age of 6 months she began to gain weight; by 8 months she weighed 14 lb. 10 oz. (6.63 kg.) and her liver was almost normal in size. Since her progress seemed much better than would have been expected of a child with a severe hepatitis the history was reviewed with her mother, who said that the baby had begun to thrive as soon as she had substituted glucose for sucrose in the feeds. She had done this because she had noticed that the patient's reaction to sucrose was similar to that of her first child (Case 2), whose history follows.

Case 2

This male child born on 26 September 1953 was breast-fed for one month and then changed to dried milk with the usual additions of sucrose. He did not take his feeds well and failed to gain weight on three different milks. A health visitor suggested that it was the sucrose which was upsetting him and advised the mother to use glucose. After this he gained weight but later developed a "screaming dislike" of sweet things, also carrots, peas, baked beans, fruit, and a variety of other foods.

A diagnosis of fructose intolerance in both children now seemed probable, and an oral fructose-tolerance test was performed by Dr. K. Simpson at Leicester Royal Infirmary (they had moved shortly after the diagnosis was suggested in London).

Comment

Case 1 was given 5 g. of fructose (0.5 g./kg. body weight). She vomited soon after her test dose and was sleepy for the rest of the day. A urine specimen during the test contained fructose. The response to the fructose was characteristic of fructose intolerance (Fig. 1). Case 2 was given 13 g. of fructose (0.5 g./kg. body weight). He became pale and drowsy and felt sick. The chemical changes in his blood were also typical of fructose intolerance.

* Consultant Paediatrician, Sheffield Children's Hospital.

† Consultant Paediatrician, Leicester Area.

A fructose-free diet was therefore prepared and the sheet was shown to the mother, but she reported that it contained little information which she and her family had not already worked out for themselves. At the time of writing both children were well and were growing normally. At the age of 3 years 11 months Case 1 weighed 35 lb. (15.9 kg.) and her height was 3 ft. 2 in. (96.5 cm.), while Case 2, aged 12 years 5 months, weighed 88 lb. (40 kg.) and was 4 ft. 11½ in. (152 cm.) tall.

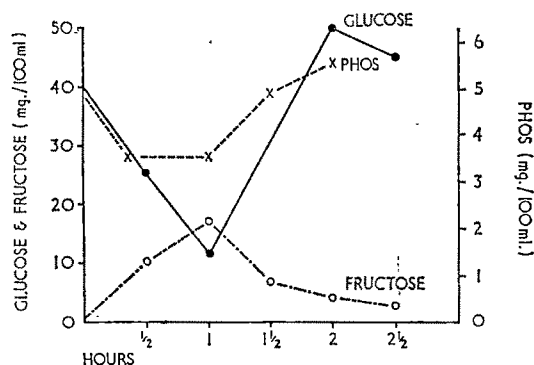


FIG. 1.—Case 1. Aged 1 year. Oral fructose tolerance test; 5 g. of fructose was given by mouth.

Subsequently the piece of liver from the biopsy preserved in the deep freeze at -35°C . was examined by Dr. A. D. Patrick in the Department of Chemical Pathology at the Hospital for Sick Children, London. Aldolase activities, with both fructose-1-phosphate and fructose-1-6-diphosphate as substrates, were estimated by the method of Leuthardt and Wolf (1955). The results (see Table) demonstrated a 50% reduction in the diphosphate aldolase activity and an almost complete absence of fructose-1-phosphate aldolase activity, giving a ratio of 6:1 instead of the normal ratio of approximately 1:1. Some of the same material was also examined by histochemical methods (Lake, 1965) and showed a reduction of aldolase activities with both fructose-1-phosphate and fructose diphosphate as substrates.

Aldolase Activity of Liver

		Activity ($\mu\text{moles NADH/min./g. Wet Wt. of Liver}$)		Activity Ratio F-1-6-P./F-1-P.
		F-1-P. Aldolase	F-1-6-P. Aldolase	
*Control 1	..	0.90	1.00	1.1
*Control 2	..	0.92	0.83	0.9
Case 1	..	0.08	0.49	6.1

* Control specimens were stored under the same conditions and for the same period as the specimen from Case 1.

Case 3

This male child born on 16 March 1964, birth weight 6 lb. 11 oz. (3.04 kg.), was the second child, both parents being healthy and unrelated. He was breast-fed for two days; the feed was then changed to a dried milk with added sucrose. He started vomiting, and at the age of 7 weeks was admitted to the Children's Hospital, Sheffield, with a provisional diagnosis of pyloric stenosis. He weighed 7 lb. 1½ oz. (3.22 kg.) and looked wasted but not dehydrated; there was no evidence of pyloric stenosis. His urine was normal to routine testing. During the next month he continued to feed poorly and did not gain weight: at the age of 11 weeks his liver was enlarged to two fingerbreadths below the costal margin, and in the next two months it increased in size. His urine contained an unidentified reducing substance on one occasion. He was very ill, and it was decided to give him a fructose-free diet without any preliminary tolerance tests. On this diet there was a steady improvement, interrupted only by a further fall in weight when sucrose was added to his feeds in error. During this setback fructose was identified in his urine and the total reducing substances in his blood were 77 mg./100 ml. with 45 mg./100 ml. of glucose:

a considerable proportion of the large difference of 32 mg./100 ml. was thought to represent fructose (a specific method for fructose was not at this time available at the hospital). He finally returned home at the age of 6 months and has been gaining weight steadily (Fig. 2). His liver was normal in size.

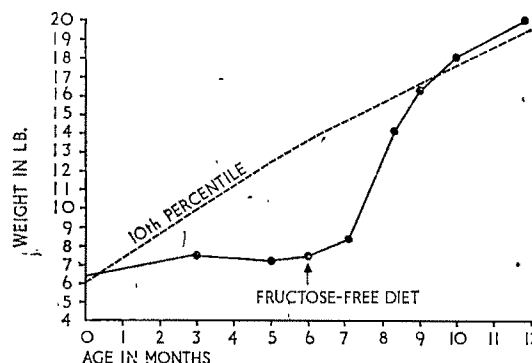


FIG. 2.—Case 3. Weight chart showing the effect of the introduction of a fructose-free diet.

The diagnosis in this child was initially obscured by the fact that his elder sister (Case 4) was diagnosed at the age of 5 years as having glycogen storage disease and had had a liver biopsy at the age of 5 years. However, examination of her notes and the biopsy sections showed no real evidence of glycogen storage. Her history follows.

Case 4

The elder sister of Case 3, born 24 May 1953, birth weight 6 lb. 11 oz. (3.04 kg.), was breast-fed for four weeks, then changed to a dried milk with added sucrose. At the age of 7 weeks she was admitted to the City General Hospital, Sheffield, with vomiting thought to be due to pyloric stenosis, but this was not confirmed. At 3 months she weighed 8 lb. 4 oz. (3.74 kg.) and her liver was three fingerbreadths below the costal margin. Her urine contained fructose on one occasion and a reducing substance, "not glucose," on another occasion. She was thought to have glycogen storage disease. At the age of 5 years a liver biopsy showed very marked fatty change, with a normal amount of glycogen. When the diagnosis of fructose intolerance was suggested in her younger brother the evidence for the diagnosis of glycogen storage disease was reviewed. On further questioning the mother said that the child had always avoided sweet things. She was then given a similar diet to that of her brother. It has not been possible to carry out any formal confirmation of the diagnosis in these children.

Case 5

A girl born on 30 September 1957, birth weight 7 lb. (3.18 kg.), was the first child of healthy unrelated parents. She was breast-fed for a few days and then changed to a dried milk. Her mother found that the addition of sucrose to the feeds upset her and therefore stopped adding it. She had always been noticed to have an aversion to sweet things. At the age of 7 years 4 months she attended the Children's Hospital, Sheffield, with a history of listlessness for a few weeks. Since she had started school dinners, which she disliked, she had been generally unwell.

She was a healthy-looking girl, of normal height and weight for her age; the only abnormality was a firm liver enlarged to two fingerbreadths below the costal margin. The urine was normal and contained no reducing substance. It was decided to do an oral fructose-tolerance test. On 12 February 1965 she was given 12.5 g. of fructose (0.5 g./kg. body weight). After one hour she felt faint and looked pale. The level of fructose rose slowly to a maximum of 24 mg./100 ml. at one and a half hours and the blood inorganic phosphorus also fell: the blood glucose level fell sharply from a fasting level of 79 mg. to 30 mg./100 ml. at one hour and 27 mg. at two hours. These results were regarded as typical of fructose intolerance. She seemed well shortly after the test was completed and was allowed to go home. One week later she refused food and two days later complained of abdominal pain: 12 days after the test she was slightly jaundiced and her liver was four fingerbreadths below the costal margin. The urine contained bilirubin and a

slight excess of urobilin, but no fructose. Serum transaminases were raised (S.G.P.T. 920 units/100 ml., S.G.O.T. 480 units/100 ml.), but other liver-function tests were normal. After this she improved slowly on a fructose-free diet, and one month later her liver was two fingerbreadths below the costal margin and transaminases were normal.

Two years after the diagnosis was made she was no longer listless, her liver was just palpable and felt normal. Her teeth had been examined by Mr. R. C. W. Dinsdale, at the Charles Clifford Dental Hospital, Sheffield, and been found to be completely free of caries.

Presentation

The presenting symptoms of fructose intolerance are extremely varied. An infant with this condition will thrive normally as long as he is wholly breast-fed: as soon as feeds containing sucrose—that is, cane sugar or beet sugar—are given, vomiting occurs or the infant may refuse to feed after sucking for a few minutes. Severe neonatal jaundice with hepatomegaly may develop, with signs of acute liver failure, just as may occur in galactose intolerance; or the vomiting may be so severe as to suggest pyloric stenosis. The condition may be fatal in infancy (Sacrez *et al.*, 1962; Levin and Snodgrass, 1965) unless the diagnosis is made promptly or the mother realizes, having had previously affected children, that glucose must be substituted for sucrose. Later the hepatomegaly may suggest glycogen storage disease. By the time school age is reached the child will have learned to exclude sweet things and root vegetables from his diet, but the necessity of eating school meals causes severe distress, which may be interpreted as a behaviour disorder or school phobia. In hypoglycaemic fits, particularly with hepatomegaly, fructose intolerance should always be considered (Levin and Snodgrass, 1965). Swales and Smith (1966) have reported fructose intolerance in an adult and have pointed out that the vague symptoms may often lead to a diagnosis of "neurotic ill-health."

Diagnosis

In many cases of fructose intolerance a detailed dietetic history may point to the correct diagnosis, and it is important not only that artificial milks and infant foods should be accurately labelled, showing the exact monosaccharide or disaccharide which they contain, but also that the physician should know what sugars are added to the feeds of the infant under his care.

It must be emphasized that the absence of fructose in the urine does not exclude fructose intolerance. Even if present, fructosuria will be missed if a glucose-specific (glucose-oxidase) method is used for screening urines. In fructose intolerance, glucose and other sugars may be present in the urine at the same time as fructose, and therefore in any suspected metabolic disorder it should never be assumed that glucose if present is solely responsible for a positive reducing reaction. Chromatography of the urine should be used to identify all the sugars present.

The symptoms in fructose intolerance are due predominantly to the severe hypoglycaemia which occurs after a dose of fructose; nausea, vomiting, and epigastric discomfort are common if the fructose is given orally. The diagnosis can be confirmed by a fructose-tolerance test or by estimating the activity of fructose-1-phosphate aldolase in fresh or frozen liver tissue obtained by biopsy. Fructose-tolerance tests can be performed after an oral dose (0.5 g./kg.), but it has been shown that more satisfactory results can be obtained by an intravenous injection of half the oral dose (Cornblath *et al.*, 1963). Characteristically the fructose level in the blood rises to or above 20 mg./100 ml.; the blood inorganic phosphorus falls, and this is followed by a rapid fall of blood glucose to a level at which symptoms or even fits or unconsciousness may occur; such

severe hypoglycaemia can be rapidly reversed by an intravenous injection of glucose, which should be immediately available during the test. Another disadvantage of the fructose-tolerance test is the delayed development of liver damage, as occurred in our Case 5.

In view of these disadvantages of the tolerance test it is not surprising that a liver biopsy should be thought to be preferable. Our experience confirms what has previously been shown (Sacrez *et al.*, 1962; Desbuquois, 1965), that orthodox histological examination of the liver may be extremely misleading, as the sections may show a "neonatal hepatitis" (Case 1), gross fatty change (Case 4), or early cirrhosis, and it would appear that there are no histological changes which are specific to fructose intolerance. Therefore the only useful investigation on biopsy material is an estimation of the fructose-1-phosphate aldolase activity in the liver.

In practice the ratio of liver aldolase activities with both fructose-1-6-diphosphate and fructose-1-phosphate as substrates is usually determined. This ratio (F.1-6-P./F.1-P.), which is approximately 1 for normal liver, increases to 6 or greater in fructose intolerance due to the almost complete absence of fructose-1-phosphate aldolase activity (Schapira *et al.*, 1961-2). The appreciable activity of fructose-1-phosphate aldolase on fructose diphosphate would account for the moderate decrease in aldolase activity which is observed with the diphosphate as substrate. A liver biopsy may well be the investigation of choice if adequate biochemical facilities are available, but it cannot be too strongly emphasized that neither a liver biopsy nor a fructose-tolerance test should be done when the patient is severely ill; this applies particularly to the newborn infant. A trial of a fructose-free diet can be easily arranged, and a dramatic improvement (Case 3) may give confirmation of the probable diagnosis without in any way prejudicing the performance of a diagnostic test when the patient's condition has improved.

The evidence that in fructose intolerance there is a considerable reduction of fructose-1-phosphate aldolase activity in the liver is based on numerous reports on biopsy material (Desbuquois, 1965). Confirmation of the expected increase in fructose-1-phosphate in the liver of affected individuals has also been provided by Milhaud (1964) and Rossier *et al.* (1966). Apart from this primary defect (Fig. 3) the accumulation of fructose-1-phosphate in the liver appears to inhibit the activity of fructokinase (Froesch *et al.*, 1959) and of fructose-1-6-diphosphate aldolase (Desbuquois, 1965), causing, respectively, a rise in fructose in the extracellular fluids and the inhibition of gluconeogenesis. There is also a block in the release of glucose from the liver; after a dose of fructose glucagon fails to produce its usual hyperglycaemic effect, though the glucagon effect is restored later (Cornblath *et al.*, 1963). It has been suggested that this interruption of glucose release from the liver is due to a failure of phosphorolytic degradation of glycogen, resulting

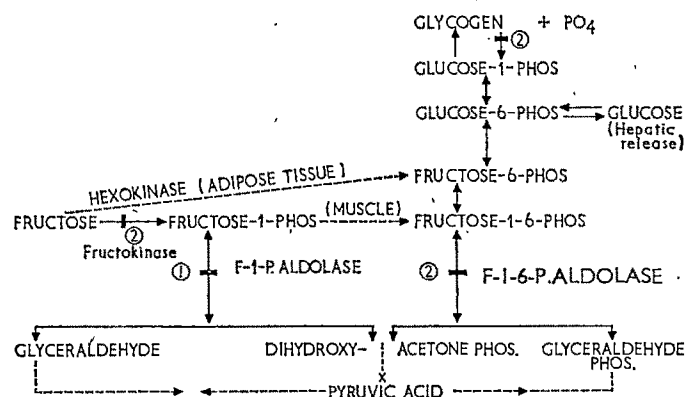


FIG. 3.—The metabolic pathways of fructose. (1) Indicates site of the primary block in fructose intolerance. (2) Indicates sites of secondary blocks.

from the depletion of intracellular phosphate after its immobilization as fructose-1-phosphate, though this is still uncertain (Desbuquois, 1965). The severe hypoglycaemia resulting from a dose of fructose appears to be the resultant of a failure of glycogenolysis in the liver, with continued peripheral utilization of glucose by the tissues. The cause of the liver damage itself remains unexplained; it is possible that the intrinsic metabolism of the liver cell is damaged, owing to depletion of cellular adenosine triphosphate (Levin *et al.*, 1963).

Treatment and Prognosis

Treatment consists in the exclusion of sucrose and fructose from the diet, with the addition of ascorbic acid, as the daily intake is otherwise likely to be low. Difficulties often arise in the prescription of medicines or antibiotic syrups, and the patients and their doctors need to be warned specifically about this point.

Severe or fatal liver damage is likely to occur in infancy if the diagnosis is not suspected. As the case histories show, the diagnosis is commonly made by an observant mother if she has already had a similarly affected infant, but the exclusion of fructose-containing substances from the diet by the mother, or later by a self-selected diet, is not usually strict enough to prevent the development of hepatomegaly. It is probable, therefore, though there is as yet no certain evidence of this, that the fatty infiltration of the liver will in due course be followed by cirrhosis. Our own observations suggest that a strict fructose-free diet in children will cause a complete return to normality, though a long follow-up has not yet been possible.

Summary

Fructose intolerance is a genetically determined metabolic disorder inherited as an autosomal recessive. It is probably as common as the more widely recognized galactose intolerance.

In affected individuals fructose given orally or intravenously causes profound hypoglycaemia, with a rise of the level of

fructose in the blood to 20 mg./100 ml. or more. The essential abnormality is an absence of the liver enzyme fructose-1-P. aldolase. The condition may present in infancy as neonatal jaundice with hepatomegaly, or with vomiting and failure to thrive: in older children hypoglycaemic fits may occur or glycogen storage disease may be suspected on account of the enlarged liver. In adults the symptoms are less obvious, and may be dismissed as "neurotic ill-health."

The diagnosis is made by an oral or I.V. fructose tolerance test or by estimation of the activity of the specific aldolase in a fresh or frozen liver biopsy.

Treatment is by the exclusion of fructose and sucrose from the diet.

Five children with this condition are described.

We wish to thank Dr. A. D. Patrick, Department of Chemical Pathology, the Hospital for Sick Children, London, for his help in the investigation of Case 1 and for his advice in the preparation of this paper. We are also grateful to Professor Sir Alan Moncrieff, Dr. R. R. Gordon, and Dr. C. B. M. Warren for allowing us access to their clinical records.

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Abnormal Splitting of the Second Heart Sound in Renal Failure

D. G. GIBSON,* M.B., B.CHIR., M.R.C.P.

Brit. med. J., 1967, 4, 141-144

Abnormally wide splitting of the second heart sound due to delay in the pulmonary component is a significant physical sign (Leatham, 1958). Though it is most frequently due to right bundle-branch block or an atrial septal defect, it may also result from any condition causing mechanical prolongation of right ventricular systole, such as pulmonary valve stenosis, or from right ventricular failure due to severe pulmonary hypertension (Shapiro *et al.*, 1965). However, delay in pulmonary valve closure by more than 0.03 second, the value usually taken as the upper limit of normal (McKusick, 1958), has been observed in a number of patients with advanced renal failure in whom none of these conditions was present. Since its recognition has proved to be of value in the management of such patients, it is documented here, and its clinical associations are defined more precisely.

Material and Methods

Observations were made during the routine management of eight patients with advanced renal failure. All had radio-

logical evidence of perihilar or interstitial pulmonary oedema, and all but one had dyspnoea, orthopnoea, and crepitations over the lungs. Further clinical, biochemical, and haemodynamic data are summarized in Table I. The haemodynamic data form part of those presented in a previous communication (Gibson, 1966). Biochemical estimations were performed by autoanalyser techniques. The total fluid loss during peritoneal dialysis was calculated from the cumulative balance of each exchange, and during haemodialysis from the weight loss of the patient. Drug therapy was not altered during the procedure, except in Case 8, where ethanol inhalations, morphine, aminophylline, and pentolinium were given without effect on the pulmonary oedema.

Phonocardiograms were recorded from the position along the left sternal edge where the splitting of the second sound was most obvious clinically. A Mingograf direct writing recorder was used, running at a paper speed of 100 mm. per second. On account of the patients' dyspnoea, it was not always pos-

* Registrar, Medical Unit, Westminster Hospital, London S.W.1. Present appointment: Registrar, National Heart Hospital, London W.1.

TABLE I.—Clinical Data

Case No.	Age	Sex	Diagnosis	Blood Pressure (mm. Hg)		Haemoglobin (g./100 ml.)		Blood Urea (mg./100 ml.)		Plasma Bicarb. (mEq/l.)		Mean Right Atrial Pressure (mm. Hg)		Mean Pulmonary Arterial Pressure (mm. Hg)		Fluid Volume Removed (–) or Administered (+) (litres)	Anti-hypertensive Agents
				A	B	A	B	A	B	A	B	A	B	A	B		
1	25	M	Chronic glomerulonephritis	130/80	160/110	6.1	12	431	215	15	235	—	—	—	—	–10.3	Methyldopa
2	60	M	Malignant hypertension	180/130	120/80	9.2	9.0	550	370	14	17	1	—	32†	—	–5.6	Nil
3	26	M	Chronic glomerulonephritis	140/90	110/70	6.1	5.4	396	258	13	21	1	1	16	17	–7.5	"
4	24	M	Chronic glomerulonephritis	240/120	220/140	6.7	5.6	560	247	11	25	4	3	30	19	–6.9	"
5	50	M	Chronic pyelonephritis	150/90	160/90	9.2	11.1	233	143	17	27	—	—	—	—	–10.0	Methyldopa
6	59	M	Streptococcal septicaemia	130/60	180/110	13	11.5	290	181	23	17	1	3	21	27	–2.6	Nil
7	26	M	Chronic pyelonephritis	150/90	150/100	5.7	8.3	238	235	25	27	—	—	—	—	+1.2	Methyldopa
8	27	M	Chronic pyelonephritis	140/80	*	6.8	7.9	200	112	22.5	21	—	—	—	—	*	Guanethidine, Pentolinium

A = Before dialysis (Cases 1–6 and 8) or transfusion (Case 7). B = After dialysis (Cases 1–6 and 8) or transfusion (Case 7).

* Please see Table III. † Peak R.V. pressure—the pulmonary artery was not entered. Pressures are expressed in mm. Hg above a point 5 cm. below the sternal angle.

sible to use an indirect carotid pulse transducer, and in these patients the aortic component of the second sound was identified from an apical phonocardiogram. For the same reason, recordings were made during spontaneous respiration rather than held expiration. The heart sounds were timed from their initial deflections. Specimen phonocardiograms are reproduced in Figs. 1–6.

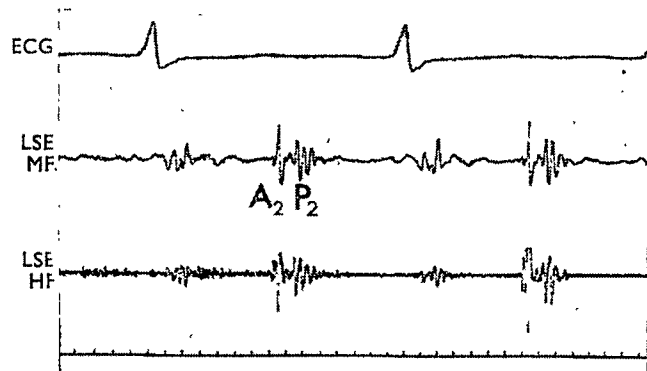


FIG. 1.—Case 2. Phonocardiogram before treatment, recorded from the left sternal edge (LSE) at high (HF) and medium (MF) frequencies. The pulmonary component of the second sound (P_2) occurs 0.055 second after the aortic (A_2), during spontaneous expiration. In this and the other phonocardiograms, the marker represents time intervals of 0.04 second.



FIG. 2.—Case 2. Phonocardiogram after dialysis.

Cases 1–6 were admitted in pulmonary oedema and were treated with hypertonic peritoneal dialysis. Phonocardiograms were recorded before and after the procedure.

Case 7.—This patient had radiographic evidence of pulmonary oedema though it was not causing symptoms. His anaemia was therefore treated with slow infusion of 1.2 litres of packed cells. This caused the appearance of abnormal splitting of the second heart sound and transient dyspnoea, but there were no other untoward effects. Phonocardiograms were recorded before and after the transfusion.

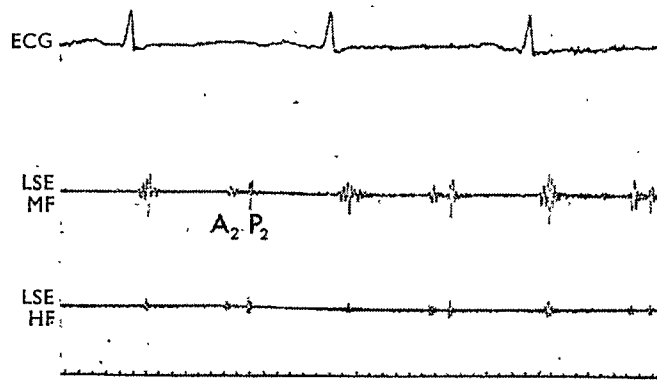


FIG. 3.—Case 3. Phonocardiogram before treatment, showing separation of the two components of the second sound by 0.06 second in expiration.

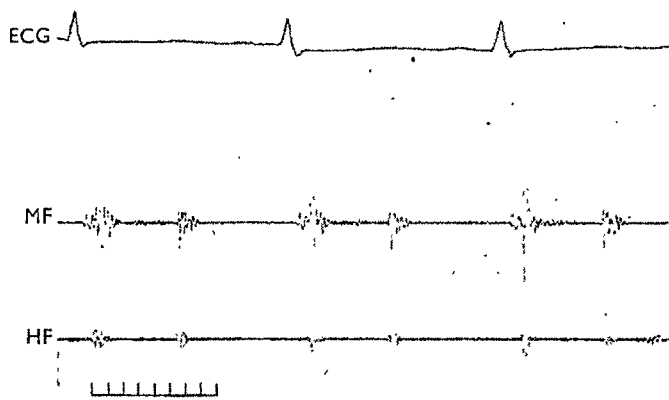


FIG. 4.—Case 3.—Phonocardiogram after dialysis.

Case 8.—This patient had radiographic evidence of pulmonary oedema, but no undue dyspnoea or orthopnoea. However, wide splitting of the second heart sound was noted clinically and recorded phonocardiographically (P.C.G. 1 in Table III and Fig. 5). To treat his anaemia a slow transfusion of packed cells was started, but after only 100 ml. had been given he developed a severe attack of acute pulmonary oedema which proved resistant to the usual methods of treatment. Haemodialysis by means of a hypertonic bath was therefore started, and within 45 minutes his symptoms had subsided,

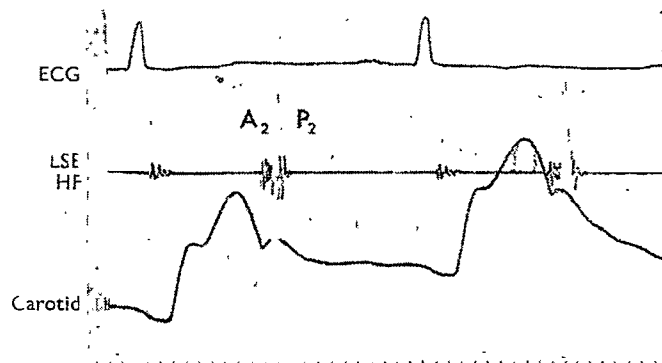


FIG. 5.—Case 8. Phonocardiogram before the initial blood transfusion, taken during spontaneous expiration. The aortic component of the second sound, occurring with the incisura on the carotid pulse recording, precedes the pulmonary component by 0.055 second.

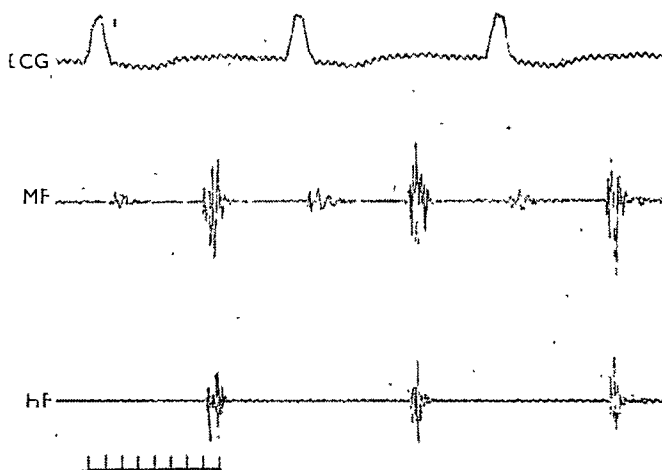


FIG. 6.—Case 8. Phonocardiogram after dialysis.

after the net removal of 500 ml. of fluid. P.C.G. 2 was recorded at this time. When the rate of infusion of the blood was increased so that the net fluid loss dropped to 200 ml. mild symptoms recurred and abnormal splitting of the second sound was again evident (P.C.G. 3), but both resolved on further dehydration. P.C.G. 4 was recorded towards the end of the dialysis.

Results

The phonocardiographic observations are summarized in Table II. Wide splitting of the second heart sound in expiration was recorded at some stage in all the patients. This was due to delay in closure of the pulmonary valve relative to that of the aortic by 0.04 to 0.06 second. There was normal inspiratory augmentation of the A_2 - P_2 interval. In Case 7 abnormal splitting appeared after blood transfusion. The relation between changes in blood volume and abnormal splitting was investigated in more detail in Case 8. In this patient the abnormality was relieved after the removal of plasma ultrafiltrate and recurred after blood transfusion. Details of the total volume of blood administered, the net fluid balance of the patient, and the phonocardiographic data are given in Table III.

Other Factors.—There was no consistent reaction between changes in the blood urea level and the development of abnormal splitting. In Cases 1-6 the blood urea was reduced during peritoneal dialysis, as the abnormality was corrected, while in Case 7 it remained unchanged as delay in pulmonary valve closure was provoked by blood transfusion. In Case 8 it fell throughout the haemodialysis as abnormal splitting was precipitated by blood transfusion and relieved by dehydration. Similarly, the return of the heart sounds to normal could be dissociated from changes in the systemic arterial pressure, or from correction of the anaemia, hyperkalaemia, or metabolic acidosis present initially in some of the patients.

TABLE II.—Phonocardiographic Data in Cases 1-7

Case No.	Before Dialysis				After Dialysis			
	Pulse Rate (Beats/min.)	Q-A2 Interval (sec.)	A ₂ -P ₂ Interval (sec.)	Inspiratory Augmentation of A ₂ -P ₂ Interval (sec.)	Pulse Rate (Beats/min.)	Q-A2 Interval (sec.)	A ₂ -P ₂ Interval (sec.)	Inspiratory Augmentation (sec.)
1	74	0.36	0.06	0	90	0.34	0.02	0.01
2	105	0.30	0.055	0.01	125	0.26	0.01	0.02
3	105	0.305	0.056	0.015	105	0.29	0.01	0.02
4	90	0.31	0.05	0.01	86	0.32	0.02	0.02
5	83	0.36	0.05	0.02	72	0.38	0.02	0.03
6	81	0.31	0.04	0.02	80	0.32	0.02	0.02
7	Before Transfusion				After Transfusion			
	Pulse Rate (Beats/min.)	Q-A2 Interval (sec.)	A ₂ -P ₂ Interval (sec.)	Inspiratory Augmentation of A ₂ -P ₂ Interval (sec.)	Pulse Rate (Beats/min.)	Q-A2 Interval (sec.)	A ₂ -P ₂ Interval (sec.)	Inspiratory Augmentation (sec.)
	88	0.40	0.02	0.02	82	0.41	0.045	0.01

The Q-A2 interval is the time interval between the initial deflection of the E.C.G. and the onset of aortic valve closure. The Q-P2 interval is the time interval between the initial deflection of the E.C.G. and the onset of pulmonary valve closure.

TABLE III.—Phonocardiographic Data in Case 8

P.C.G. No.	Time After Start of Haemodialysis (min.)	Blood Pressure (mm. Hg)	Volume of Blood Given (ml.)	Net Fluid Balance* (ml.)	Phonocardiogram			
					Pulse Rate (Beats/min.)	Q-A2 Interval (sec.)	A ₂ -P ₂ Interval (sec.)	Inspiratory Augmentation of A ₂ -P ₂ Interval (sec.)
1	—	140/80	0	0	70	0.39	0.055	0.015
2	50	180/100	200	-500	100	0.26	0.02	0.02
3	105	200/130	800	-200	102	0.26	0.04	0.01
4	255	210/130	1,600	-900	103	0.26	0.02	0.03

* Net loss of fluid from the patient is expressed as a negative balance.

Discussion

In the present series of patients, right bundle-branch block as a cause of the abnormal splitting of the second heart sound could be excluded by the absence of the characteristic E.C.G. pattern. There was no supportive evidence of an atrial septal defect, or other congenital heart disease, and, in any case, normal splitting was observed at some stage in all the patients. In no case was there any clinical evidence of severe pulmonary hypertension causing right ventricular failure, and in four patients it was excluded by direct measurement of the right atrial and pulmonary arterial pressures. There was, however, strong correlation with the degree of hydration of the patients. Abnormal splitting was relieved in all patients in whom it was initially present by dehydration, while in two patients the abnormality developed after the administration of blood. Alwall *et al.* (1953) have stressed that pulmonary oedema in renal failure is also a manifestation of fluid overload, and have demonstrated resolution of the radiographic appearances with dehydra-

tion, even in the presence of a rising blood urea. It was therefore of interest that though abnormal splitting was sought in a large number of patients with renal failure it was found only in the presence of pulmonary oedema: in particular, it was not found in patients with gross peripheral oedema due to the nephrotic syndrome, in the absence of pulmonary oedema.

The mechanism by which fluid overload causes delay in pulmonary valve closure is not clear. Theoretically, it might be due to prolongation of right ventricular activation, isovolumic contraction, or ejection. With a normal E.C.G. it is unlikely that selective prolongation of right ventricular activation occurred. In the absence of mechanical obstruction to right ventricular ejection, pulmonary hypertension, or a left-to-right shunt, prolongation of either right ventricular isovolumic contraction or right ventricular ejection implies impairment of the function of the right ventricle relative to that of the left. This might be due to the effect of some toxic metabolite retained as a result of the renal failure. Though the results in Case 8 suggest that external fluid balance is important, such prolongation of right ventricular systole does not occur in normal subjects after the administration of relatively small volumes of fluid. Alternatively, impairment of right ventricular function may be caused by reflex activity. It has been demonstrated that stimulation of the carotid sinus baroreceptors (Daly and Luck, 1958) and also of efferent fibres in the vagus (Daggett *et al.*, 1966) may lead to a reduction in ventricular contractility. In the abnormal circulatory state present in these patients, such reflex activity might have been present.

Delay in the pulmonary component of the second sound has been recorded in a number of similar clinical situations. Though abnormal splitting appears to be unusual in the presence of pulmonary oedema due to left ventricular failure or mitral stenosis, it has been recorded inconstantly in association with the pulmonary oedema of high altitude (Fred *et al.*, 1962), and also under certain circumstances in cholera (Greenough, 1966). In the former condition, cardiac catheterization has revealed high pulmonary arterial pressures, which would provide a satisfactory explanation of a prolonged right ventricular ejection time. In cholera, acute pulmonary oedema, gallop rhythm, and wide splitting of the second heart sound may be provoked by the administration of excess saline in the presence of an uncorrected metabolic acidosis. Though haemodynamic and phonocardiographic data are not yet available, the clinical picture has features in common with that occurring in renal failure. In severe systemic hypertension the interval between the Q wave on the E.C.G. and aortic valve closure is often longer than that predicted from the pulse rate; yet splitting of the second heart sound is usually normal. It has been pointed out that the concomitant delay in pulmonary valve closure has not been adequately explained (Shah and Slodki, 1964). Since seven out of the eight cases described in

the present series were hypertensive, it is possible that a similar mechanism was involved.

In a study of the second heart sound in 118 cases of ostium secundum atrial septal defect, Aygen and Braunwald (1962) found that the mean A_2-P_2 interval was 0.05 second and that if the inspiratory augmentation of the A_2-P_2 interval was less than 0.01 second then the split might be regarded as "fixed." Thus the abnormality described in the present series of patients is comparable to that seen in the average case of atrial septal defect, and is readily apparent on auscultation. Though its absence does not exclude the presence of fluid overload, its presence appears to be a sign of incipient pulmonary oedema. In such circumstances fluid should be administered with caution, since the transfusion of even small amounts has led to the development of acute pulmonary oedema (as in Case 8) or epileptic fits.

Summary

Abnormally wide splitting of the second heart sound, due to delay in the pulmonary component, is described in eight patients with advanced renal failure. In seven the abnormality was relieved after the removal of extracellular fluid by peritoneal dialysis or haemodialysis, and in two it was provoked by blood transfusion. Though the mechanism of its production is not clear, it appears to be a useful sign of fluid overload in the uraemic patient.

I am grateful to the Department of Chemical Pathology for permission to reproduce the results of biochemical investigations; to Mrs. D. Winter, of the Department of Cardiology, for assistance with the phonocardiography; to Dr. P. R. Fleming for helpful discussion; and to Professor M. D. Milne for constructive criticism of the manuscript and for permission to publish observations made on patients admitted under his care.

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Effect of Glucagon on Intravenous Glucose Tolerance

D. A. TURNER,*†‡ M.Sc.; T. K. AUDHYA,* B.Sc.; D. G. CRAMP,* A.I.M.L.T.
C. D. HOLDSWORTH,†§ M.D., M.R.C.P.; NEIL MCINTYRE,†|| M.B., B.Sc., M.R.C.P.

Brit. med. J., 1967, 4, 145-146

The plasma insulin response to intestinally administered glucose is greater than that elicited by the same quantity of glucose given intravenously (McIntyre *et al.*, 1965). McIntyre and his colleagues suggested that the most likely explanation is the release from the intestine of a humoral factor which stimulates insulin secretion. The identity of this hormone remains speculative, but the intestinal hormones secretin (Pfeiffer *et al.*, 1965; Dupré *et al.*, 1966; Unger *et al.*, 1966b), pancreozymin (Ketterer *et al.*, 1966), and glucagon (Samols *et al.*, 1965a, 1965b) have all been reported to stimulate the release of insulin.

Glucagon is an attractive possibility. Its presence in the gastrointestinal tract has been indicated by biological (Kenny and Say, 1962; Makman and Sutherland, 1964) and immunochemical techniques (Samols *et al.*, 1966; Unger *et al.*, 1966a). Samols *et al.* (1965a) demonstrated that the injection of 1 mg. of glucagon into normal fasting humans produced a rise in plasma insulin that could not be accounted for by elevation of blood glucose. In addition, glucagon has been shown to stimulate the release of insulin from isolated pancreatic tissue (Candela *et al.*, 1963; Turner and McIntyre, 1966). Furthermore, a rise in plasma glucagon levels was found after the oral administration of 100 g. or more of glucose (Samols *et al.*, 1965b; Lawrence, 1966), though Unger and Eisentraut (1964), Lawrence (1966), and Young and Jenkinson (1966) have observed a fall in plasma glucagon after the ingestion of 50 g. (or 1 g./kg.) of glucose.

McIntyre *et al.* (1965) found that the higher insulin response to intestinal glucose was associated with improved glucose tolerance; arterial blood glucose levels were lower during intestinal infusion than during intravenous infusion of the same quantity of glucose. This effect was also demonstrated in two patients after end-to-side portacaval anastomosis, and could not therefore be accounted for by the removal of ingested glucose from the portal circulation on its initial passage through the liver, as suggested by Scow and Cornfield (1954).

If the intestinal release of glucagon is responsible for the enhanced insulin secretion associated with oral glucose it might also be responsible for the superiority of oral over intravenous glucose tolerance. Such an effect would at first sight seem unlikely, as glucagon administration normally produces glycogenolysis and hyperglycaemia. However, Samols *et al.* (1965a) found that the high plasma insulin levels which resulted from the injection of 1 mg. of glucagon were associated with an increased rate of assimilation of a simultaneously administered rapid intravenous injection of glucose. It seemed possible that a similar effect of glucagon on glucose disposal might be seen with more prolonged infusions of glucose and glucagon, simulating the relatively slow absorption of glucose after oral administration. This possibility was tested in the following studies.

Methods

Eight healthy volunteers were given two separate intravenous infusions of the same quantity of 10% glucose after an overnight fast. On one occasion the glucose was given alone, and on the other glucagon was added to the glucose to give a rate of glucagon infusion of 0.6-12 µg. per minute. The actual quantities given to each subject are shown in the Tables. Glucose was given at a rate of 900 or 600 mg. per minute by means of a constant infusion pump.

Arterial blood was sampled through an indwelling Riley needle. Blood glucose was measured by an automated glucose oxidase method (Cramp, 1967) and plasma insulin by radioimmunoassay (Samols and Bilkus, 1964). Plasma samples were normally stored at -15° C. before insulin assay; those from the glucose-plus-glucagon infusion in Subject 6 were inadvertently left at room temperature and insulin assays were not performed on these samples.

Several subjects experienced nausea at the end of the glucagon infusion. A reaction characteristic of hypoglycaemia was also seen after cessation of the infusion; relief with glucose was rapid.

Results

Plasma insulin results are presented in Table I. In all seven studies in which plasma insulin was measured the levels were higher during the infusion of glucose plus glucagon than with glucose alone. The difference was evident at five minutes and continued to increase during the whole period of sampling. The greatest effect of glucagon on insulin secretion was seen in those subjects who received the largest dose of glucagon. This was particularly striking in Subject 2, in whom the insulin rose very rapidly with the glucagon load and reached a level of 204 µu./ml. at 20 minutes while the equivalent level with glucose alone was only 36 µu./ml.

The blood glucose values are presented in Table II. All subjects showed a more rapid rise in blood glucose during the first 30 minutes of the infusion of glucose plus glucagon than during the first 30 minutes of the infusion of glucose alone, while two of the subjects (Nos. 1 and 6) showed higher levels during the first 90 minutes. In the other six subjects the curves crossed and the blood glucose levels were lower at the end of the glucagon plus glucose infusion. In five of the six subjects the cross-over occurred between 30 and 70 minutes, while in the sixth it did not occur until after 105 minutes.

The magnitude of the difference in glucose levels during the first 30 minutes was, like the insulin response, related to the dose of glucagon administered. In the three subjects (Nos. 6-8) who were given 0.6 or 0.8 µg. of glucagon per minute the blood glucose did not rise more than 17 mg./100 ml. above the corresponding level which resulted when glucose alone was infused. In those subjects who received 2 µg. per minute or more the maximum difference for each individual during the first 30 minutes was not less than 41 mg./100 ml.

Discussion

In these studies glucagon did not produce an early improvement in glucose tolerance, despite the higher plasma insulin levels obtained when glucagon was infused with glucose. Glucose levels were actually higher during the first 30 to 45 minutes of the infusion of glucose plus glucagon than during

* Alexander Simpson Laboratory for Metabolic Research, St. Mary's Hospital, London W.2.

† Lecturer in Medicine, Royal Free Hospital, London W.C.1.

‡ Present address: Department of Medicine, Guy's Hospital Medical School, London S.E.1.

§ Present address: St. Leonard's Hospital, London N.1.

|| Present address: Gastrointestinal Unit, Massachusetts General Hospital, Boston, Mass., 02114, U.S.A.

TABLE I.—Plasma Insulin Response to Slow Intravenous Infusion of 10% Glucose With and Without Infusion of Glucagon

Subject	Age	Rate of Glucose Infusion (ml./min.)	Rate of Glucagon Infusion (μg./min.)	Plasma Insulin (μu./ml.)												
				Fasting		5'	10'	15'	20'	30'	45'	60'	75'	90'	105'	120'
1	22	6.0	0 12.0	8	8	14	—	—	17	13	21	26	24	34	41	41
				11	11	29	38	46	57	77	111	128	172	230	205	250
2	21	9.0	0 10.0	13	15	33	35	34	36	46	48	62	62	71	83	90
				11	8	60	130	169	204	260	299	307	373	424	478	461
3	22	9.0	0 10.0	7	8	19	17	15	23	26	24	27	56	50		
				9	10	24	32	45	54	89	155	200	223			
4	22	9.0	0 2.0	10	18	29	25	29	23	38	27	61	69	75	80	88
				14	15	45	50	63	62	56	76	100	155	174	200	190
5	27	9.0	0 2.0	8	16	49	52	51	60	76	88	104	144	155		
				20	18	78	81	75	103	128	232	324	336	404		
6	26	6.0	0 0.8	—	—	—	—	—	—	—	—	—	—	—	—	—
				—	—	—	—	—	—	—	—	—	—	—	—	—
7	21	6.0	0 0.6	14	8	21	19	43	42	44	53	60	61	94		
				16	20	42	65	86	91	113	142	174	155			
8	21	6.0	0 0.6	16	16	24	29	28	31	34	35	38	56	62		
				14	14	26	35	43	45	53	86	90	150	189		

TABLE II.—Blood Glucose Response to Slow Intravenous Infusion of 10% Glucose With and Without Infusion of Glucagon

Subject	Rate of Glucose Infusion (ml./min.)	Rate of Glucagon Infusion (μg./min.)	Arterial Blood Glucose (mg./100 ml.)													
			Fasting			5'	10'	15'	20'	30'	45'	60'	75'	90'	105'	120'
1	6.0	0	76	80	82	120										
		12.0	100	94	90	137	160	184	146	165	175	225	225	240	275	270
2	9.0	0	50	78	75	126	130	160	170	190	195	200	240	230	198	180
		10.0	75	78	75	117	173	190	191	207	196	170	205	190	195	170
3	9.0	0	80	70	71	120	135	160	176	195	230	251	255			
		10.0	75	81	85	140	168	195	210	240	255	236	230	300		
4	9.0	0	66	66	66	99	107	123	146	163	184	191	212	176	173	162
		2.0	69	73	66	113	137	165	187	198	194	182	186	147	149	137
5	9.0	0	62	62	62	94	125	147	159	176	214	245	258	264	273	272
		2.0	66	66	68	110	147	195	220	258	275	277	286	280	280	264
6	6.0	0	75	75	77	95	100	106	115	130	145	145	140	138	140	
		0.8	80	80	80	95	110	115	122	145	160	150	145	140	115	100
7	6.0	0	90	92	90	130	152	160	180	180	205	198	168	160	121	
		0.6	90	95	92	130	155	172	187	192	170	160	160	140	121	86
8	6.0	0	90	90	94	116	125	130	140	155	165	182	180	140	140	100
		0.6	85	90	90	110	125	136	150	168	182	175	164	150	115	85

the infusion of glucose alone. It would seem that the hyperglycaemic-glycogenolytic effect of glucagon initially overcame the glucose-lowering effect which should have resulted from the increased insulin levels. In four of the subjects there was a change in the shape of the glucose curves during the infusion of glucose plus glucagon; the arterial blood glucose level fell and reached values below those found during the infusion of glucose alone. This suggests that when the short-lived glycogenolytic effect was over the effect of high insulin levels on peripheral glucose uptake could become manifest.

The glycogenolytic effect of glucagon seen in these studies suggests that it is unlikely that glucagon is the intestinal beta-cell stimulant suggested by McIntyre *et al.* (1965). A clear enhancement of insulin secretion can be obtained with 50 g. of oral glucose; elevation of plasma glucagon levels, however, has been consistently demonstrated only with the ingestion of larger doses. In addition, no glycogenolytic effect appears to occur with oral glucose; such an effect was presumably the cause of the higher blood glucose levels which we observed when glucagon was added to an infusion of glucose. Though we made no measurement of plasma glucagon the small amounts of glucagon infused should have produced plasma levels similar to those obtained with oral glucose (Samols *et al.*, 1965b).

Further evidence against the role of intestinal glucagon has been presented by Samols *et al.* (1966). They have claimed that glucagon of intestinal and pancreatic origin can be differentiated immunologically and that the rise in plasma glucagon which occurs after oral glucose is due to pancreatic glucagon. They suggest that stimulation of insulin secretion after oral glucose is enhanced by a high local concentration of glucagon following its release from the alpha cells of the islets of Langerhans. If this hypothesis proves to be correct it will leave unexplained the mechanism by which the signal for enhancement of glucagon, and thus insulin, secretion is trans-

mitted from the intestine after the administration of oral glucose.

Summary

When glucagon and glucose were infused intravenously the rise in plasma insulin was greater than that found when glucose was infused alone. Blood glucose levels were also higher during the first 45 minutes of glucose and glucagon infusion, indicating that under these conditions the blood glucose level was more affected by the glycogenolytic action of glucagon than by the greater insulin release due to glucagon. It is thus unlikely that glucagon-induced elevation of plasma insulin levels is responsible for the superiority of oral over intravenous glucose tolerance.

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The Thyroid and Fibrinolysis

N. B. BENNETT,* M.D.; C. M. OGSTON,† M.B.; G. M. McANDREW,‡ M.B., M.R.C.P., M.R.C.P.ED.

Brit. med. J., 1967, 4, 147-148

The profound influence of thyroid dysfunction on metabolic processes is well recognized but only recently has its relation to fibrinolysis been studied. Using a whole blood clot lysis technique, Hume (1965) showed that overall blood fibrinolytic activity is diminished in hyperthyroidism and increased in hypothyroidism; it was suggested that the increased fibrinolytic activity provides a protective mechanism by which the untreated hypothyroid patient is spared the consequences of occlusive vascular disease. We have extended these findings by measuring the individual components of the fibrinolytic enzyme system in patients with hyperthyroidism and hypothyroidism and by observing the changes in the levels of these components during treatment of both disorders.

Methods

Plasminogen Activator.—Euglobulin clot lysis times were estimated by the method of Nilsson and Olow (1962), and the results were expressed by plotting the values logarithmically against units of fibrinolytic activity (Sherry *et al.*, 1959), 10 units being equated arbitrarily with a lysis time of 50 minutes. Such an assessment of plasminogen activator level has been shown to correlate well with specific assays of plasminogen activator (Fletcher *et al.*, 1964).

Plasma Plasminogen.—This was measured by the caseinolytic method of Remmert and Cohen (1949) as modified by Alkjaersig *et al.* (1959). The results were expressed in Sherry units.

Plasma Fibrinogen.—This was estimated by a modification (Ogston and Ogston, 1966) of the method of Ratnoff and Menzie (1951).

Plasma Antiplasmin.—This was assayed by the technique of Sherry *et al.* (1959) with activator-free plasmin prepared by spontaneous activation of plasminogen (Kabi Pharmaceuticals Ltd.) in 50% glycerol. Results were expressed as percentage inhibition of the standard plasmin preparation.

Plasminogen Activation Inhibitor.—This was measured in serum by the method of Bennett (1967). This technique measures an inhibitor of the activation process distinct from antiplasmin.

Subjects

All 18 hyperthyroid patients studied had an elevated four-hour gland uptake of radioactive iodine (range 44–80%, mean

64% of administered dose). All 16 hypothyroid patients showed depressed serum protein-bound iodine levels (range 1–3 µg./100 ml., mean 1.9 µg./100 ml). Patients with infections, inflammatory conditions, or disorders such as renal disease, which are known to alter the fibrinolytic system, were excluded. Inhibitors were not measured in the first 10 subjects studied. The control subjects were age-matched to the thyroid patients, and comprised members of the medical staff, healthy volunteers, and patients convalescent from a number of minor disorders not known to affect fibrinolysis. No formal studies of thyroid function were carried out on these control subjects, but they were clinically euthyroid and free of symptoms or signs of vascular disease.

Results

The mean levels and standard deviations of the components of the fibrinolytic system and fibrinogen are presented in the Table.

Plasminogen Activator Levels.—The mean blood activator level of the hyperthyroid group, 1.7 units, was significantly lower than that of the control subjects, 4.7 units, but the hypothyroid patients had a mean activator level, 5.4 units, only slightly greater than the control group, and the difference was not significant.

Inhibitor of Plasminogen Activation.—Patients in the hypothyroid group had a mean inhibitor level of 1.6 units, which is significantly lower than that of the controls, while the hyperthyroid patients had a mean level of 4.3 units, which is significantly higher than that of the euthyroid subjects. This inhibitor does not appear in the euglobulin fraction, and therefore cannot directly influence activator levels as measured by the euglobulin method.

Plasminogen.—The mean plasma plasminogen level in the hypothyroid group was higher than in the control group, and that in the hyperthyroid group was lower than in the control group. Both differences were significant.

Antiplasmin and Fibrinogen.—In contrast with the other components of the fibrinolytic system, antiplasmin levels did not differ in the three groups. Mean fibrinogen levels were greater in both hyperthyroid and hypothyroid groups than in the control subjects, the elevation in the hyperthyroid patients just reaching the 5% significant level, while the elevation in the hypothyroid subjects did not differ significantly from the controls. The difference between the mean fibrinogen levels of the hyperthyroid and hypothyroid groups themselves was not significant.

Levels of Components of Fibrinolytic Enzyme System and Fibrinogen in Hyperthyroid, Euthyroid, and Hypothyroid Subjects

	Hyperthyroid			Sig. of Diff. between Hyperthyroid and Euthyroid Subjects	Euthyroid			Sig. of Diff. between Hypothyroid and Euthyroid Subjects	Hypothyroid		
	No.	Mean Level	S.D.		No.	Mean Level	S.D.		No.	Mean Level	S.D.
Activator (units)	18	1.7	0.8	P < 0.001	34	4.7	1.9	P > 0.1	16	5.4	1.7
Plasminogen (casein units/ml.)	14	3.58	0.56	P < 0.001	34	4.37	0.38	P < 0.01	14	4.70	0.33
Activation inhibitor (units)	13	4.31	0.98	P < 0.001	34	2.42	0.41	P < 0.001	11	1.58	0.39
Antiplasmin (% inhibition)	13	47.3	2.2	P > 0.1	34	46.4	4.9	P > 0.1	11	45.8	5.2
Fibrinogen (mg./100 ml.) . .	18	380	55	P < 0.05	34	347	53	P > 0.1	16	368	72

* Lecturer in Medicine, University of Aberdeen.

† Research Fellow in Medicine, University of Aberdeen.

‡ Senior Medical Registrar, Aberdeen Royal Infirmary.

Serial Studies During Treatment

The serial changes in the components of the fibrinolytic system were measured in one hyperthyroid and one hypothyroid subject during the first six weeks of treatment.

Fig. 1 shows the changes which took place as thyroid overactivity was controlled. Activator levels rose progressively while activation inhibitor fell during the six-week period of observation. Plasminogen, after a very slight fall, rose steadily. All these changes represent a return towards normal levels. Fibrinogen, after a moderate fall during the first two-week

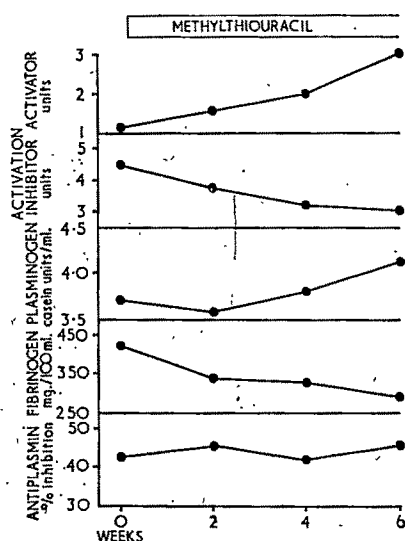


FIG. 1

FIG. 1.—Changes in levels of components of the fibrinolytic system in a hyperthyroid subject during treatment with methylthiouracil. FIG. 2.—Changes in levels of components of the fibrinolytic system in a hypothyroid subject during treatment with L-thyroxine.

period, remained unchanged and antiplasmin levels showed no trend.

Fig. 2 shows the changes which occurred during treatment of the hypothyroid patient with L-thyroxine. During the period of study the observed changes were the reverse of those found during the control of thyroid overactivity, levels again returning toward the mean normal values.

Discussion

Altered fibrinolytic activity may be implicated in the formation of intravascular thrombi, and Hume (1965) suggested that the depression of fibrinolytic activity after administration of L-thyroxine might be important in causing acute coronary occlusion in treated hypothyroidism. However, the role of the fibrinolytic system in occlusive vascular disease remains speculative, and it is probable that this system has fundamental functions unrelated to the pathogenesis of coronary artery occlusion. The changes which we have observed in thyroid disorders represent fundamental alterations in the balance of the system. Plasminogen, plasminogen activator, and an inhibitor of activation show changes in opposite directions in hyperthyroid and hypothyroid subjects. In addition, the levels of these factors return to normal as the euthyroid state is restored by treatment with antithyroid drugs or L-thyroxine. The results presented in this study suggest that the fibrinolytic

system is a further metabolic process influenced by thyroid hormones. Further, they suggest that the activity of the normal thyroid gland may influence physiological changes in fibrinolysis, the regulation of which is as yet not understood.

Summary

Hypothyroidism is associated with an increase in plasminogen, a decrease in an inhibitor of plasminogen activation, and a possible increase in plasminogen activator, whereas hyperthyroid

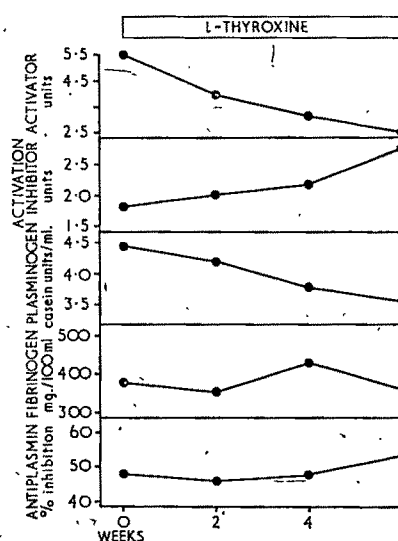


FIG. 2

patients show opposite changes in the blood fibrinolytic enzyme system. These changes may play some part in the association between treated hypothyroidism and occlusive coronary disease. More fundamentally they suggest that the thyroid has a regulating influence on fibrinolysis.

We are grateful to Professor H. W. Fullerton and Dr. T. N. Morgan for permission to study patients in their care, and to Dr. D. Ogston for his advice in the preparation of this paper.

This work was supported by a grant from the Tobacco Research Council on the recommendation of the British Heart Foundation, and was carried out during the tenure of a Medical Research Council Junior Research Fellowship by N. B. B.

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Injury, Serum Lipids, Fat Embolism, and Clofibrate

M. O'DRISCOLL,* F.R.C.S.; F. J. POWELL,† M.Sc., A.R.I.C.

Brit. med. J., 1967, 4, 149-151

The mechanism of fat embolism following injury has excited much controversy since it was first described by Zenker in 1862. Two theories seek to explain it—the classical mechanical theory, which is supported by Sevitt (1962), and the metabolic theory, which is supported by Evarts (1965). The mechanical theory suggests that following trauma fat is liberated from the marrow cavity into the venous sinusoids, whence it passes in the form of globules into the systemic circulation. The metabolic theory suggests that tissue injury may initiate changes in the physicochemical state of the blood, and that this alters the emulsion stability of the blood lipids. Together with the activation of a lipid-mobilizing hormone by trauma this results in the formation of fat globules.

Fat embolism follows trauma (usually to bones). There is a lucid interval of variable duration and then signs of respiratory and systemic fat embolism develop, together with changes in the mental state and level of consciousness; a petechial rash also occurs on the head, neck, and thorax.

In this study, firstly, an attempt was made to try to establish whether there was any change in the serum non-cholesterol lipids after trauma; secondly, the incidence of all degrees of the syndrome of fat embolism was investigated; and, thirdly, the effect of Atromid (clofibrate) on the serum lipids and the incidence of fat embolism was studied. Clofibrate was used because it has an effect on the lipids of the hyperlipaemic patient and has also been found to depress postprandial lipaemia.

Material and Methods

The patients were inmates of the orthopaedic unit at St. James's Hospital, Leeds, either as a result of injury serious enough to warrant admission or because they were undergoing orthopaedic surgery. They were divided into two groups (Table I). One group received standard therapy, and the other received clofibrate as well, as soon as they were able to take capsules. The dosage of clofibrate used was 750 mg. by mouth followed by 500 mg. six-hourly for two days, then 250 mg. six-hourly for three days, then 250 mg. twice daily for two days, and finally 250 mg. daily for two days. The dose was tailed off to prevent any rebound effects. Eight patients who had had operations on non-bony structures also received clofibrate.

Laboratory Estimations

Plasma total lipids were estimated by the rapid turbimetric method of Kunkel *et al.* (1948), giving normal ranges between 340 and 640 mg./100 ml. and a 5 % error against standard sera. Cholesterol levels were measured by the method of Carr and Drekter (1956) on the first 30 samples and subsequently by direct estimation on an autoanalyser (Kenny and Jamieson, 1963). Cholesterol levels were then subtracted from the total levels to give the non-cholesterol lipid levels.

Sputum was examined for fat globules by adding scharlach R and then by direct microscopy. Urine (end samples) were examined by centrifugation for five minutes, adding scharlach R to the deposit, and then by direct microscopy. Specimens of

sputum from 10 patients with chronic bronchitis in acute exacerbation and samples of urine from six patients with prostatic hypertrophy and urinary infection were examined as controls.

Blood was drawn from an arm vein, with tourniquet, of all patients on arrival in the casualty department, or immediately preoperatively in patients undergoing orthopaedic operations.

TABLE I.—Patients in the Series and Injuries Sustained

Type of Patient	Standard	Clofibrate
Closed fracture tibia and fibula	10	8
Compound " " " " " " " " " "	11	4
Closed fracture femur " " " " " " " "	10	8
Compound " " " " " " " " " "	0	5
Pelvis fracture " " " " " " " " " "	9	0
Multiple upper-limb fracture " " " " " "	5	0
Crush fracture vertebrae " " " " " "	2	0
Multiple injuries:		
Compound fracture tibia and rupture spleen	0	3
" " " " " " " " " " " " " "	5	1
Closed " " " " " " " " " " " " " "	0	3
Compound tibia + rupture liver " " " "	1	0
" " " " " " " " " " " " " "	1	0
Compound " " " " " " " " " " " " " "	0	2
Compound tibia + upper-limb fracture + rupture kidney + chest injury " " " "	3	0
Compound tibia + upper-limb fracture + rupture spleen " " " " " " " " " "	0	1
Multiple upper-limb fracture + bilateral tibial fracture " " " " " " " " " "	0	1
Compound femur + hinge pelvis + accidental haemorrhage and foetal death in utero	0	1
Degloving injury lower limb + pelvis fracture	1	0
Operative cases:		
Laminectomy " " " " " " " " " "	3	0
Kunschner nailing femur fracture " " " "	2	0
Arthrodesis knee and hip " " " " " "	3	0
Hip arthroplasty " " " " " " " " " "	4	4
Nail plating fracture neck femur " " " "	4	1
Bone grafting (Phemister) ununited fracture femur or tibia " " " " " "	5	5
Total	79	46

Further samples were taken on the next five or six days, with the patients fasting. Blood was also drawn from the femoral vein of the injured limb in nine patients with fractures of the leg—before, during, and after manipulation, when the patients were anaesthetized for the manipulation.

Clinical Examination

Features noted were (a) mental and conscious state ; (b) skin and conjunctivae for petechiae ; (c) the results of chest examination, particularly for central rales and other signs of pulmonary oedema (radiography being performed on the slightest evidence of abnormality and the x-ray film being compared with the earlier chest x-ray film) ; (d) neurological examination ; and (e) pulse and respiration rate and any signs of so-called "fracture fever"

Necropsy was carried out on the patients who died.

TABLE II

Major Fat Embolism	Minor Fat Embolism
(a) Post-mortem findings of fat embolism	(a) Fat globules in sputum
(b) Petechial rash	(b) Haemoptysis
(c) Confusional states lapsing into coma	(c) Signs of central pulmonary oedema
(d) Respiratory insufficiency with snow-storm chest x-ray change, which must be bilateral	(d) Chest radiographic change of milium zone mottling, patchy consolidation—which must be bilateral
	(e) Fat globules found in end samples of urine

* Orthopaedic Registrar, Central Middlesex Hospital, London N.W.10.

† Head Biochemist, St. James's Hospital, Leeds 9.

Though the florid syndrome of fat embolism is easy to diagnose, many subclinical cases occur, with few if any of the classical signs, and may be diagnosed only by chest radiography (Berrigan *et al.*, 1966). We have therefore classified our patients into two groups (Table II).

To make the diagnosis of fat embolism we required one major plus one minor criterion; or three or more minor criteria, of which one had to be the presence of changes in the chest radiograph.

Results

Serum Lipids

Daily estimation of the serum non-cholesterol lipid levels showed minimal or no deviation from the normal on any of the six days after operation in the control group; graphs were plotted of the lipid levels of all the subjects: Fig. 1 shows that in those not receiving clofibrate there was an appreciable rise

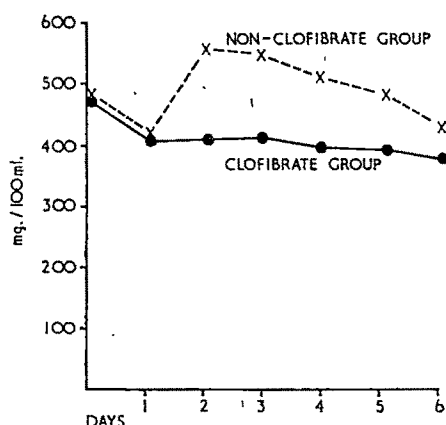


FIG. 1

Fig. 1.—Serum lipids of total cases. Fig. 2.—Serum lipids of patients on clofibrate for one procedure and not for another.

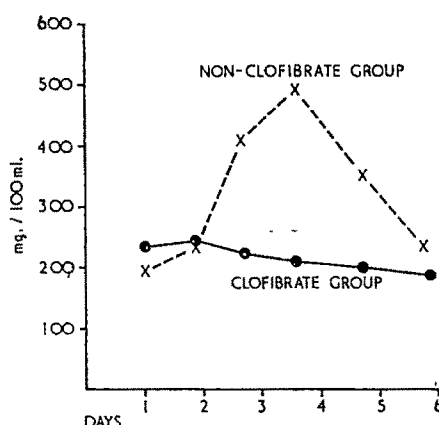


FIG. 2

to the third and fourth days, which fell off slowly. In the patients receiving clofibrate, on the other hand, lipid levels did not rise. The difference was statistically significant. Moreover, when the seriously injured patients were considered separately the difference in lipaemia between those receiving clofibrate and those not was even more apparent. This difference was noted again in seven patients, each of whom underwent two operative procedures of comparable severity, one being covered by treatment with clofibrate and the other not (Fig. 2).

Samples of blood were obtained from the femoral vein in nine patients, of whom four had closed fractures of the femoral shaft, three had closed fractures of the tibia and fibula, and two had compound fractures of the tibia and fibula. The samples were taken with wide-bore needles from the vein of the affected limb, high up against the inguinal ligament to catch blood issuing from the profunda femoris vein as well. Three

any stage. Of the total of 125 patients, seven were found to have fat in their urine, and it did not appear until the fourth day.

Of the patients who did not receive clofibrate, 30 had chest signs, usually in the mid-zone, or raised respiratory and pulse rates, or haemoptysis, or combinations of these. Pleuritic pain, usually left-sided, was also noted in eight cases. Of the clofibrate-treated patients three had fat in their sputum, increased respiratory and pulse rate, and rales; one patient also had pleuritic pain. Of the patients with abnormal chest signs and fat in the sputum, 27 had chest x-ray changes compatible with pulmonary oedema. No patients treated with clofibrate had chest x-ray changes.

The presence of a petechial rash was looked for in a good light. It was found in seven patients of the non-clofibrate group (five of whom also had confusion and marked chest x-ray changes). Nevertheless, the rash was not present in one patient who died of fat embolism. None of the clofibrate-treated patients developed a rash.

Coma, which carries a grave prognostic sign in fat embolism, occurred in one patient in the non-clofibrate group after a lucid interval of 24 hours. Four other patients became very confused, requiring sedation for several days, and becoming normal again only after several weeks. Two of these patients had temporary loss of sphincter control.

Six patients died in the non-clofibrate group (three from fat embolism), and none in the clofibrate group.

Stainable fat globules in sputum are thought significant of fat embolism (Robb-Smith, 1941).

TABLE III

Injury	Serum Lipids (mg./100 ml.)			
	Arm Vein	Femoral Vein, Pre-manipulation	Femoral Vein During Manipulation	Femoral Vein, Post-manipulation
Femur fracture (closed)	170	160	120	120
	500	500	500	490
	857	857	744	800
	515	494	494	510
Tibia and fibula fracture (closed)	686	695	686	686
	770	725	720	700
	445	415	410	387
Tibia and fibula fracture (compound)	214	208	195	190
	528	479	429	460

Diagnosis of Fat Embolism

The diagnosis was made by using our system of criteria. In the non-clofibrate group three had fat in the sputum and chest signs, but no x-ray changes, so were not thought to have fat embolism. Twenty-seven other patients had either one or more major signs, or three or more minor signs, with x-ray changes, and hence were thought to have fat embolism.

A careful note was made of the day on which the features of fat embolism were sufficient to warrant diagnosis; from Day 1 to Day 6 the numbers of cases were 2, 7, 13, 4, 1, and 0 respectively. These figures corresponded with the distribution of the maximum serum-lipid concentration (Fig. 3).

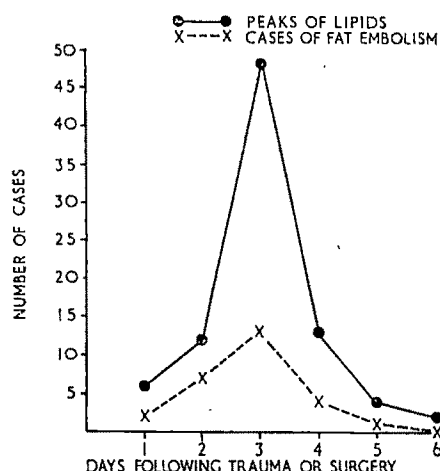


FIG. 3.—Comparison of days of onset of fat embolism and days of peak of lipids.

Illustrative Case

A youth aged 19 was involved in a motor-cycle crash. He was not knocked out, but on admission was clinically shocked though fully conscious and alert. He had sustained a compound fracture of the mid-shaft of the right femur, a compound fracture of the right patella penetrating the knee joint, and a compound fracture of his right tibia and fibula. He needed a transfusion of 3 pints (1.7 l.) of blood before he was fit enough for wound toilet, patellectomy, and manipulation of the fractures—which were done under general anaesthesia, the fractures being immobilized on a Thompson splint and using plaster-of-Paris. Postoperatively he remained well for 24 hours, after which he became confused and comatose within three hours. Fat embolism was diagnosed in view of the history of injury; the absence of signs of intercranial haemorrhage, the presence of rales, and a petechial rash on examination; and the appearances suggesting pulmonary oedema on chest x-ray film. He also developed ankle clonus, a raised pulse rate, and a temperature of 100° F. (37.8° C.).

He was treated with intermittent positive-pressure respiration and hypothermia. For five days he made some improvement on this regimen, but deterioration occurred and he died on the sixth day after injury. Necropsy showed gross petechial haemorrhages throughout the brain, particularly in the pons and medulla, and, histologically, intracapillary fat globules were present in the brain and in the lung vessels.

Discussion

Much evidence shows that fat embolism is not entirely due to fat getting into the circulation mechanically. The existence of lipaemia after trauma was demonstrated as long ago as 1921 (Bloor, 1921). Johnson and Svanborg (1956) and Bergentz (1961) have demonstrated this in animals, while Gottlieb (1964) has described this in patients who did not have a fracture.

We have shown that a definite lipaemia exists after injury or operation to bone, which rises to a maximum three to four days later and then falls off fairly rapidly. The degree of lipaemia was found to have no relation to the occurrence of fat embolism, but in those patients who had some degree of fat embolism it was at least double the earliest concentration determined. On the other hand, there was a definite correlation between the peak of the lipaemia and the onset of signs of fat embolism. The incidence of clinically recognizable fat embolism was high in the non-clofibrate group (34.2%), and there were three deaths (3.75%)—a figure which agrees with other series (Sevitt, 1962; Evarts, 1965). In the clofibrate group, on the other hand, there were only two cases (4.3%), and no deaths occurred.

Since clofibrate appears to have diminished both lipaemia and fat embolism, it is logical to suggest that the relation between the last two may be causal. Barrett (quoted by Thorpe, 1962) believes that clofibrate acts by virtue of its affinity for serum albumin, resulting in the reduction of the adrenaline-stimulated release of free fatty acids from the fat stores. This in its turn suggests that adrenaline may be implicated in the pathogenesis of fat embolism. Baur and Ludin (1950) found that irradiation of the spine of patients with ankylosing spondylitis caused a rise in the serum histamine concentration as a result of bone-marrow damage. Histamine is known to mobilize adrenaline, and this further mobilizes fat from fat depots. Since bone marrow is damaged by trauma, this could be a possible sequence leading eventually to fat embolism.

A further point in favour of a metabolic cause for fat embolism is our finding on the femoral vein samples. In none of these samples were we able to demonstrate the presence of a shower of fat; in fact, if anything the fat levels in blood draining from the injured limb were lower than those in concomitantly taken arm vein samples.

Summary

A significant lipaemia was found in 79 patients who were followed for a period of six days after trauma, and corresponded at its peak to the onset of fat embolism. There were 27 patients with some degree of fat embolism, three of whom died. A series of 46 patients with bone injury were treated with clofibrate. Lipaemia was substantially reduced and only two instances of fat embolism occurred.

We would like to thank Mr. R. Broomhead, Mr. J. M. Fitton, and Mr. F. W. Shea, orthopaedic surgeons, St. James's Hospital, Leeds; Dr. J. Goldie and the staff of the pathology department, St. James's Hospital, Leeds; Mr. J. M. O'Mahoney and Mr. D. Macwilliams; Mr. J. G. Bonin and Mr. A. J. Howse, of the orthopaedic unit, the Central Middlesex Hospital, London; and Dr. S. L. Lewis for their help.

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Behçet's Syndrome with Aortic Aneurysms

ELIZABETH A. HILLS,* M.B., M.R.C.P.

Brit. med. J., 1967, 4, 152-154

The coexistence of mouth and genital ulceration with hypopyon mentioned by Hippocrates and described by various workers in the early part of this century was first defined as a syndrome by Behçet in 1937. The place of the syndrome as part of a systemic disorder is now clearer, and the underlying pathology appears to be a vasculitis. The disease runs a chronic course, blindness being the greatest disability and central nervous system involvement a cause of death. Thrombophlebitis is fairly frequent, France *et al.* (1951) giving an incidence of 25% and Dowling (1961) 12%; superficial thrombophlebitis migrans and thrombosis of large veins, including venae cavae (Thomas, 1947; Boohkos, 1960) are recorded.

Little attention has been paid to arterial involvement (Schneider, 1965). Mishima *et al.* (1961) described resection of an aortic aneurysm in a 38-year-old man with Behçet's syndrome, and since then have seen a patient with a femoral artery aneurysm (personal communication); Oshima *et al.* (1963) record two aneurysms of smaller arteries; Shikano (1966) mentioned that one of his patients died of a ruptured aortic aneurysm. Mounsey in a clinicopathological conference (*Brit. med. J.*, 1966) described a case of ruptured aortic aneurysm in Behçet's syndrome, treated by aorto-iliac graft: in this case the aortic aneurysm was presumed to be secondary to osteomyelitis of the lumbar spine, though the possible association between aortic aneurysm and Behçet's syndrome was raised.

A further case is reported here, in which arterial aneurysms appeared to form part of this generalized disease.

Case Report

The patient's illness began in 1954, when he was in an Army unit containing men who had been serving in Egypt. He had fever and abdominal pain, appendicectomy was performed, but his symptoms continued for three months. Prolonged pain in the left wrist followed minor trauma, and six months later pains developed in the neck, shoulder, and back, with radiation down the back of the thigh. This was attributed to Scheuermann's disease, and after six months in hospital he was discharged from the Service, wearing a plaster jacket. He began to work in the following year, and was well until 1958. He then had osteomyelitis of the jaw after dental infection. Two weeks later he was admitted to hospital with fever and abdominal pain, followed by fleeting joint pains and a rash resembling erythema nodosum. Intensive investigations did not provide a diagnosis, and he was treated for six weeks with bed rest, aspirin, antibiotics, and corticosteroids, and was discharged well. From this time onwards he had recurrent ulcers of the mouth, penis, and scrotum. In 1960 he had an unexplained venous thrombosis of the left leg, and one year later had a right femoral vein thrombosis. Biopsy of the long saphenous vein showed gross thickening of the vein and infiltration with inflammatory cells, particularly around nutrient vessels (Dr. J. G. Leopold). Because of this, long-term anticoagulant therapy was instituted. In 1962-4 he had episodes of haziness of vision, and in 1964 had bilateral iritis and later a vitreous haemorrhage. He was seen by Mr. Vine Cole, who suggested the diagnosis of Behçet's syndrome, based on the association of aphthous mouth and genital ulceration, panuveitis, and thrombophlebitis. Corticosteroid therapy was begun.

In October 1964 the first recognized pulmonary infarct occurred. Since then he had experienced numerous episodes of febrile pleurisy associated with haemoptysis and transient radiological shadowing. Possibly these are due to thrombosis in pulmonary vessels rather than to embolization. During treatment with steroids and anticoagulants he had a haematemesis and later melaena; anticoagulants were withdrawn. In 1965 right-sided loin pain and haematuria were attributed to renal infarction. In April 1966 he complained of severe continuous pain at the base of the spine and a lesser pain in the shoulders. There was associated severe constipation and rectal bleeding. Barium enema was normal. During five weeks in hospital no cause for the pain was found. After discharge from hospital the pain continued, and in August 1966 became so severe that he was admitted to the Cardiff Royal Infirmary, very ill, Cushingoid in appearance, with a temperature of 37° C., blood pressure 130/80, and dusky, scaling nodules, 0.5-1 cm. in diameter, on both legs. There was some tenderness over the sacroiliac joints but no other arthropathy. He had aphthous ulcers on the lateral border of the tongue and inner surface of the lip. In the right fundus there were many haemorrhages, and central retinal artery thrombosis, and in the left eye less marked vasculitis. Carotid and radial pulses were normal, but the left femoral pulse was weak and the right femoral pulse absent. The abdominal aorta was palpable well to the right of the epigastrium and a bruit could be heard. The abdomen was diffusely tender, and slight movement in bed caused severe lumbar and sacroiliac pain. Psoas spasm was present.

Investigations.—Haemoglobin 12.4 g./100 ml.; white cells 12,200/cu. mm. (polymorphs 55%); platelets 453,000/cu. mm. Plasma fibrinogen 650 mg./100 ml. Total serum proteins 7.5 g./100 ml. (albumin 3.8 g.); electrophoresis showed slight increase in globulin. No L.E. cells present. No evidence of bacterial, mycoplasmal, or viral infection. E.C.G. normal. Chest x-ray film showed heart of normal size; shadowing in the right mid-zone.

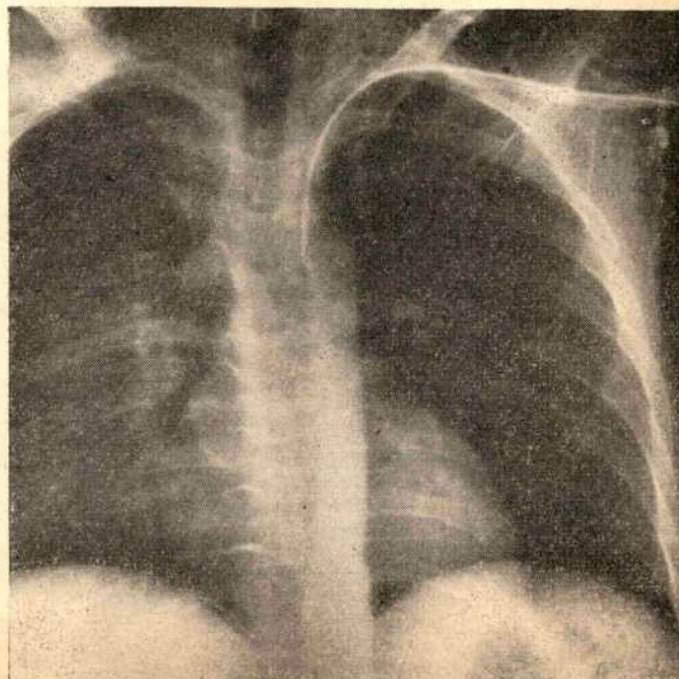


FIG. 1.—Thoracic aortogram. Fusiform dilatation of lower portion of aorta.

* Senior Medical Registrar, the Royal Infirmary, Cardiff.

The pain became worse and the abdomen more distended. Pressure over the aorta produced severe pain in the back.

Aortograms (Figs. 1 and 2) (Dr. G. de B. Hinde) showed fusiform dilatation of the thoracic aorta, extending to the level of the renal arteries. Below the renal arteries a segment of aorta appeared narrow, and distal to this a large aneurysm involved the superior

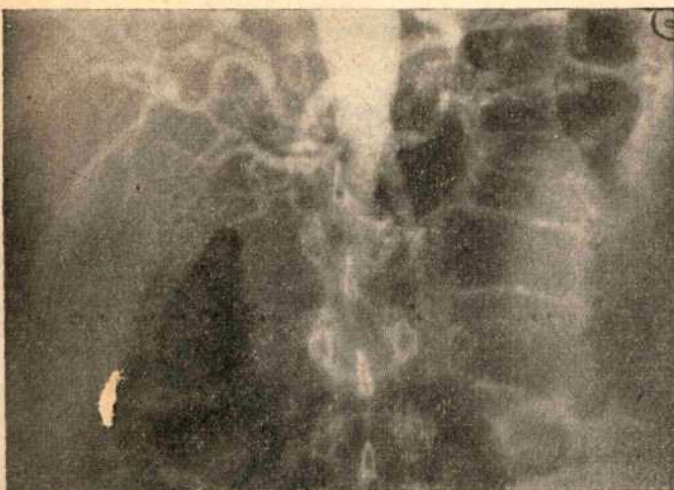


Fig. 2.—Upper abdominal aortogram. Fusiform aortic dilatation extending to level of renal arteries.

mesenteric artery, extending to the level of the inferior mesenteric artery.

At laparotomy Mr. Gordon Heard found the aorta and its branches grossly thickened and inflamed, and only $\frac{3}{4}$ in. (2 cm.) at the level of the renal arteries appeared relatively normal, aneurysmal changes extending above and below. Adjacent lymph nodes were somewhat enlarged. No source of infection could be found. Because the aorta was densely adherent to the posterior abdominal wall resection was not attempted, but a bypass graft was inserted from below the renal arteries to the common iliac arteries. An excised lymph node showed nonspecific reactive hyperplasia.

After operation there was some delay before bowel function was satisfactory, but no other problems. He was maintained on prednisolone, 20 mg. daily, with injections of A.C.T.H. 40 units on alternate days. On smaller doses of corticosteroids his vision deteriorated and mouth ulceration was very painful. He had pain between the shoulder-blades which probably differed from that associated with his episodes of pulmonary infarction. A recent penetrated chest radiograph showed less dilatation of the lower thoracic aorta than was seen in the aortogram.

Discussion

Behçet's disease is not very rare in this country; the patients attend ophthalmological, dermatological, or gynaecological departments or do not seek medical advice. Episodes of unexplained fever and arthralgia are soon forgotten and the manifestations of the disease will be separated by such long intervals that several years elapse before their relation as part of a systemic disorder is recognized. If a young patient has arthritis, fever, and an arteritis, a diagnosis of polyarteritis nodosa or systemic lupus erythematosus is usually made. Oral or genital ulceration is not usually mentioned unless specific inquiry is made for these symptoms, and at this stage uveitis may not be present to help the diagnostician.

In young patients aneurysms may not be suspected, particularly now that syphilis and tuberculosis are less common. Had the possibility of aneurysms in Behçet's disease been recognized an earlier diagnosis might have been made in this case. The diagnosis made in April 1966 was of intestinal obstruction, but investigation showed no mechanical cause and

the condition improved. This transient bowel obstruction was probably due to involvement of the inferior mesenteric artery, and in an elderly man the possibility that this event associated with severe back pain was due to aortic aneurysm would not be overlooked. The severe lumbar pain, which is probably due to inflammatory stretching of the arterial wall, may be confused with pain of spinal origin. Arthropathy, possibly spondylitis, is part of the syndrome; many patients are taking corticosteroid therapy, which may cause vertebral collapse. If there are no radiological changes in the spine and pain is persistent, acute inflammatory disease of the aorta should be considered.

It was suspected that the aneurysm was due to acute infection, perhaps associated with corticosteroid therapy, but careful search failed to reveal source of infection. The macroscopic appearances of the aorta can only be explained by acute inflammatory disease, unlike the granulomatous changes which may be seen in the aorta in Takayasu's disease, associated with distant tuberculosis, or the more chronic destructive lesions seen in tertiary syphilis. Both these latter conditions may be regarded as immune response to infection, in which a delayed sensitivity reaction is found in the aortic wall. In Takayasu's disease antibodies to the aorta are found (Ito, 1966). It is very likely that a search for aortic antibodies in Behçet's disease will give positive results, as antibodies to oral mucosa have been demonstrated (Lehner, 1967), and by immunofluorescent staining of peripheral blood films (Shimizu *et al.*, 1965) less specific cytoplasmic antibodies have been found.

The cytoplasmic antibody was similar to those occurring in polyarteritis nodosa, rheumatoid arthritis, and dermatomyositis, in contrast to the antinuclear factor found in systemic lupus erythematosus. These immunological findings support the clinical impression that Behçet's syndrome is related to the collagen diseases. Aneurysms of the aorta are described in polyarteritis nodosa (Wolff, 1936) and with giant-cell arteritis (Gilmour, 1941; McMillan, 1950); it must be remembered that division of these syndromes is often artificial, and firm rules may not be stated that only large or small arteries are involved in certain diseases. The evidence for viral infection in Behçet's disease (Sezer, 1956; Evans *et al.*, 1957) has not been conclusive, but the histological appearances could be due to such infection.

Until the cause of the disease is known treatment is empirical. The immediate treatment of the aneurysms must be surgical. Corticosteroids appear to suppress troublesome general symptoms of the disease in some patients, but there is no evidence that they halt the basic underlying disease process. Indeed, it is possible that this therapy may have played some part in the pathogenesis of the aneurysms. The other possible measure is immunosuppression with a drug such as azathioprine, but this will rest on less sure ground than its use in systemic lupus erythematosus. Such therapy is still experimental in this condition, in glomerulonephritis, and in rheumatoid arthritis, but might be tried in patients who have Behçet's disease with life-threatening complications.

The possible association of aortic aneurysms with Behçet's syndrome is suggested by an increasing number of reports, mostly of isolated cases, in the world literature. This complication should therefore be borne in mind in the management of Behçet's syndrome.

Summary

A case is described of aortic aneurysms occurring in a patient with a 12-year history of Behçet's disease. Their relation to the disease is discussed. It is suggested that specific symptoms of the syndrome should be sought in young persons with aneurysms. Aneurysm formation, a possibly fatal complication,

should be considered as a possible cause of pain in Behçet's disease. Treatment is discussed.

My thanks are due to Dr. William Phillips for permission to publish this case, and to the staff of other hospitals for their helpful information.

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Medical Memoranda

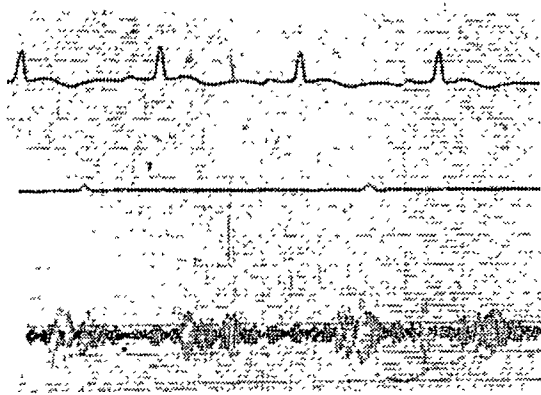
Murmur over Liver in Cases of Severe Anaemia

Brit. med. J., 1967, **4**, 154

A murmur may be audible over the heart and blood vessels in cases of anaemia. A systolic murmur was heard over the liver in three cases of severe anaemia. To our knowledge no reference to such a murmur has been made previously.

CASE REPORTS

The patients were female aged 38, 40, and 12 years suffering from nutritional macrocytic anaemia with ankylostomiasis, nutritional macrocytic anaemia, and thalassaemia. The chief complaints were weakness, pallor, palpitation, exertional dyspnoea, and dependent oedema. Their haemoglobin levels varied from 1.45 to 2.9 g./100 ml. The pulse was of water-hammer type and the rate varied



Phonocardiographic record of murmur over the liver.

between 120 and 130 a minute. The respiratory rate was 20 to 26 a minute. Their blood pressures were 60/0, 115/45, and 110/40 mm. Hg. The neck veins were very distended. The sites of apical impulse were the fifth intercostal space 1 cm. outside the mid-clavicular line, left sixth space 2.5 cm. outside the midclavicular line, and left fifth space on the midclavicular line. One patient had a diastolic gallop. There was no murmur in peripheral vessels. In two patients a soft systolic murmur was heard over the pulmonary area. Their electrocardiograms did not reveal any significant abnormality. The liver was non-pulsatile, tender, and enlarged to 3-4

fingerbreadths below the right costal arch. It was soft in two cases and firm in one. There was a systolic high-pitched murmur over the liver, best heard about 2.5 cm. below the costal arch in the continuation of the right midclavicular line. Application of pressure over the area by the chest-piece of the stethoscope made the murmur a little louder. A phonocardiogram taken in one of the cases recorded the systolic murmur (see Fig.).

In the first case transfusion of 300 ml. of whole blood precipitated pulmonary oedema. Partial exchange transfusion of 400 ml. of concentrated red cells with simultaneous withdrawal of 500 ml. of blood saved her. The other two patients had a very slow transfusion of 200 ml. of concentrated red cells. With transfusion of blood the patients became less dyspnoeic, their pulse rates came down, blood pressures improved, the size of the livers diminished, and the murmurs disappeared within a few hours.

COMMENT

The murmur was probably produced in the hepatic artery owing to accelerated circulation of blood through it as a manifestation of hyperkinetic circulatory state. After appropriate blood transfusion along with improvement of the circulatory state, the size of the liver was reduced and the murmur disappeared.

The murmur was best heard over the liver about 2.5 cm. below the costal arch in the continuation of the right mid-clavicular line. This site suggests that the origin of the murmur was in the hepatic artery. The murmur was not a transmitted one from the heart or the abdominal aorta, as in none of these cases was there a murmur in the abdominal aorta and that heard over the pulmonary area was never very pronounced.

We are grateful to Dr. K. C. Sarbadhikari, Principal-cum-Superintendent, Medical College and Hospitals, Calcutta, for allowing us to publish these cases. Our thanks are due to Dr. R. N. Roy for haematological investigations; to Dr. C. R. Maiti for phonocardiography; and to Dr. P. C. Mitra and Dr. S. B. Dutta, of the Central Blood Bank, Calcutta, for performing partial exchange transfusion.

N. R. KONAR, M.D., M.R.C.P.,
Professor-director.

S. K. DATTA, M.B., B.S., B.S.C.,
House-physician.

A. NAG, M.B., B.S., B.S.C.,
Senior House-physician.

A. KONAR, M.B., B.S.,
Research Scholar.

Department of Medicine,
Medical College, Calcutta 12.

Carbamazepine-induced Jaundice

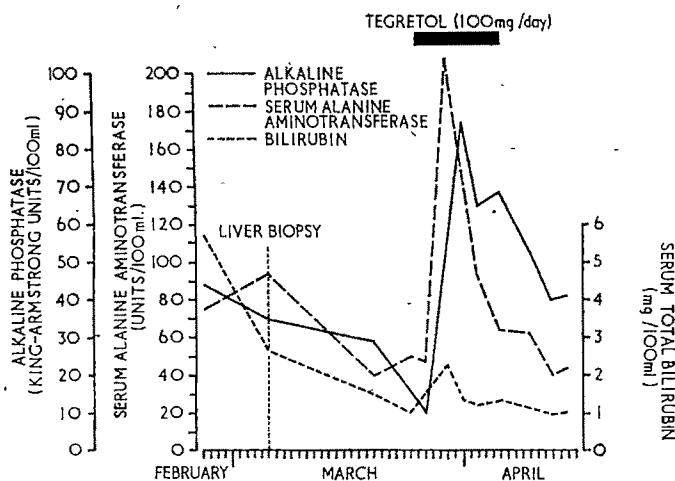
Brit. med. J., 1967, 4, 155

Carbamazepine (5-carbamyl-5H-dibenzazepine; Tegretol) has been shown to be effective in the treatment of trigeminal neuralgia (Blom, 1962, 1963; McArdle, 1963; Taylor, 1963; Spillane, 1964; Vanderfield, 1964; Burke, Grant, and Selby, 1965; Campbell, Graham, and Zilkha, 1966). Apart from two fatal cases of aplastic anaemia (Spillane, 1964; Donaldson and Graham, 1965) and one case of Stevens-Johnson syndrome (Coombes, 1965) the other side-effects of the drug have been of a relatively trivial nature, such as transient giddiness, drowsiness, ataxia, diarrhoea, anorexia, and an itching erythematous rash (Blom, 1963; Spillane, 1964; Vanderfield, 1964; Burke *et al.*, 1965; Graham and Zilkha, 1966). Obstructive jaundice occurring on the 20th day of treatment with carbamazepine was described by Spillane (1964), but as the patient had had an antecedent gall bladder dyspepsia for 18 months it could not be conclusively proved that the jaundice was drug induced.

In the following case jaundice was associated with the administration of carbamazepine and recurred after a drug challenge.

CASE REPORT

A man aged 65 was admitted to hospital on 14 January 1965 with a history of several days of severe right-sided trigeminal neuralgia, which he had suffered from intermittently for 15 years. His attacks of pain were not relieved by phenobarbitone 60 mg. eight-hourly and pethidine 100 mg. six-hourly. On 21 January



Graph showing liver-function tests before and after a drug challenge with 100 mg. of carbamazepine (Tegretol) daily.

carbamazepine was started in a dose of 100 mg. b.d., increasing gradually up to 200 mg. q.i.d., by which time his pain had completely disappeared. He was sent home on 11 February.

On 24 February he was readmitted with a history of anorexia for 10 days, dark urine for seven days, epigastric pain for three days, and jaundice for one day. He had no pruritus. He had continued taking carbamazepine in a dosage of 200 mg. q.i.d. and had had no further attacks of trigeminal neuralgia. There was no history of contact with infectious hepatitis and he had received no injections except venepuncture, by means of disposable needles, during his last admission. The only abnormalities on examination were jaundice and a smooth tender liver, palpable two fingerbreadths below the costal margin.

The carbamazepine was stopped and the following investigations were carried out: Hb 14.8 g./100 ml., W.B.C. 5,400/cu. mm. (differential normal, eosinophils 1%), E.S.R. (Westergren) 50 mm./1st hour, serum albumin 3.1 g./100 ml., serum globulin 4.1 g./

100 ml., with prominent peaks in the α_2 , β , and γ globulins and prothrombin time 11 seconds (control 14 seconds). The urine contained bile and urobilinogen. The initial and subsequent liver-function tests are shown in the Chart.

On 5 March a liver biopsy was carried out. Histological examination showed normal architecture with slight widening of the portal tract and the presence of sparse chronic inflammatory infiltrate. The cells of the limiting plate appeared normal. The hepatic cell plates showed some reduplication and the cells contained considerably increased amounts of pigment.

Because it was by no means certain that his jaundice was due to carbamazepine and because his neuralgic symptoms had responded so dramatically to the drug, it was decided, with the patient's willing co-operation, to give a dose of 100 mg./day and do serial liver-function tests. As can be seen in the Chart, within four days his bilirubin was up to 2.2 mg./100 ml., serum alanine aminotransferase (S.G.P.T.) to 210 units/100 ml., and alkaline phosphatase to 87 units/100 ml. Some bile and a trace of urobilinogen were present in the urine. On stopping the drug the biochemical abnormalities began to improve, but it was not until four months later that the alkaline phosphatase had fallen to 16 units, still slightly above the upper limits of normal.

COMMENT

The association of jaundice with the administration of carbamazepine was shown by a further drug challenge. The jaundice was probably of a mixed cholestatic/hepatic type because both the alkaline phosphatase and the serum alanine aminotransferase were elevated. The liver biopsy was unhelpful as it was done three weeks after the onset of the initial jaundice and the residual histological changes were nonspecific. It is not known why the liver-function tests at the time of drug challenge started to improve while the patient was still on carbamazepine, but this phenomenon has been described in patients receiving chlorpromazine (Haubrich, 1965).

It is of interest that carbamazepine is chemically related to the antidepressant drug imipramine (Tofranil), which may cause a sensitivity type of intrahepatic cholestatic jaundice similar to that produced by the phenothiazines, such as chlorpromazine (Hoaken, 1964).

I am grateful to Dr. Nigel Compston for permission to publish details of this case, to Dr. Roger Williams for his helpful criticism, and to Dr. A. G. Signy and Dr. E. J. F. Spicer for their comments on the liver histology.

IAN D. RAMSAY,* M.D., M.R.C.P., M.R.C.P.E.D.

St. Mary Abbot's Hospital, London W.8.

* Present address: King's College Hospital, Denmark Hill, London S.E.5.

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IgG Myeloma in Cerebrospinal Fluid with a Total Protein of 32 mg./100 ml.

[WITH SPECIAL PLATE ON FACING PAGE]

Brit. med. J., 1967, 4, 156

The following case is reported because of the finding of an IgG myeloma revealed electrophoretically and immunoelectrophoretically in a lumbar cerebrospinal fluid with a total protein of 32 mg./100 ml.

CASE REPORT

A 47-year-old man had been in good health apart from occasional attacks of "funny feelings" which had troubled him for nine years. These occurred at varying intervals of about three a day to one a month, lasting for 5 to 30 seconds and clearing spontaneously. He said that during these episodes "things go different, things seem to change, and everything looks distant." For the past few years he had also been subjected to grand mal attacks occurring about every two months. He was investigated at Maida Vale Hospital in December 1962, a diagnosis being made of temporal lobe epilepsy. The blood count was within normal limits but the E.S.R. (Westergren) was 20 mm. In September 1965, five months before his second admission, he first noticed attacks of dizziness, especially on looking up, and a tendency to fall to the left coming on about three times a week. In addition, he complained of tinnitus in the right ear.

On examination he was found to be fully alert, and his intelligence was normal. The optic fundi were healthy. The cranial nerves were normal, and so were the upper limbs, trunk, and lower limbs. There was no abnormality in the respiratory, gastrointestinal, and cardiovascular systems.

The E.E.G. was abnormal predominantly in the right anterior temporal region, where episodes of spike and slow-wave discharges occurred. In one of these episodes the patient was apparently unable to respond to command. The air encephalogram and x-ray films of the chest, skull, pelvis, abdomen, and soft tissues were not remarkable. Routine testing for urinary protein was negative, but Bence Jones thermosoluble protein was present in trace amount. E.S.R. (Westergren) 22 mm. Spinal fluid: clear and colourless; 2 cells per cu. mm. (small lymphocytes); total protein 32 mg./100 ml.; Wassermann negative.

A diagnosis was made of temporal lobe epilepsy with no evidence of a space-occupying lesion.

Electrophoretic and Immunoelectrophoretic Studies.—On two occasions we were able to carry out C.S.F., serum, and urinary protein electrophoresis and immunoelectrophoresis. For the simple electrophoresis Kohn's (1958) cellulose acetate technique was used. Three microlitres of serum or C.S.F. (this latter concentrated approximately 100 times) were applied under 120 v. constant current for 45 minutes. A barbitone buffer of pH 8.6 and ionic strength of 0.05 was used. The immunoelectrophoretic studies were conducted by the Scheidegger (1955) modification of the immunoelectrophoretic technique developed by Grabar and Williams (1953) in the serum and by Gavrilescu *et al.* (1955) in the cerebrospinal fluid. Protein was concentrated by the Mies (1953) method. For the immunoelectrophoresis use was made of horse and rabbit anti-normal human sera as well as anti-IgG (Immunology Inc., Chicago). The C.S.F. electrophoresis (Special Plate, Fig. 1a) showed an elevated compact band in the gamma region characteristic of IgG myeloma. This finding was fully confirmed by immunoelectrophoresis (Special Plate, Fig. 1b), which showed the abnormality affecting the gammaglobulin in the corresponding electrophoretic position—namely,

reduplication in the lower part and thickening in the upper arc. These perceptible differences in antigenic specificity were located in the "high speed" area of the gammaglobulin. Fig. 1c (Special Plate) shows the C.S.F. protein immunoelectrophoresis with IgG antiserum bringing up once more the characteristic image of an IgG myeloma. The total serum protein was 9.1 g./100 ml., the electrophoresis and immunoelectrophoresis were showing the same IgG abnormalities as the C.S.F.

A sternal marrow puncture carried out by Dr. M. Batata showed an average normal cellularity with a slight increase in morphologically normal plasma cells but with the presence of a large number of abnormal cells (Special Plate, Fig. 2). These latter were of three types: (a) cells which resembled though were not identical with plasma cells 7–12 μ in diameter (mature variety); (b) large cells 20–30 μ in diameter with abundant pale or dark blue cytoplasm and a large round or oval nucleus, fine chromatin, and sometimes nucleoli; and (c) giant cells with two or more nuclei, the cytoplasm often containing azure granules, clear vacuoles, or having a clear perinuclear zone. The marrow was normoblastic, granulopoiesis was normal, and the megakaryocytes were normal. The appearances were regarded as being consistent with myelomatosis.

COMMENT

The finding of IgG myeloma in a C.S.F. with a total protein of 32 mg./100 ml. is noteworthy. In view of the fact that no symptoms or signs were present to indicate the presence of a myeloma—as so often happens—and that other tests gave no indication either, the importance of the electrophoresis and immunoelectrophoresis is apparent. As the total C.S.F. protein was within normal limits and the blood-brain barrier was apparently unaffected, the protein abnormality found in the C.S.F. is unlikely to have been conveyed through the blood stream, and one must consider the likelihood of its being the local product of myeloma tumour cells.

Plasma cell tumours within the cranial cavity are exceptional, but French (1947) described such a tumour in the third ventricle impinging on the chiasm, but examination of the bone marrow was not made. In our case there was no evidence of a space-occupying lesion within the cranial cavity. In a case of multiple myeloma involving bone marrow and lymph node Kramer (1963) described a tumour within the right temporal lobe consisting of a perivascular proliferation of reticulo-endothelial cells evolving in the same way as in the marrow.

We want to thank the Medical Research Council and the Multiple Sclerosis Society for our respective grants. We are grateful to Mr. V. Logue, Professor W. H. McMenemey, and Dr. H. C. Grant for help and advice.

KETTY GAVRILESCU, B.Sc., DIP.MED.CHEM., F.I.C.
A. PAPAKRIVOPOULOS, M.D.

Department of Pathology,
Maida Vale Hospital for Nervous Diseases,
London W.9.

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K. GAVRILESCU AND A. PAPAKRIVOPoulos: IgG MYELOMA IN CEREBROSPINAL FLUID

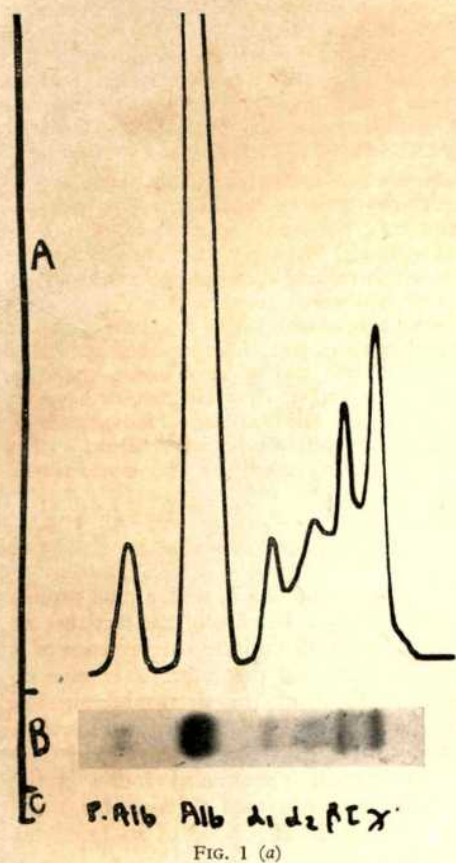


FIG. 1 (a)

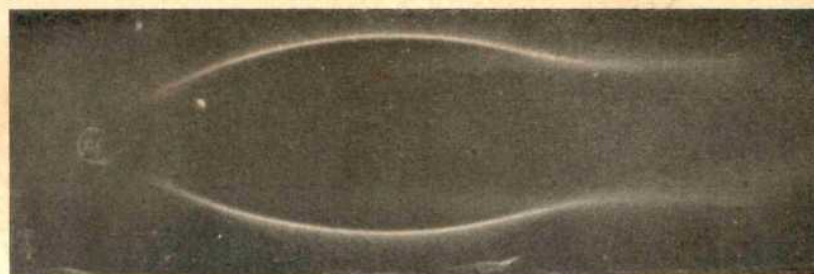


FIG. 1 (c)



FIG. 1 (d)

FIG. 1

(a) C.S.F. electrophoresis.

(c) Anti-IgG showing IgG myeloma.

(b) Immunoelectrophoresis.

(d) Normal C.S.F./IgG.

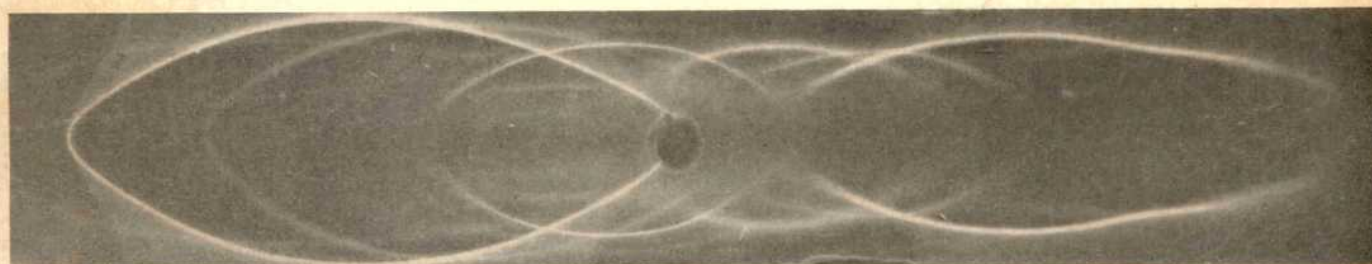


FIG. 1 (b)

FIG. 2.—Sternal marrow smear showing a group of abnormal cells resembling plasmablasts ("myeloma cells").

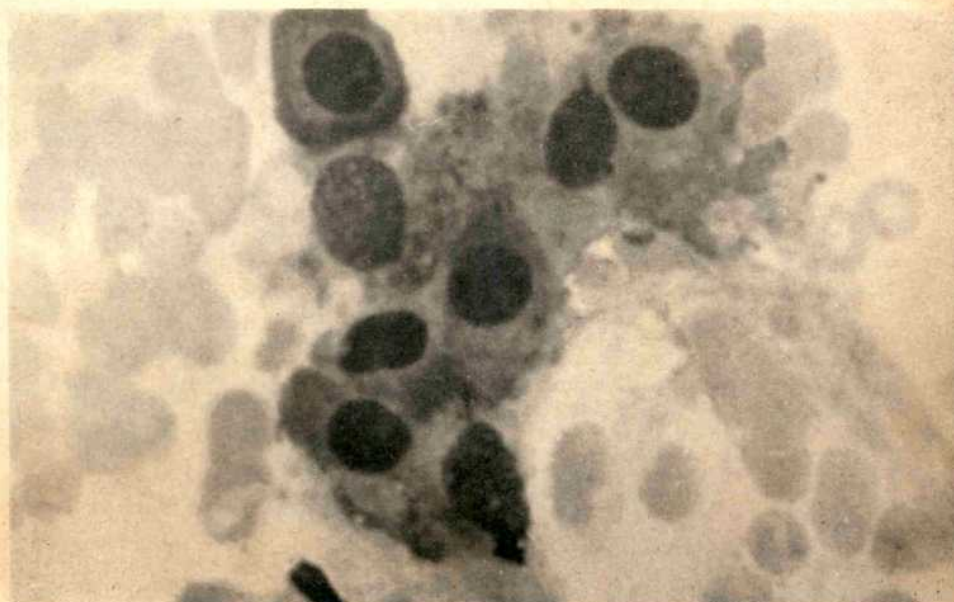


FIG. 2

NORMAN BROWSE: SPARE-PART SURGERY



FIG. 1

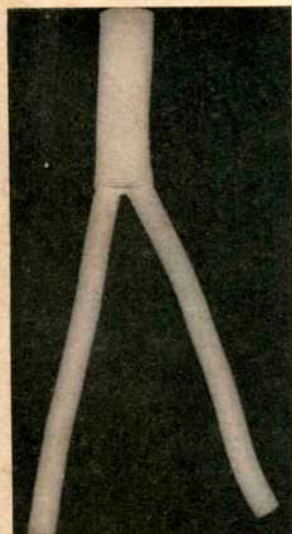


FIG. 2



FIG. 4

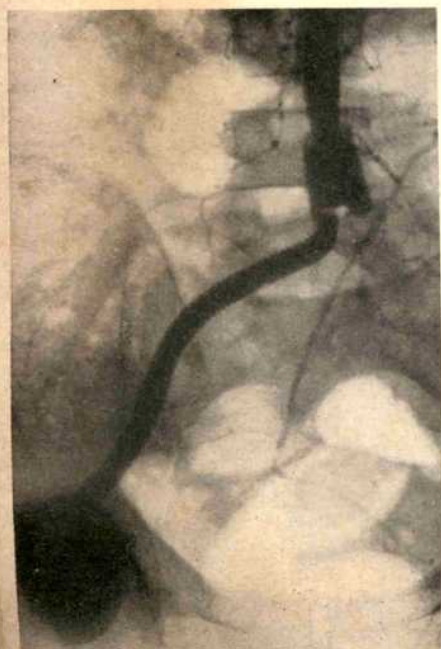


FIG. 3

FIG. 1.—An artificial hip joint (Ring prosthesis) inserted by a member of the Orthopaedic Department of St. Thomas's Hospital. The patient was an elderly woman with disabling arthritis of the right hip. Hip movements and mobility a year later are excellent.

FIG. 2.—A Dacron bifurcation aortic graft used after resection of an aneurysm or to bypass atherosclerotic blocks.

FIG. 3.—An aortogram of a bifurcation graft, similar to that shown in Fig. 2, five years after its insertion. Note the progression of the disease in the host aorta, the occlusion of the left limb, and the aneurysm at the end of the right limb.

FIG. 4.—A Starr-Edwards artificial heart valve. The anchoring stitches are placed through the soft cushion at the base.

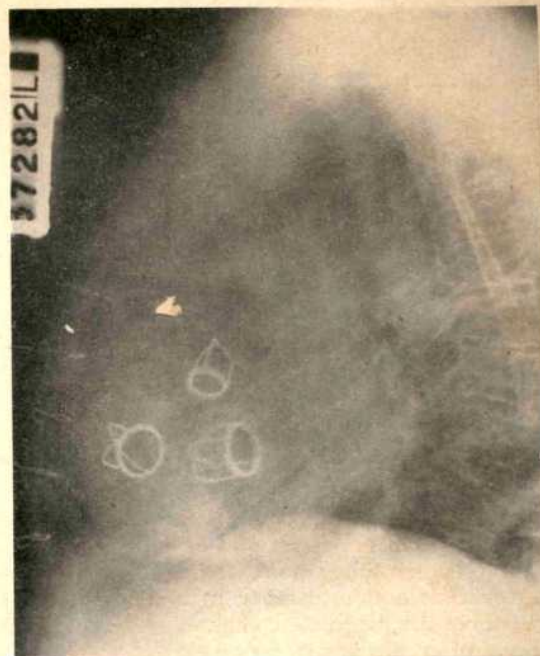


FIG. 5.—Chest x-ray film following a triple-valve replacement (aortic, mitral, and tricuspid) performed by Mr. M. V. Braimbridge, of St. Thomas's Hospital, in June 1966. The patient is alive and well.

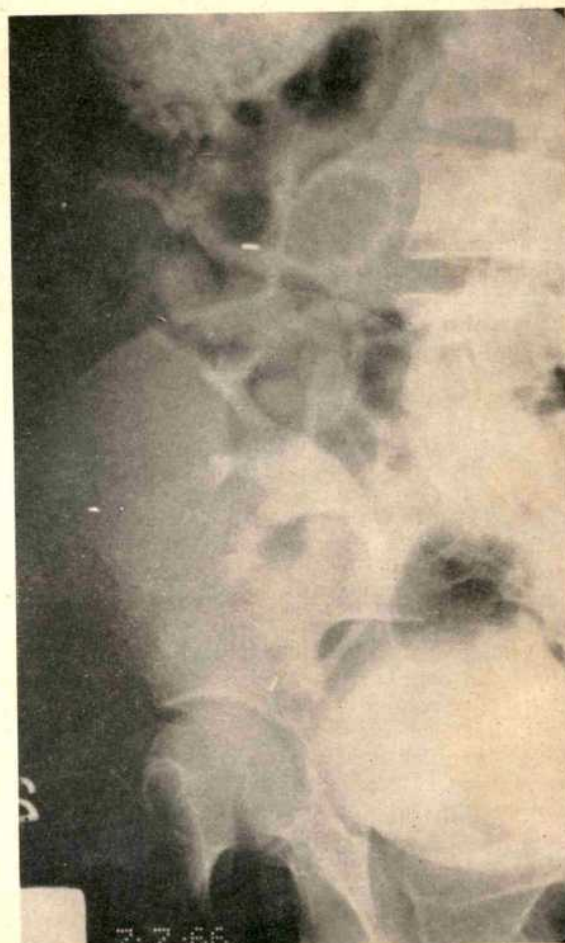


FIG. 8.—An intravenous pyelogram of a transplanted kidney, inserted by Professor R. Y. Calne, of Cambridge. Note the healthy calices indistinguishable from those of a normal kidney. (Reprinted by kind permission of Edward Arnold Ltd. from *Renal Transplantation*, second edition.)

Middle Articles

GROWING POINTS

Spare-part Surgery

NORMAN BROWSE, M.D., F.R.C.S.*

[WITH SPECIAL PLATE ON FACING PAGE]

Brit. med. J., 1967, 4, 157-161

Spare-part surgery began when the first prehistoric man to survive a traumatic amputation of a limb attached a piece of wood to the remaining stump to help himself to walk or grasp. It remained in this phase, with a few exceptions, until the present century, when the combined advances of many different aspects of medicine made possible the insertion of artificial materials and living tissues *into* rather than on to the body.

A notable exception to this recent development is the ancient use of skin grafts. It is often quoted that as long ago as the sixth century B.C. Indian surgeons were moving pedicles of skin from the forehead to the nose to repair severe nasal defects (usually a result of the punishment of "cutting off the nose"). The Italian, Tagliacozzi, gives a description of rhinoplasty using pedicle grafts from the arm in a work published in 1597, and the *Madras Gazette* of 1792 describes in detail the rotation of a forehead flap to the nose. The old maxim "there is nothing new in medicine" comes to mind yet again.

Spare-part surgery can be divided into three sections. Firstly, the attachment of devices to the outside of the body to replace missing parts (*external spare parts*); secondly, the insertion of parts made of foreign dead material into the body; and, thirdly, the insertion of foreign, living, functioning tissue into the body (*internal spare parts*). Each present their own problems, the last being by far the most complex.

External Spare Parts

This aspect of spare-part surgery is well known and it is not intended to discuss the tremendous advances that have been made in this field. Artificial limbs are being improved continually. For example, it is possible to make a power-driven upper limb that can be controlled by the patient from the electrical potentials developed in the muscles of the stump. Although such complex prostheses are seldom required by adults, they may be valuable to children, and the cripples of the thalidomide disaster have been a great stimulus and challenge to the limb-makers. One must not forget that spectacles, hearing aids, false teeth, and even wigs can be defined as external spare-parts. The benefit to mankind of this type of spare-part medicine is incalculable.

For the future this branch of spare-part medicine holds promise of the development of other artificial sense organs. Many years hence we may see an artificial eye relaying its message to the brain, for preliminary experiments have already been performed with this object in mind. Such progress will

be especially important in the replacement and bypassing of organs incapable of repair, such as the optic and auditory nerves.

Internal Spare Parts

Dead and Inert Foreign Materials

Artificial spare parts of metal, plastic, or dead tissues have been of most value in the replacement of those parts of the body that have a simple, relatively inert, mechanical function, such as arteries and joints. Three problems face the surgeon. The first is to insert the prosthesis without infection, for infection around a foreign body almost always results in its extrusion from the host. Secondly, the material inserted must be acceptable to the tissues. The chemical and the physical properties of a prosthesis are important. Vitallium and stainless steel evoke little tissue reaction, and most of the newer plastic materials based on nylon, Terylene, or polyethylene none at all. Nevertheless, even an inert material if it is porous will evoke a foreign-body reaction in response to the changes of tissue and surface tension in and around the pores, and any constituent that is at all water-soluble may cause a chemical inflammatory response. Thirdly, but by no means least, the material must be strong enough to withstand the enormous stresses of daily life. The strains placed on an artificial hip joint by a few years' weight-bearing are far in excess of the stresses and strains that we expect our motor-car engines to withstand. Fortunately the newer metals and plastics are both inert and strong; indeed, much of this field of spare-part surgery could not have developed without the brilliant discoveries of the chemical and other industries.

Artificial Joints

Since 1938, when Smith-Petersen found Vitallium to be a suitable metal for inserting into the body, many types of hip prosthesis have been made. Metal cups have been inserted between the joint surfaces; the head of the femur has been replaced; and in recent years complete joints, acetabulum, and head of the femur have been inserted. Fig. 1 (Special Plate) is a radiograph of a Ring prosthesis, which consists of a cup screwed into the acetabulum and an artificial head of femur. The problem of wear due to friction, not so serious in the older operations where one surface was living and capable of self repair, has not been completely solved and at the moment these prostheses are being inserted only in elderly patients. Time will tell how successful such operations can be. The production of a "frictionless" joint is now being pursued by many workers,

* Honorary Consultant and Assistant Director, Surgical Unit, St. Thomas's Hospital, London S.E.1.

and the complete replacement of the hip joint will probably soon be a common routine procedure.

Apart from the problem of wear at the joint surfaces the orthopaedic surgeon has also to solve the problem of making a permanent joint between the prosthesis and the bone. Occasionally the metal wears right through the bone or, more often, just becomes loose. Much work will have to be done before we have a prosthesis that the skeleton will accept without complaint. Probably this aim will not be achieved until the growth and turnover of the host bone around the prosthesis can be controlled, and the stresses can be transmitted from the prosthesis to the host in a more physiological manner.

Many other joints have been replaced, the finger joints in patients with severe rheumatoid arthritis, the elbow, and the knee. The problems are similar but greater than those of hip prostheses; fixing metal to bone becomes more difficult as the bones get smaller and the mechanics of the joint more complex.

Artificial Arteries

The replacement of arteries with artificial tubes has developed over the last 15 years. The techniques of vascular anastomosis have been understood since the beginning of the century, but suitable materials with which to make artificial arteries have become available only recently. Fifteen years ago the enterprising surgeon simply sewed together two strips of man-made fibre cut almost literally from his shirt-tails, but now we have a vast array of vascular prostheses. Fig. 2 (Special Plate) shows an aortic bifurcation prosthesis made of Dacron (Terylene). One difficulty with these tubes is that they kink when bent, and we still hope to develop a more flexible elastic graft. With such prostheses one can replace a segment of vessel knowing that the holes in it will be effectively stopped by blood clot; that a firm fibrous reaction will develop at the suture line to bind it to the host vessel; and that, provided there is enough blood flowing through, it will not become occluded with thrombus.

These grafts are not perfect. Fig. 3 (Special Plate) is an aortogram of a Dacron aortic bifurcation graft that was inserted five years ago. The left side has become occluded, but the right is patent and looks the same as the day it was inserted. Thus, though the material is strong enough to withstand the arterial blood pressure for many years, it does not conduct blood as well as a normal vessel and thrombosis is a hazard. Two other points must be noted: the disease in the host aorta is still present and slowly advancing towards complete aortic occlusion; and the right femoral artery has been destroyed by the combined effect of the underlying disease and turbulent flow at the anastomosis, so that it has become aneurysmal. Thus partial replacement of an organ may fail because of the progression of the primary disease. As total replacement of the vascular tree is impossible, we will continue to have late failures until we can also cure or arrest the underlying disease. It follows, therefore, that the aim of spare-part surgery should be the complete removal and total replacement of a diseased organ or system.

Artificial Heart Valves

The aortic valve is often so extensively destroyed by disease that repair is impossible. In such circumstances the damaged valve must be replaced with an artificial one or one from another person. The valve most commonly used is the Starr valve (Fig. 4, Special Plate), made entirely of metal and plastic, but freeze-dried aortic valve homografts, taken at necropsy soon after death, are also used. Both may be considered as inert foreign material, for the cells of the freeze-dried valve are dead and disorganized and do not cause an immune response.

Fig. 5 (Special Plate) is a chest x-ray film of a patient with three artificial valves—aortic, mitral, and tricuspid. This is as near as we can go at present towards giving a patient an

artificial heart, but it is unlikely to be long before an artificial pump will be inserted as a long-term replacement for the myocardium.

The heart valve presents another complication of spare-part surgery. The materials of which it is made are inert when placed in soft tissues, but not when placed in a continuous stream of blood. Whereas the normal valve falls back away from the mainstream of blood ejected from the ventricle during systole, the ball of the Starr valve lies right in the middle of the stream. Turbulent flow around the valve may cause sufficient haemolysis to produce anaemia, and if the thrombus around the valve becomes infected a condition identical to sub-acute bacterial endocarditis will develop, which may be fatal.

It is in many ways surprising that either artificial or freeze-dried valves function so well; some Starr valves have been in position for as long as five years and the one-year success rate for these operations is now well above 70%.

Artificial Hearts

The "heart-lung" machine is both an artificial heart and an artificial lung, and is used extensively during cardiac surgery. It is only recently that very small pumps have been devised that can be left connected to the conscious patient to replace or aid the myocardium for long periods.

Fig. 6 shows the principle of these devices. When perfected they will be used when the myocardium is so weak that it is

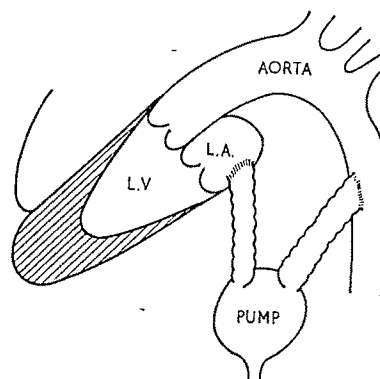


FIG. 6.—Diagrammatic illustration of an artificial left ventricle used to take the strain off a failing heart in the early postoperative period. Blood is taken from the left atrium and pumped directly into the aorta.

unable to function properly following the repair or replacement of chronically diseased valves, or after myocardial infarction. Thus this device is not an artificial heart, just a temporary artificial left ventricle—though it represents the beginning of another new field of spare-part surgery.

Artificial Nerves

For the Heart.—The commonest conducting system to be replaced with an artificial device is the conducting system of the heart. Failure of ventricular contraction due to a permanent or transient heart block results in hypotension and collapse. Conversely, an excessively fast ventricular rate, as occurs in ventricular tachycardia or auricular flutter, will also cause hypotension and collapse. In either case, whatever the cause, it is necessary to control the heart rate to maintain life. The cardiac pacemaker takes over the role of the sino-auricular node and conducting system. The battery and timing device replace the natural pacemaker (sino-auricular node) and the wires the conducting bundles, the ends of the wires being placed on that portion of the heart that one wishes to control—usually the ventricle.

The problems of implanting wires and fixing them to the heart are no different from those already discussed, but a new

problem arises—the source of power. Early models had the wires coming to an external electrical source, and temporary pacing is still done in this way. This is unsuitable as a permanent method, as the site at which the wires come through the skin is extremely susceptible to infection. Permanent pacing is therefore achieved with either long-life implanted batteries (needing regular renewal) or by induction. In the latter system the wires from the heart are brought to a coil beneath the skin and current is induced therein from an overlying primary circuit (Fig. 7). The source of power is then external, removable, and without any direct connexions with the internal secondary circuit. This overcomes the problems of sepsis, breakage of wires, and renewal of power supply. Recently attempts have been made to harness electric current produced within the body as a source of power.

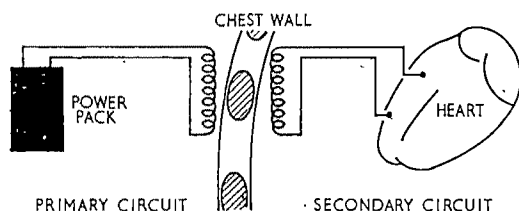


FIG. 7.—Diagram of the electrical circuit of an inductive cardiac pacemaker.

Perhaps we are not far from the day when a patient may have three artificial heart valves and an artificial left ventricle paced by a pacemaker, which is in turn fired from the electrical activity of right ventricular systole. This, I suspect, is as near as we will get to a truly artificial heart, at least for the next 50 years.

Other Sites.—The development of the cardiac pacemaker is far ahead of all other artificial nerve implants. Electrodes have been implanted on the bladder to stimulate micturition in paraplegics, and attempts have been made to control the sphincter of the bladder to prevent incontinence of urine. Anal incontinence has also been studied, and the most promising approach is the stimulation of the sphincter from the outside with a dumbbell-shaped electrode fitted into the anal canal. These efforts will no doubt lead to the development of permanently implanted electrodes with external inductive power circuits to maintain sphincter competence but which allow it to relax on demand.

A final example of the way in which man is attempting to take over the nervous control of the body is the study of methods of pacing the nerve to the carotid sinus. In the previous examples the battery and wire has replaced an efferent motor nerve. Stimulation of the carotid sinus nerve, on the other hand, is an attempt to mimic the afferent impulses coming from the baroreceptor endings. This aims to effect some degree of regulation of the blood pressure.

Living Autogenous Tissue

In many instances we have within ourselves the tissues required to fashion a spare part. Pedicles of skin can be fashioned into new noses, the ileum can be made into a bladder, the colon can become an oesophagus.

The use of autogenous tissues depends to a large extent on the ingenuity and technical skill of the surgeon. Provided the blood supply of the part remains intact or is re-established, the tissue will live, and often shows a remarkable degree of adaptation to its new function.

Living Foreign Tissue

The problems of placing living foreign tissue into the body are those outlined for inert materials, with the addition of

several greater ones, all yet to be fully resolved. Thus, firstly, one must obtain suitable material. Secondly, the latter must be kept alive during transit from donor to host. Thirdly, it must be kept alive within the host. These problems are best discussed in the context of renal transplantation.

Source of Materials

Organs for transplantation must be living and healthy. The obvious source is another living person, as tests of function can be performed preoperatively and the organ removed at leisure and at a time most suited to the well-being of the donor, recipient, and surgeon. Is it morally and ethically right to ask or expect a healthy subject to donate a kidney? This problem does not arise with other organs such as the liver, heart, or lungs, for the living have none to spare; but, as it is well known that man can live a normal life with one kidney, relatives are often eager to volunteer as donors. Donation is not, however, free from risk. Nephrectomy has its hazards, such as haemorrhage, in addition to those associated with all operations, such as pneumonia and pulmonary embolism. After the donor has survived the operation there is still the possibility of an accident or disease process affecting the function of the remaining kidney. Against these problems must be set the undoubted fact that transplants from live, related donors do better than those from dead, unrelated donors. The problem is one for the individual surgeon concerned. Cadaveric donation has its problems. The best source is the recently dead young person, but there are legal problems concerning the rights of the relatives. Most relatives agree to the removal of a kidney, but it is an essential precaution when the donor is a patient dying in the hospital that the surgeon has nothing to do with the donor's care, lest he should be accused of hastening death in order to obtain the kidney.

Preservation of Organs

Whatever organ is used, and whatever its source, it inevitably undergoes a period of ischaemia between removal and insertion. The effects of this ischaemia are minimized by keeping it as short as possible and by keeping the organ cool. A cold kidney (4° C.) can survive six hours or more of total ischaemia and function. A warm kidney is severely damaged after 30 minutes, but may still recover after one and a half hours of ischaemia.

Any organ must of course be removed in aseptic conditions, and if the donor is alive this is done as an elective procedure in an operating-theatre adjoining that in which the recipient is being prepared. The kidney is then carried from one room to the next, and the ischaemia time is that which is needed to make two vascular anastomoses (10–20 minutes). With cadaveric donors the preparation of the recipient takes longer, as it is begun as an emergency after the donor has died. The kidney is therefore washed through with cold heparinized saline solution and kept in ice until the recipient is ready.

In ideal conditions a transplanted kidney will produce urine as soon as the clamps are removed from the blood vessels. There may follow a diuretic or anuric phase, depending upon the degree of tubular necrosis.

The problems of short-term preservation of the liver, lung, and heart have not yet been solved. To do this the organs will probably have to be artificially perfused with oxygenated blood. In the future one hopes to see banks of viable organs ready for insertion, but the problems of long-term preservation are enormous.

Preparation of the Recipient

Surgeons like to operate on a fit patient, for an ill one is more susceptible to all the common postoperative com-

plications. Patients in renal or hepatic failure are not usually subjected to operation, but in transplantation these are the very subjects with whom the surgeon has to deal. The immediate success of renal transplantation is entirely dependent upon the efficiency of preoperative dialysis. Careful use of the artificial kidney gives a fit patient who can withstand surgery and the postoperative medication with cytotoxic drugs. Without preparation with chronic dialysis the mortality rate is high.

There is no machine to replace the hepatic function, and hence liver transplantation is performed on sick patients. Passing the patient's blood through a pig or human cadaveric liver has not been outstandingly successful in the treatment of hepatic coma. Once an artificial liver is available to prepare the patient liver transplantation will become a practical proposition.

Surgical Techniques

The anastomosis of the vessels of the graft to those of the host is a fairly simple procedure requiring the basic skills of vascular surgery. A kidney is placed in the iliac fossa and its vessels anastomosed to the internal or common iliac vessels. The ureter is either joined to the bladder or to the host ureter. Fig. 8 (Special Plate) shows an intravenous pyelogram of a kidney transplanted to the right iliac fossa; it is indistinguishable from that of a pyelogram of a normal kidney in the loin.

The transplantation of other organs, such as the liver or the lungs, is more difficult, as there are more (usually smaller) vessels to anastomose.

The development of the techniques of transplantation have depended upon work in animals. Many thousands of canine renal, liver, heart, and lung transplants have been performed and techniques perfected, so that the practical problems of inserting the graft into the recipient are now the least of the transplanters' worries.

Prevention of Rejection

Once inside the recipient, perfused with recipient blood, the transplanted organ is subjected to the major hazard of this whole problem—namely, that of host rejection.

From a very early stage in interuterine growth special cells develop, particularly in the thymus, which are capable of recognizing any protein which is foreign to the body. They then migrate to populate the reticuloendothelial system. These "self-recognizing" cells can initiate a series of responses by which any "non-self" material is destroyed. This, in very simple terms, is the basis of immunity. Any cell capable of initiating an immune response is called an immunologically competent cell.

Foreign tissue is destroyed either by antibody production or a local cellular reaction. It is thought that the local cellular response is the most important line of defence. Circulating antigens are released by implanted tissues, but in small amounts, so that there are probably only low levels of circulating antibody.

If one accepts this mechanism of graft rejection then a number of methods of preventing this response become apparent; they are shown diagrammatically in Fig. 9. Only two are of practical value today.

Make the Graft Non-antigenic.—Homozygous twins have an identical genetic make-up. Tissue grafted from one to the other is totally accepted. The results of kidney transplants between identical twins are excellent, some functioning 6–8 years after transplantation. Such good results justify the use of a living donor, but regrettably few patients with renal failure have an identical twin.

Attempts are being focused on ways of typing the tissues of both the donor and recipient to get the best degree of immunological compatibility. These studies are in their infancy and involve many sophisticated techniques.

Recipient and donor should have the same blood group. Leucocytes can also be "typed" in the same way as red cells, but this is a much more difficult procedure.

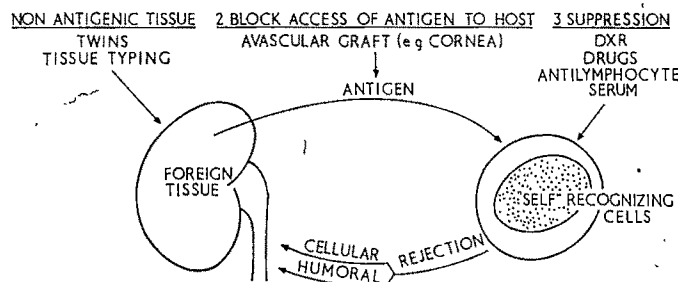


FIG. 9.—The ways of overcoming the immune response.

A host-versus-graft reaction can be detected before transplantation by injecting the recipient's lymphocytes into the skin of the donor and observing the local reaction. This test can be used only with living donors.

The presence or absence of histocompatibility antigens can also be detected by studying the effect of known specific antigens against donor and recipient lymphocytes. The preliminary results of these attempts at tissue typing are encouraging and suggest that they will have an important role in determining the success or failure of a transplant. If tissue typing is to be used with cadaveric donors the donor will have to be studied before death, so that the methods used will have to become rapid and simple.

Any attempt to destroy the antigenicity of the graft before transplantation always causes death of the transplant.

Prevent the Host Recognizing "Non-self" Material.—Once a foreign tissue is in the body and fully vascularized there is only one way to stop the host recognizing and starting an immune reaction against it—to destroy those cells involved in the recognition process. This is known as immunosuppression. The small lymphocytes are the target cells and there are three possible methods of attack.

Irradiation.—Total body irradiation was the first method to be tried, but was given up when it was found that the dose required to achieve effective immunosuppression invariably killed the host. Local irradiation of the graft is used occasionally to help suppress a severe rejection phase.

Cytotoxic Drugs.—Many drugs have been studied, but by far the most successful is azathioprine (Imuran). Imuran will destroy all types of white cell, and complete depression of marrow and lymph node activity can occur if the dose is not carefully controlled. Cortisone has an inhibitory effect on the reticuloendothelial system and is used in combination with azathioprine. The other cytotoxic drug in common use is actinomycin C.

The present-day successes of renal transplantation are due either to chance histocompatibility or the control of rejection by azathioprine and cortisone, but better substances are needed.

Antilymphocyte Serum.—The wholesale destruction of bone marrow and lymphoid tissue is a blunderbuss approach. Antilymphocyte serum can specifically destroy those cells believed to be responsible for graft rejection. It is made by injecting human white cells into the horse and then preparing the antiserum in just the same way that the antisera against many bacteria are made. Preparations can now be made of pure antilymphocyte globulin. As white cells from many different subjects have to be pooled to get enough for an adequate antigenic stimulus, the antiserum is species—but not individual—specific.

Studies with this substance in man are just beginning ; those experiments that have been performed show great promise. Antilymphocyte serum is the only specific immunosuppressive agent yet developed and those patients who have received it both preoperatively and postoperatively have shown a worthwhile improvement in their tolerance to the grafted kidney.

Current Practice following Renal Transplantation

The usual practice following a kidney transplant is to start the patient on azathioprine and corticosteroids immediately. Renal function is watched carefully. A reduction of renal function indicates the development of the rejection process within the kidney. The earliest change is a reduction of renal plasma flow. The doses of azathioprine and corticosteroids are immediately raised and actinomycin C is added. The signs of rejection usually subside within a few days, and drug doses are then reduced. Episodes of rejection get less frequent and less severe as the months pass, but the patient must be very closely observed for six months, and then seen frequently for the next 12 months. If immunosuppression fails the kidney gets bigger, function fails, the small intrarenal vessels thrombose, and the kidney dies.

In addition to all these problems the surgeon has to manage a patient with a low leucocyte count, who is taking corticosteroids, and who has a wound, drains, and a urethral catheter. The chance of infection is high. These patients are usually barrier-nursed in special units until all the impedimenta of the postoperative period have been discarded.

The one-year survival rate of the graft in good centres is continually improving. Figures of 80 and 90% have been claimed, while the overall world figure for living related donors is about 70%—for unrelated cadaveric donors the figure is about 50%.

Liver Transplantation

A few livers have been transplanted between humans and many have been exchanged between dogs. The latter work has shown the procedure to be technically possible and that the problems of rejection can be met in the same way as kidney transplants. Many animals have survived six months, some as long as a year and a half, but there are no long-term survivors in man.

The functions of the liver are more complex than that of the kidney and certainly less well understood. Thus, though the blood of a man in hepatic coma can be passed through another human or pig liver to lower the concentration of bilirubin and ammonia, there is often no change in the level of coma. A fully functioning transplanted liver would presumably restore a patient in liver failure to normal, but this has rarely been achieved for even a short term with extracorporeal liver perfusion techniques.

At present anyone attempting liver transplantation for hepatic failure must work with a very ill recipient, and the chances of success are slight. With the kidney this problem was overcome by the development of the artificial kidney ; little progress can be expected with liver transplantation until we have an effective artificial liver. It would help in the making of such a machine if we understood the biochemistry of hepatic coma.

Liver transplantation may be valuable to some patients not in liver failure. For example, the patient with an extensive, locally infiltrating, primary carcinoma of the bile duct could be cured if the surgeon could remove the porta hepatis and the liver *en masse*. Liver transplantation may make this possible. The patient, though jaundiced, would not be in hepatic failure and the chances of success would seem to be moderately good.

Liver transplantation will become a practicable procedure when the problems of temporary support for the patient in liver failure and the rapid collection and perfusion of the cadaveric donor liver have been solved.

Other Organs

The transplantation of the heart, lung, pancreas, gut, and endocrine glands are all technically feasible procedures. An ape heart has been inserted into a man, though its function quickly failed. One patient has had a successful pancreas transplant, which is reported to be functioning four months after operation. So continued progress is being made. Any organ that can withstand ischaemia for 30 minutes may be transplanted, and as our knowledge of the immune reactions increases so these transplants can be kept alive for longer periods.

Other Tissues

Perhaps the most important body tissue to be transplanted, and certainly the one that has made all the recent developments of transplantation possible, is blood. Blood transfusion is a form of tissue transplantation, the value of which is inestimable. A major part of modern surgery could not be done without it. The transfer of blood-cell-producing tissues, the bone marrow, has not been so easy. It is beset with all the problems of organ transplantation. Experiments have shown that antilymphocyte serum will improve the results of bone-marrow exchange. If a diseased haemopoietic system could be completely destroyed and replaced with a healthy one a great number of diseases such as aplastic anaemia and leukaemia might become curable.

The future of transplantation is bright. Solving the problems of immunity will solve many of the fundamental problems of cellular biology. Transplanting organs successfully will give life to many. All this will repay the singlemindedness and courage of the few who have pressed on in this field during the last 20 years in the face of failures, discouragement, and seemingly insurmountable barriers.

CONFERENCES AND MEETINGS

Paediatric Neurology

[FROM A SPECIAL CORRESPONDENT]

A conference on paediatric neurology was held at the Royal College of Physicians of London on 5 and 6 October. Opening the first session on some aspects of progressive brain disease in childhood, Professor D. V. HUBBLE (Birmingham) observed that no area of paediatrics was more retarded than paediatric neurology. However, the recent genetic and biochemical developments in this field had drawn more attention to it.

Sphingolipidoses

Dr. J. WILSON (London) discussed the neuropilidoses and leukodystrophies, both of which result from derangement of neuronal and glial elements by the abnormal storage of lipids. The neuropilidoses included Tay-Sachs disease, various forms of a similar syndrome of later onset formerly grouped together as "amaurotic family idiocy," Niemann-Pick disease, and Gaucher's disease, in all of which the lipid storage affected mainly the neurones. In the leukodystrophies the white matter was affected; these included metachromatic leukodystrophy, Krabbe's disease, and sudanophilic diffuse sclerosis. The term sphingolipidoses covered both these groups and their many eponymous variations. They presented similar problems, and dementia was a common characteristic. The rate of progression was variable. Early evidence of the syndromes was failure to thrive, arrest of development, and loss of skills already acquired. An acute presentation, perhaps after a febrile illness or an accident, could cause further confusion.

Tay-Sachs disease was the commonest, said Dr. Wilson. The condition was not confined to Jews, and the cherry-red spot at the macula was not specific; it was due to the thinner fovea showing up pink against the surrounding lipid-laden retina. In the group with late onset fits were common, speech was usually affected, and myoclonic jerks were often severe. Blindness occurred late. True cerebellar incoordination and pyramidal lesions could confuse the diagnosis. Onset later than the age of 2 was rare in Niemann-Pick and Gaucher's diseases, and visceral involvement was usually obvious. In the leukodystrophies fits were a less prominent feature and there was peripheral nerve involvement, but the dementia was still the most important feature. In Krabbe's globoid cell sclerosis the onset was before 6 months; the head might enlarge and the legs stiffen, making hydrocephalus and cerebral palsy possible misdiagnoses. Diagnostic investigations included enzyme studies, electroencephalography, and biopsy. Brain biopsy was extremely helpful for guiding the parents and for genetic counselling in atypical cases and in the diseases where other investigations were less definite. Genetic counselling depended on the fact that many of these diseases were transmitted as autosomal recessives and on the increasing ability to identify carriers by biochemical or other tests.

An account of electroencephalographic studies in this group of diseases was presented by Dr. G. PAMPIGLIONE (London). This investigation was important for diagnosis of individual diseases, for screening, for following the evolution of the disease, and for correlation with clinical and biochemical findings. Showing serial E.E.G. tracings in several cases, Dr. Pampiglione illustrated how the E.E.G. was seldom abnormal before there were clinical signs, though the rectal biopsy could be positive before this. However, the E.E.G. was of value in showing that the cerebral disturbance was generalized.

Laboratory Methods

Dr. A. CLAIREAUX (London) said that the histologist was now presented with a wide variety of tissues with which to diagnose sphingolipidoses. Brain biopsies gave the greatest range of information, and at Great Ormond Street Hospital a good-sized piece was usually obtained and divided for routine histology, histochemistry, chemical analysis, and electronmicroscopy. Both grey and white matter was necessary. Between 1962 and 1966 about half of 34 brain biopsies had been positive, while rectal biopsies had given only 30% positive results in 165 cases.

Chemical Classification

Professor J. N. CUMINGS (London) classified the sphingolipidoses according to the chemical groups attached to sphingosine. Techniques were now available to analyse the lipid composition of the grey and white matter. There was no variation between the sexes, but considerable variation at different ages. Specific abnormalities had been found on thin-layer chromatography in Gaucher's disease (though central nervous involvement was rare) and Niemann-Pick disease, but in metachromatic leukodystrophy and Krabbe's disease the abnormality was in the ratio of lipid components. Abnormal quantities of ganglioside were found in Tay-Sachs disease and the amaurotic family idiocy group. Of 178 brain biopsies 77 (43%) had been diagnostic, 37% abnormal but not diagnostic, and 20% normal. There had been no deaths and only occasional fits. At necropsy the area of brain had been found to be healed and the positive diagnoses confirmed.

Management of Progressive Disease

For the session on the management of progressive neurological disease Dr. D. WILLIAMS (London) took the chair. Dr. J. N. WALTON (Newcastle upon Tyne) discussed progressive muscular dystrophy and spinal muscular atrophy. He said that there was no specific treatment for these conditions and accurate diagnosis was the only safe guide to prognosis and genetic counselling.

Clinically the pattern and selectivity of muscle weakness and wasting was important for diagnosis. The electromyogram was more valuable in differentiating myopathy from neuropathy than in diagnosing individual myopathies. Serum enzyme estimations were valuable diagnostically, and muscle biopsy was useful in showing changes not only characteristic of muscular dystrophy and regeneration of denervation but also of recently recognized conditions such as central core disease.

A major problem clinically was the differential diagnosis of the "floppy" infant who was hypotonic from birth. Amyotonia congenita was not a diagnosis but a symptom of many disorders, including central nervous disease, spinal muscular atrophy, myopathies, some benign and not progressive, and diseases of joints and connective tissue. Arthrogryposis multiplex congenita was a complication of similar multiple aetiology.

Dr. Walton went on to outline the general principles of management, which were to avoid inactivity or immobilization even if the child was ill, to watch for contractures and to delay them by stretching the muscles, and to avoid skeletal deformities by the use of light plastic jackets which did not embarrass respiration.

Dr. K. HOLT (London) divided progressively handicapped children into those whose lesions were static, but who nevertheless fell further and further behind their normal fellows, and those whose condition was deteriorating. The latter often had progressive impairment of intellect as well as of physical ability, but this was not always so. Help had to be positive. Training was important to stimulate activity, and ability could improve while the deformity became worse. The ability to do just a little, such as manage one course of a meal alone, was of great value to the patient in morale. If skills were lost other ways had to be found to replace them. In prescribing aids doctors should try to provide things that the patient could manage independently, such as a motorized wheel chair. It was more frustrating to sit in a chair waiting to be pushed than not to have one at all. The morale gained could be easily lost by thoughtless treatment on hospital visits—for example, by being examined by many people as "an interesting case." Steady and continuing care needed a great deal of planning, Dr. Holt concluded. This theme was carried further by the next speaker, Miss M. E. ATKIN (London), who discussed help for the family of the progressively handicapped child. The social worker's job was to share the concern and fears of the parents. The stress of waiting for a diagnosis might be replaced by shock when it came, particularly if an older child already suffered from the same disease. Drawing on her experience of patients at Great Ormond Street, Miss Atkin illustrated how much emotional help was needed, particularly by the mother. In addition, there were many mundane practical problems. Parents' groups

had proved useful for self-help and sharing of problems, and there was scope for much more of this sort of solution.

Vulnerability of the Immature Nervous System

Starting from the hypothesis that slowing the rate of growth of the brain at a time when it was growing fastest would lead to permanent retardation, Dr. J. DOBBING (London) presented experimental evidence that there was a growth spurt in the brain and that interfering with it nutritionally caused lasting effects. Adult animal brains were found not to be affected by such stresses. Thus the brain weight of pigs at one year could be reduced by 33% below that of well-fed litter mates, and after two further years of good feeding it still remained 20% below the controls. Less drastic deprivation occurred in rat litters when 15 infants were fed by one mother and three by another. The overcrowded family was much smaller in both body and brain analysis at weaning and never caught up even on the best subsequent feeding. In humans the fastest rate of brain growth was some time before birth, and Dr. Dobbing thought it possible that the small-for-dates babies might well suffer at the critical time.

Dr. G. PAMPIGLIONE again discussed electroencephalographic findings, this time in the maturation of the puppy, human baby, and piglet. Such studies could be repeated at intervals without harm. Well-recognized patterns of development in each species emerged, which were partly related to the stage of development at birth.

In considering neonatal illnesses leading to chronic brain damage, Professor J. P. M. TIZARD (London) pointed out that some people had to have intelligence quotients below the mean and that most survived the perinatal period unscathed, so that it was important to be wary in attributing causes to deficits. Brain damage appeared to occur in many cases without neonatal illness, and must therefore have occurred in foetal life. Professor Tizard cited experiments in animals in which breathing pure nitrogen caused first dyspnoea, then primary reversible apnoea, spontaneous gasping, and finally terminal apnoea. In monkeys brain damage was found to occur only if the stage of terminal apnoea had been reached. Professor Tizard illustrated the complexities of research into the neonatal period by referring to an old report of the use of oxygen therapy, in which 21% were affected by retrolental fibroplasia and only 4% by spastic diplegia, while another series collected after the dangers of high oxygen therapy were known gave 1% with retrolental fibroplasia and 19% with diplegia. Since 1964 Professor Tizard's unit had monitored the arterial oxygen level in all neonates with respiratory illness, trying to maintain it at

about 75 mm. Hg and not exceeding 160 mm. Of the babies born before 35 weeks' gestation there were 57 survivors, none with retrolental fibroplasia, and four cases of cerebral palsy.

Behavioural Aspects

Dr. P. P. G. BATESON (Cambridge) discussed sensitive periods in the development of animal behaviour. The "critical periods" of the embryologists of 40 years ago had been succeeded by the knowledge that learning was not "all-or-nothing," so the term sensitive was preferable. This could be illustrated by experiments on birds learning to sing. The chaffinch from Somerset learnt a different dialect from the Cambridge one and the song was simpler if the bird was isolated during the first three weeks of life. It could even be taught by a taperecording to sing the final flourish in the middle at this period.

Professor B. M. FOSS (London) said that what was important was to make practical use of the identification of sensitive periods. Unfortunately, the effects of what happened during the sensitive period were not observable for a long time, and there was some confusion in individual instances about whether it was the onset or the offset of the sensitive period which was important. The factors affecting the onset of the sensitive period were probably organic development of the nervous and endocrine systems, passing through the stages of development in correct sequence, and previous learning—for example, to read a child has to be able to look from left to right in steps down the page. The time of offset might be affected by competition between habits, as when congenital cataracts were operated on, and competition between motivation or drives. By analogy with Dr. Dobbing's thesis behaviour might be most vulnerable when developing most rapidly.

Dr. E. J. M. BOWLBY (London) considered the effect of deprivation in early life in those left in a bad institution, and the effect of the disruption of affectional bonds already made. Progressive backwardness could result. In the first group there was inadequate novelty and change, with too many people involved in the child's care. Social responses appeared at the usual time but tended to fade away. Studies had shown that a group fostered by mentally defective women did better in school and subsequently than those with no mother-figure at all. The longer children were left in an institution the less likely they were to settle satisfactorily in a foster home. The bonds to the mother-figure were established between the third and seventh months. It was inadequate and misleading to assume that these bonds were merely related to feeding and pain. Investigation of psychopaths showed a high incidence of the disruption of these bonds. In one series the mother had been absent for more than six months in the first five years

of life in 35% of the psychopaths, but in only 6% of controls. There was a marked tendency for depressives, alcoholics, and addicts to have lost mother or father in the first 15 years of life.

Teale Lecture

Dr. D. B. CLARK (University of Kentucky) gave the Teale Lecture on the subject "Some Speculations on the Pathogenesis of the So-called 'Brain-damaged Syndrome.'" Dr. Clark said that the diagnosis of minimal brain damage was popular, even among grade schoolteachers in America. However, he pointed out, it was certainly not minimal in respect of disability or functional deficit, affecting as it did the abilities which distinguished man from animals. The minimal element was presumably the amount of actual brain damage causing the deficit. However, if this was small it should be possible to localize it. To try to do this he had selected 55 patients with minimal brain damage according to the following rigid criteria. There had to be no affected relatives, no deprivation, no primary emotional factors, no recurrent seizures, no birth trauma, no past or present gross motor defect, no complications, if premature, and an age of less than 30 months at the first visit. Clinically 41 were "clumsy," 18 had mild pyramidal signs, 15 strabismus, and chorea was seen in four. Thirty-six were hyperactive, four emotionally labile, and perseveration was seen in three. Speech was abnormal in all but nine. The E.E.G. was abnormal in 85%.

Clearly several levels of cerebral function were implicated, affecting both sides, and lesions would be slight. Suspicion fell on the brain stem and thalamus—areas seldom examined in the routine necropsy. Examination of brains of babies who died after precipitate labour had shown lesions in the territory of the vertebrobasilar arterial blood supply. Injection of radio-opaque fluid showed that the vertebral artery closed off completely when the head was rotated 35° in the opposite direction. It was recognized that the normal development of nerve cells depended on adequate stimulation, and that nerve cells grew differently after deafferentation. At birth the human thalamus was known to be mature, but the cortex was packed with small immature cells with few processes and few branches. If the thalamic area was destroyed columns of cortical neurones should be affected. Dr. Clark therefore postulated that turning the head during delivery could cause ischaemia in the region of the vertebrobasilar distribution. Some deaths would result but in others the loss of neurones could be minimal, but even losses of 5–10% of cortical cells might be enough to produce the minimally brain-damaged child, while the loss of total brain substance might remain undetectable.

Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Gastritis

D. N. CROFT,* D.M., M.R.C.P.

What is gastritis? There are many and varied answers. To the layman it is epigastric discomfort and vomiting, particularly related to heavy alcohol consumption. Clinicians find gastritis a convenient term when dealing with virtually any upper abdominal symptom, for it provides a quasi-scientific label with which to satisfy the patient. The gastroscopist's definition of gastritis depends on a visual appearance which has been shown to correlate poorly with the histological state of the mucosa, except when there are acute haemorrhagic erosions. The pathologist diagnoses gastritis by criteria such as the presence of inflammatory cells and the degree of atrophy, but these histological changes may bear little relation to the patient's symptoms. To the haematologist gastritis implies the total gastric atrophy characteristic of pernicious anaemia.

In context the term is reasonable when used by any of these individuals, but because it embraces such a variety of situations gastritis has come to be almost meaningless as a concept of disease. In relation to clinical medicine the term gastritis is best considered as embracing two distinct and probably unrelated entities: *acute gastritis*, which is the transient reaction of the gastric mucosa to irritants, and *atrophic gastritis*, in which the mucosa is permanently altered and its normal function impaired. In both conditions the lesion is diffuse and inflammatory cells are present to a greater or lesser degree, but these two features are the only similarities between acute and atrophic gastritis. In this article the clinical aspects of acute and atrophic gastritis will be considered in relation to recent work on the histology and physiology of the gastric mucosa.

Gastric Cells and Gastric Function

Before considering these diffuse lesions of the stomach it is worth recalling the normal architecture of the gastric mucosa. Our knowledge of the mucosal structure in man has increased greatly in recent years through the use of blind suction gastric biopsy.¹ By this technique samples of mucosa may be simply and safely obtained, and fixed before autolysis of the cells occurs.

The surface of the gastric mucosa facing the gastric lumen is covered with mucus-producing columnar (surface epithelial) cells. These cells are formed by mitoses in the base of the gastric pits and they migrate up the walls of the pits to the surface, where they are extruded into the lumen of the stomach (Figure). In man the life span (or turnover) of these cells is two to four days, and it has been estimated that there is a continuous loss into the gastric lumen of half a million cells per minute.² This active turnover of epithelial cells functions to protect the mucosa from damage.

Below the gastric pits is the glandular or secreting part of the mucosa, where the cells are of a very different type. The two important cells in this part of the mucosa are the large

parietal or acid secreting cells, and the smaller zymogenic or pepsin secreting cells. In terms of turnover these cells are static cells and mitoses are not seen in them. Intrinsic factor, which is required for vitamin B₁₂ absorption, is also produced in this part of the mucosa, possibly from the parietal cells themselves. At the two ends of the stomach, the cardia and the antrum, the normal histological picture is different, for acid and pepsin secreting cells are missing and the mucosa is mainly

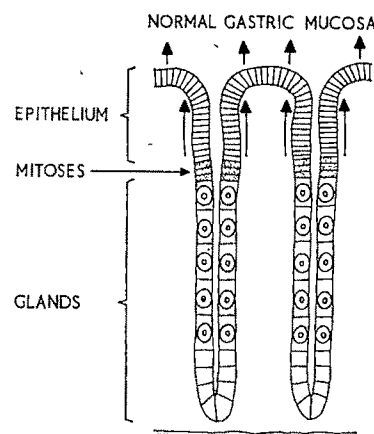


Diagram of a histological section through normal gastric mucosa. The epithelial compartment is a dynamic structure composed of columnar cells which are continuously produced by mitoses at the base of the gastric pits. This high turnover of cells probably functions to protect the mucosa from external insults. The cells of the glandular or secreting portion of the mucosa are static; the large circular ones represent parietal or acid secreting cells, and the smaller ones the zymogenic or pepsin secreting cells.

composed of mucus secreting surface epithelial cells arranged as a glandular structure. Gastrin, the hormone which stimulates gastric acid secretion, is produced in the antrum, but from which cell is not known.

Thus the mucosa is composed of two main compartments, a dynamically active surface epithelium which serves to protect the mucosa, and a glandular portion containing static cells which secrete hydrochloric acid, pepsin, and intrinsic factor. Acute gastritis is a transient lesion which affects predominantly the surface epithelium, leaving the gland cells intact. In atrophic gastritis there is permanent destruction of the glandular portion and also important changes in the surface epithelium.

Acute Gastritis

The physiological response of the gastric mucosa to irritants is to exfoliate surface epithelial cells. This was demonstrated in the dog³ in response to 5% ether and 5% clove oil, and in a patient with a gastrostomy in response to 95% alcohol, copper sulphate, hydrochloric acid, and a 1 in 30 suspension of mustard in water.⁴ More recently a similar effect has been shown when three soluble aspirin tablets suspended in 50 ml. saline were

* Senior Medical Registrar and Clinical Chief Assistant to the Radioisotope Department, St. Thomas's Hospital, London.

left in contact with the human stomach for five to ten minutes.⁵ It seems likely that many other substances may have a similar irritative effect on the gastric mucosa; but mild acute gastritis, even to the extent of epithelial cell exfoliation, produces no pain or gastric symptoms. Under these circumstances it is a physiological effect and no clinically significant blood loss or gastric lesion occurs, presumably because of the regenerative capacity of the surface epithelium. Some patients, however, develop epigastric pain and discomfort when they ingest particular irritants, such as aspirin, but this pain is more likely to be due to the presence of a peptic ulcer.

Nevertheless, acute gastritis following the ingestion of irritants can have clinical significance. The patients may present with epigastric pain, nausea, and vomiting as the main features, or with overt or occult gastrointestinal bleeding.

Acute Gastritis Without Bleeding.—This occurs when the stomach is subjected to a large dose of a gastric irritant and may be a feature of ingestion of certain poisons such as lysol. In clinical practice the two most common substances involved are alcohol and staphylococcal endotoxin.

The symptoms of alcoholic gastritis may occur within hours of ingestion but are commonly notable the following morning, when the subject experiences nausea, epigastric discomfort, and vomiting. Gastric biopsy performed during this phase demonstrates damage and denudation of the surface epithelium, with the glandular epithelium left intact.⁶ These histological alterations are transient and the mucosa returns completely to normal in a few days. One or two teaspoonfuls of sodium bicarbonate dissolved in half a glass of warm water and taken immediately on waking offers some relief for alcoholic gastritis.

Staphylococcal gastroenteritis presents with vomiting and diarrhoea. The onset is abrupt and occurs four to six hours after eating contaminated food. Similar alterations in the gastric mucosa to those of acute alcoholic gastritis have been noted, with return of the mucosa to normal within 96 hours.⁶ Staphylococcal gastroenteritis is a self-limiting condition, and though the patient may be acutely uncomfortable for some hours the symptoms subside spontaneously within 12 to 24 hours. Dehydration can occur during the acute phase and may require treatment with intravenous fluids.

Acute Gastritis With Bleeding.—There is now overwhelming evidence that there is an association between haematemesis and melaena and recent consumption of aspirin.⁷ The lesions responsible for this bleeding are haemorrhagic erosions which are probably initiated by the exfoliative effect of aspirin on gastric surface epithelial cells. Haemorrhage occurs with both soluble aspirin and plain aspirin tablets, but as there is evidence that undissolved aspirin particles can "burn" larger holes in the gastric mucosa, it is sensible to advise all patients to take soluble aspirin dispersed in half a glass of water. Alcohol has a similar effect, for it is not uncommon to find diffuse haemorrhagic erosive gastritis when patients are gastroscopied during the acute bleeding induced by an alcoholic bout.

Haematemesis or melaena or both caused by alcohol or aspirin consumption may require urgent blood transfusion, but most of these acute bleeds stop spontaneously within 36 hours, with complete healing of the erosions within a few days. Because of this it is important to establish in a patient with a haematemesis and melaena whether alcohol or aspirin in any form has been taken during the previous few days. If this history is forthcoming and there is no clinical evidence of a chronic peptic ulcer it should incline the physician towards conservative, non-surgical management. A few of these patients, however, will continue to bleed, and under these circumstances an emergency operation will be needed, but the surgical management of these patients can be extremely difficult, particularly if there is bleeding from multiple gastric erosions.

Occult oozing of blood from the stomach occurs in 70% of subjects who ingest two to three aspirin tablets four times per day, usually for rheumatoid arthritis.⁸ This bleeding occurs

whether or not the aspirin is in the soluble form. In most subjects it is of no clinical significance, but in a minority the blood loss may be more than 10 ml. per day, and these individuals are prone to develop chronic iron deficiency anaemia. The bleeding can be substantially reduced by giving enteric-coated aspirin, which can be used in these subjects as long as it controls their rheumatic symptoms. It does not always do so, probably because of erratic absorption. Patients taking aspirin habitually should have regular haemoglobin estimations performed and may require oral or parenteral iron.

Atrophic Gastritis

Unlike acute gastritis, in which the gastric mucosa suffers a transient episode from which it makes a complete recovery, the histological changes of atrophic gastritis are permanent. Atrophic gastritis occurs in association with pernicious anaemia, and also without pernicious anaemia, in which case it is called simple atrophic gastritis. It may involve the whole mucosa or only parts of it. Three main alterations in the histological picture are present.

Atrophy occurs primarily in the glandular portion of the mucosa and may be partial or complete. In pernicious anaemia it is invariably complete with total absence of parietal cells, resulting in histamine-fast achlorhydria.

Inflammatory cell infiltration occurs both in the epithelial compartment and beneath it. Many of the cells are lymphocytes, but polymorphs may be seen infiltrating between surface epithelial cells.

The surface epithelial cells are commonly stunted and abnormal. In severe forms of atrophy the mucosa may alter in such a way as to look like intestinal epithelium with finger-like projections similar to intestinal villi, a condition termed intestinal metaplasia. The turnover of epithelial cells is increased in atrophic gastritis, for there are more mitoses in epithelial cells and a higher loss of these cells into the gastric lumen.²

Cause of Atrophic Gastritis

There is no one cause of atrophic gastritis, but a number of factors are known to be associated with its presence. Age is clearly one of the most important of these, for simple atrophic gastritis is uncommon under the age of 40 and becomes progressively more frequent with advancing age.⁹ Constitutional factors also play a part. The well-known tendency for the gastric atrophy of pernicious anaemia to run in families is one indication of these, and another is the higher incidence of simple atrophic gastritis in subjects with blue eyes.

Gastric autoantibodies occur in the blood of patients with pernicious anaemia and simple atrophic gastritis, which suggests that these conditions are caused by an autoimmune process. However, it may be that the gastric autoantibodies may be merely a secondary phenomenon related to the presence of an abnormal mucosa.

Environmental factors also play a part, for simple atrophic gastritis is commoner in those of low social class. Other environmental factors include heavy alcohol consumption, smoking, hot tea drinking, and possibly habitual aspirin consumption.⁹ An individual over the age of 60 who smokes and drinks heavily has a 60% chance of having simple atrophic gastritis.

Clinical Significance

The most important association between atrophic gastritis and clinical disease is in the case of pernicious anaemia. In this condition there is total gastric atrophy, histamine-fast

achlorhydria, and failure of the stomach to secrete adequate amounts of intrinsic factor. Without intrinsic factor vitamin B₁₂ cannot be absorbed in the terminal ileum; the body runs out of vitamin B₁₂ in the course of four to five years and megaloblastic anaemia ensues.

Most patients with atrophic gastritis do not have gastric symptoms. Some clinicians believe that epigastric pain or discomfort, nausea, and anorexia can be ascribed to this histological change, but there is no real evidence that this is the case. A higher incidence of atrophic gastritis has been found in patients with non-ulcer dyspepsia—indigestion and negative barium meal and/or, negative gastroscopy. However, as atrophic gastritis is commonly associated with gastric ulcer it is possible that these subjects have a gastric ulcer which was missed by barium meal or gastroscopy. In our present state of knowledge it is better to regard atrophic gastritis as predisposing to gastric ulcer.

Rarely, patients with simple atrophic gastritis suffer from recurrent bleeding from gastric ulceration.¹⁰ This is certainly not the case in most patients with this condition; in fact there is some evidence that subjects with atrophic gastritis may be protected against aspirin-induced occult gastrointestinal bleeding.⁸ On the other hand, haematemesis and melaena induced by aspirin do appear to occur from acute erosions which have developed in areas of atrophic gastritis.¹¹ This suggests that under certain circumstances aspirin initiates acute bleeding from susceptible, atrophic areas of the gastric mucosa.

For many years it has been known that patients with recurrent iron deficiency anaemia may be achlorhydric, and more recently they have been found to have a higher than expected incidence of atrophic gastritis. Iron deficiency associated with atrophic gastritis cannot be adequately explained by chronic bleeding or failure of iron absorption. Other possible mechanisms involved include the production by gastric mucosa of an iron binding protein, or an excessive rate of loss of iron into the gastric lumen in exfoliated gastric epithelial cells. With regard to the latter it is interesting to note that patients with simple atrophic gastritis associated with iron deficiency anaemia have higher than normal cell loss from the gastric mucosa as measured by gastric D.N.A. (deoxyribonucleic acid) rates.²

Some 5–10% of subjects with pernicious anaemia develop carcinoma of the stomach. Even in patients without pernicious anaemia carcinoma of the stomach arises in atrophic gastric mucosa. A factor predisposing to cancer in atrophic gastritis is probably the higher than normal turnover of epithelial cells in this condition. The turnover of epithelial cells is particularly high in areas of intestinal metaplasia² which are the sites of atrophic mucosa that are most premalignant.¹²

Atrophic gastritis, even when diagnosed by gastric biopsy, does not merit treatment. Its finding should alert one to the possibility of associated conditions such as gastric ulcer, carcinoma of the stomach, pernicious anaemia, or recurrent iron deficiency anaemia, which require their own specific treatment. The recent finding that administration of corticosteroids will improve the secretory capacity and histological appearance of the atrophic mucosa of pernicious anaemia in no way implies that these drugs should be used to treat patients with atrophic gastritis.

Rare Forms of Gastritis

Menetrier's disease is a diffuse disorder of the stomach in which the mucosa becomes thickened and hyperplastic. Radiologically giant rugal folds are seen. An important feature of this condition is that patients may present with oedema due to

hypoproteinaemia. The hypoproteinaemia has been shown to be due to excessive loss of protein from the abnormal gastric mucosa. The disease is very rare, but is notable as it was the first condition in which protein-losing gastroenteropathy was described.

True infective gastritides have been described due to bacteria, syphilis, and tuberculosis. These are extremely rare and can only be regarded as medical curios.

Conclusion

To the clinician the term gastritis embraces two distinct and probably unrelated entities.

(1) Acute gastritis is a transient response of the gastric mucosa to the ingestion of irritating substances such as alcohol, staphylococcal endotoxin, and aspirin. The symptoms of excessive intake of these substances include epigastric discomfort, nausea, and vomiting. Haematemesis and melaena may occur from gastric erosions, and in Britain it is particularly associated with aspirin consumption.

(2) Atrophic gastritis is a permanent atrophy which affects part or all of the gastric mucosa. Total atrophy is a feature of pernicious anaemia. The cause of simple atrophic gastritis is not known, but in susceptible individuals it occurs particularly over the age of 50 and appears to be related to heavy alcohol consumption and smoking. It is commonly associated with other clinically important conditions; in particular with gastric ulceration, recurrent iron deficiency anaemia, and gastric carcinoma. The alteration in the gastric mucosa may be involved in the pathogenesis of these conditions, but only research will determine their exact relationship one to another.

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Hazards of High Flying

Q.—I understand that air hostesses on some lines are grounded for six months' rest after two years' flying. Why is this, and what, if any, are the hazards to their health from (1) pressurized cabins, and (2) radiation?

A.—The work of air hostesses may be physically tiring. They carry out their duties at the equivalent altitude of 5,000–6,000 ft. (1,524–1,828 m.). On short sectors their work load is heavy, because of the limited time available to serve a full complement of passengers. On long-haul operations they may be flying to, through, and from the tropics, with irregular hours, irregular meals, and without sufficient time to acclimatize or adapt themselves to environmental changes. Flying east or west may also cause upset to the normal circadian rhythm and an associated disturbance to the sleep pattern. These factors, which may predispose to fatigue, are easily remedied by adequate pre-flight and postflight rest periods.

There is, however, no valid medical reason why air hostesses should be grounded for six months' rest after two years' flying. It is possible that some airlines may temporarily employ air hostesses on the ground for special training or other reasons, but this would not be dictated by medical considerations. In fact, many of the international airlines have a 10-year flying contract for their air hostesses.

There is no known hazard to health from flying in pressurized aircraft where the simulated altitude is of the order of only 5,000–6,000 ft. The cabin temperature is controlled, and the rate of change of air in the existing V.C.10 is over 1 lb. (0.45 kg.) of fresh air per person per minute. The Olympic Games in Mexico City will be held at a similar altitude, and there are many other areas of the world above these altitudes where non-acclimatized visitors suffer no ill-effects.

There is no hazard to health from radiation in travelling by modern jet aircraft at altitudes of up to 40,000 ft. (12,192 m.). Many reliable airlines continue to monitor their aircraft cabins, and no hazard has been found to exist for passengers or crew. Even with the advent of supersonic aircraft operating at 60,000 ft. (18,288 m.) radiation will not be a problem, except possibly from solar cosmic events. These occur probably only once or twice in a year of maximum solar activity in the 11-year solar cycle. Such occasional and remote phenomena may lead to some operational limitations, but no radiation exposure hazard to passengers or crew will be acceptable.

Cobalt-labelled Vitamin B₁₂

Q.—Are the recently available ⁵⁷Co-labelled cyanocobalamin capsules adequate in the performance of the Schilling test?

A.—Radioisotopic cobalt-labelled vitamin B₁₂ has been used for some time in the investigation of the macrocytic anaemias.

More recently the isotope ⁵⁷Co has been used to label the vitamin. This isotope has a half-life of 270 days. It emits no particulate energy but one gamma ray (0.123 MeV). Though it has a longer half-life than ⁵⁸Co, its emission is probably safer for human use, since the liver irradiation produced by ⁵⁷Co is about one-tenth of that produced by the same dose of ⁵⁸Co.¹

Workman and Rusche,¹ investigating serum levels of ⁵⁷Co-labelled vitamin B₁₂ as a basis for an absorption test, compared the new method with the Schilling test. They gave 0.56 µg. vitamin B₁₂ labelled with 0.56 µCi ⁵⁷Co to fasting patients in the form of a capsule. A 24-hour urine collection was started immediately. 1,000 µg. of non-radioactive vitamin B₁₂ was given parenterally two hours after the ⁵⁷Co-labelled B₁₂. The total urine volume was measured and a 100-ml. aliquot counted in a 2 by 2 in. (5.1 by 5.1 cm.) crystal well-type scintillation counter. The dose excreted was 7 to 37% of the ingested dose in normals, whereas patients with pernicious anaemia never excreted more than 7%.

Vitamin B₁₂ labelled with ⁵⁷Co has also been used by Forshaw and Harwood in a similar investigation. It was evident that ⁵⁷Co vitamin B₁₂ was satisfactory for the Schilling test, though this test will, of course, still suffer from the inherent disadvantages of inaccuracy in patients with poor renal function, or in those who are unable to collect a complete sample of urine, and from the need to give a large dose of vitamin B₁₂ as a flushing dose.

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Drugs, Diet, and Porphyria

Q.—What drugs and foods are contraindicated in a patient with porphyria?

A.—The following drugs are contraindicated in hepatic porphyria: any barbiturate or sulphonamide; drugs containing oestrogen (for example, oral contraceptives); griseofulvin; glutethimide; phenytoin sodium; meprobamate; bemegride; methsuximide and phensuximide; methyprylone; chloroquine; tolbutamide and chlorpropamide; possibly methyl dopa; and dichloralphenazone. In addition, there are several drugs not in current use which are contraindicated—for example, apronal, sulphonal, and trional. This list is based on clinical and experimental studies,¹⁻³ and more recently on an in-vitro screening technique which allows the testing of the effect of drugs on the porphyrin synthesis of chick embryo liver cells.⁴

These drugs should not be used for patients, or near relatives of patients, with hepatic porphyria, which is the most common and important type of the disease and includes acute intermittent porphyria, porphyria variegata, cutaneous hepatic porphyria, and hereditary coproporphyria.

There is no evidence that drugs have adversely affected the very rare congenital erythropoietic porphyria, in which the bone marrow but not the liver is involved in the porphyrin dyscrasia. There is some evidence that in the much more common erythropoietic protoporphyria the porphyrin metabolism of the liver as well as of the bone marrow is abnormal. For this reason the drugs noted above should be avoided in this disease.

No item of diet, apart from alcohol, is contraindicated in porphyria. There is evidence, however, that a diet ample in carbohydrate and protein is beneficial to patients with porphyria.⁵ In my experience one patient developed a very severe attack of acute porphyria when she put herself on a very low calorie diet for obesity.

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Inheritance of Amyotonia Congenita

Q.—A woman has had two children, of which the first had amyotonia congenita (and died in infancy) and the second is normal. What are the chances of (1) further children of the woman being affected, and (2) the children of the normal boy being affected?

A.—Amyotonia congenita of the form which is best called "infantile progressive muscular atrophy" is an autosomal recessive condition.¹ Therefore the chance of recurrence in future children of this woman is one in four, and the chances of the offspring of the normal boy being affected are small. By the time he grows up it may be possible to test whether he is a heterozygote and, if so, whether his fiancée is also a heterozygote.

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Clothing for Tropics

Q.—Is underwear and clothing made of synthetic material better for tropical wear than wool or cotton material?

A.—Cotton and wool fibres absorb water, but synthetic materials such as orlon, nylon, etc., do not. In a hot climate the sweat rate is high, and it is uncomfortable to wear vapour- or water-impermeable clothes.

The earliest version of nylon shirts were distinctly unsatisfactory to wear, since sweat accumulated underneath the shirt. Since then techniques of weaving have improved, mixtures of cotton and synthetic fibres are used, and the disadvantage of water-impermeability has been reduced, though it cannot be abolished.

The advantages of clothes made from synthetic fibres include light weight, ease of washing, and durability. In practice, a useful compromise is to have cotton underwear and suits made of synthetic fibres, preferably mixed with wool or cotton.

Book Reviews

Adrenal Function

The Adrenal Cortex. Edited by Albert B. Eisenstein, M.D. (Pp. 685+xiv; illustrated. £8.) London: J. & A. Churchill. 1967.

So much of our modern knowledge of adrenal function is based on work done in the United States that a textbook on the subject from that country is an event of major importance. Practically all the 26 contributors to this volume have already gained world-wide renown for their experimental work in this field, and all students of the adrenal cortex will recognize its authority from the names of Baulieu, Liddle, Luetscher, Migeon, and Yates, to give but a few representative examples.

Although mainly a review of existing knowledge, the book does contain an appreciable amount of original work, as, for example, in the chapter on physiological control of adrenal cortical secretion. This section, using computer analogy, regards the mechanism as "a restricted signal, multiple input closed loop control with cortisol sensitive and insensitive pathways." The emphasis tends to be rather more on physiological background than on strictly clinical applications, but the scope is so wide that there

is inevitably a fund of information of direct interest to all clinical endocrinologists. Treatment aspects are particularly well handled in the chapters on adrenal insufficiency and on adrenogenital syndromes, both of which deal thoroughly and clearly with their difficult subjects.

An excellent and informed chapter on the synthetic analogues reveals how intense has been the research, and how great the knowledge gained of the effects on activity of structural modifications to the hydrocortisone molecule. In contrast a chapter on general metabolic effects reveals how little we yet know about the action of corticosteroids on immune phenomena and on thymus function, and a chapter on electron-microscopic changes in adrenal cells leaves one with the impression that an explanation of the changes in terms of function is still very uncertain. Perhaps the most stern test of a review of disorders associated with altered aldosterone secretion is its handling of the oedematous states. Even by this criterion this section

is wholly admirable. Indeed, all the sections are constructively critical in a way which is possible only to those who, by personal research in the subject, have developed a true "feel" for their problem.

British workers on adrenal problems may be surprised to read that fluorimetric methods of plasma corticosteroid estimation are regarded as requiring too much care and caution for the average clinical laboratory. The important analysis of the mode of action of triparanol on the adrenal which was carried out by one of the contributors is not referred to in another chapter where the subject is discussed. It is of interest to compare the chapter on Cushing's syndrome, which offers only one non-U.S. reference, with that on adrenogenital syndrome, where 130 of 384 references are to non-American sources.

But these are minor criticisms. This volume will be needed by all medical libraries, even though expensive, and will be very frequently referred to by all adrenal endocrinologists. It is clearly destined to become a standard work of reference on its subject.

C. L. COPE.

Amphetamine Effects

The Amphetamines. Toxicity and Addiction. By Orania Josseau Kalant, Ph.D. (Pp. 151+xii. 48s.) London: Oxford University Press. 1967.

Dr. Kalant has produced a valuable review of the literature concerning the toxicity of amphetamines in man and the characteristics of amphetamine abuse.

She considers the effects of acute and chronic amphetamine intoxication, giving representative case histories, and, drawing on Connell's 1958 study of 42 cases, describes amphetamine psychosis. She comments that it is impossible to judge from the literature how many people take amphetamines habitually without suffering any ill effects. At the same time she warns that psychotic reactions from the use of amphetamine are more common than is perhaps still realized, and that routine chemical tests for amphetamines in schizophrenic patients are important.

There is a useful review of the vexed question of what is meant by the terms drug addiction, habituation, and dependence. Dr. Kalant concludes that addiction to amphetamines does occur. She discusses the effects of amphetamine abuse on the individual and society, both in Great Britain and in other countries. Finally she discusses the dangers of amphetamine-like drugs.

This is a well written, up to date, objective review of a subject which is all too often distorted by prejudice and purple journalism.

PETER DALLY.

Radiotherapy

The Biological Basis of Radiation Therapy. Edited by Emanuel E. Schwartz, M.D. (Pp. 624+xvi; illustrated. £7.) London: Pitman. 1967.

During the last 50 years radiotherapists have accumulated a vast practical experience in the radiation treatment of cancer. Since the second world war the growing number of hospital physicists have helped to transfer this practical experience from one radiotherapy centre to another by accurately measuring the radiation dose distribution in the treatment field, so that the observed clinical responses could be related to accurate physical measurements of radiation dose. In more recent years a new phase of development of radiotherapy has occurred in which the basic disciplines of biology, biochemistry, and biophysics have played an interlocking role. Although these developments have not yet had a great deal of impact on clinical practice, apart from a few notable exceptions such as the oxygen effect, they are beginning to give a better understanding of why the radiotherapy techniques built up from years of practical experience have been so effective.

The book under review contains 10 chapters, each written by a specialist, dealing with different aspects of the biological basis of radiotherapy. The first two chapters contain reviews of the biophysical and biochemical effects of radiation at the molecular level, and the third chapter is concerned with radiation effects at the cellular level. These subjects are the basis of radiotherapy, and in this book the individual authors deal com-

petently with their material in the 120 pages available to them.

There is some overlap between the next two chapters, which deal with the pathological effects of radiation and radiation injury in man, but this is not sufficient to make either of the chapters unnecessary.

In the sixth chapter, the longest in the book, Dr. L. Cohen has undertaken the difficult task of relating the principles of radiobiology obtained from experiments at the cellular level to the clinical practice of radiotherapy. The term R.B.E. is unfortunately given two different meanings in this chapter. In Table 6-2, R.B.E. is used in the conventional manner, whereas in Table 6-5 the reciprocal of this value is also called R.B.E. Again there is some confusion about which word is abbreviated to E. In the original paper on this subject, published in 1931, Failla and Henshaw definitely used "effectiveness" and not "efficiency" as in this chapter. However, these are minor criticisms of a chapter which should prove extremely interesting to those practising radiotherapy.

The next chapter deals with modifications of radiation response by means of oxygen or chemical compound techniques, which are becoming more widely used in clinical practice. The biochemistry of cancer cells is reviewed in the eighth chapter. As yet cellular biochemistry has had little bearing on clinical practice, but undoubtedly a better understanding of it could lead to more efficient treatments in the future.

The last two chapters review the influence of the host on tumour growth and the influence on radiotherapy of the experimental

treatment of tumours in animals. These two chapters emphasize that there are many factors which may influence the growth of tumours other than the tumour cells *per se*.

In summary this book contains a wealth of information which is indicated by the number of references given at the ends of each chapter amounting to more than 2,300. It should be particularly useful to those starting in the field of radiotherapy and a valuable teaching aid in medical schools.

G. W. DOLPHIN.

Factual Account of Communicable Diseases

Infectious Diseases. By A. Melvin Ramsay, M.A., M.D., and Ronald T. D. Emond, M.B., Ch.B., M.R.C.P., D.T.M.&H. (Pp. 306+xii; illustrated. 63s.) London: William Heinemann, 1967.

For some years there has been a need for a well-illustrated text on British practice in communicable diseases and this book by Dr. Ramsay and Dr. Emond fills the gap satisfactorily. It is an essentially factual account. The few opinions expressed are of necessity dogmatic in a book designed for students, but the factual approach does lack the impact of descriptive writing. For example, a student who has never seen a case of mononucleosis is not presented with any clear pictures of what such a patient actually looks like. Perhaps this is a harsh criticism, as medicine can only really be learnt at the bedside. The virology is up to date and nicely presented with excellent electron photomicrographs. Considering the price is only three guineas the colour reproductions are more than satisfactory and many of them are very helpful. At the end of the book there are useful tables concerning isolation and quarantine practice and the brief chapter on "P.U.O." gives excellent advice on the investigation of this common problem.

Brevity leads to dogmatic statements with which not all would agree. For example, "the downward course of the eruption (in measles) is so constant that any other course would exclude the diagnosis"; "exposure to chicken-pox sometimes causes herpes zoster"; "vaccination does not offer protection against haemorrhagic smallpox"; and "scarring in flat smallpox is deep." Desquamation of the severity shown on Plate 7 nowadays follows other erythemas much more frequently than scarlatina, so the caption is somewhat misleading. In the chapter on meningitis no indication of the quantity of cellular and biochemical changes in the cerebrospinal fluid is given and, more important, there is no mention of the very real diagnostic difficulty of the "half-treated" case which can so readily mimic aseptic meningitis. Surely few of us now use parenteral, as opposed to oral, penicillin in the routine treatment of streptococcal infections.

The references are somewhat unbalanced (for example twenty-four for "rubella," none for "acute meningitis") and do not always fall into the category of "recommended further reading for students."

These are minor criticisms which do not detract from the general value of the text,

over which a great deal of care has clearly been taken. The authors and publishers are to be congratulated on producing a well-illustrated book containing up-to-date information about the common communicable diseases in Great Britain at a remarkably reasonable price.

G. DONALD W. MCKENDRICK.

What is Known about Lymphocytes

The Lymphocyte in Immunology and Haemopoiesis. Symposium, Bristol, 1966. Edited by J. M. Yoffey. (Pp. 376+viii; illustrated. £6.) London: Edward Arnold, 1967.

The Lymphocytes. By Michael W. Elves, B.Sc.(Notts), Ph.D.(Manch.). (Pp. 303; illustrated. 50s.) London: Lloyd-Luke, 1966.

Until comparatively recently the lymphocyte was looked upon by haematologists as a blood cell of characteristic morphology but dubious function and by histologists as being concerned in an ill-defined way with the body's responses to chronic infection. Now, as one result of the almost explosive development of the science of immunology, it is regarded as a cell of key importance, and a great deal of research on its functions is being undertaken by medical scientists and biologists.

The larger of the two volumes under review—*The Lymphocyte in Immunology and Haemopoiesis*—records the proceedings of a large-scale international symposium which was held in Bristol in April 1966 under the general direction of Professor J. M. Yoffey. In summary, it consists of 43 short to medium-length papers, with references but without discussion, and without index, which cover a representative but very wide field of experimental studies in relation to lymphocyte physiology and function. Among the main topics dealt with in well illustrated and documented papers are the morphology and embryology of lymphocytes, the response of normal and pathological lymphocytes to phyto-haemagglutinin, lymphocyte kinetics and circulation, the possible role of "lymphocytes" as pluripotential stem cells, their role in immunity, including the homograft reaction, experiments with anti-lymphocyte serum, and the thymus and lymphocytes.

The completed volume is a valuable record for the research worker in the lymphocyte field, but the reading of it is likely to prove hard going for the general physician or clinical haematologist, who may feel disappointed that of the subjects in which he is particularly interested the lymphoproliferative diseases are not dealt with in detail and the syndromes associated with deficient lymphocytopoiesis and the nature of the lymphocyte response in infectious mononucleosis are not mentioned. The reviewer would have welcomed, too, a final chapter summarizing the whole subject, admittedly not an easy task in a rapidly expanding field.

In the smaller of the two volumes, *The Lymphocytes*, Dr. M. W. Elves has attempted to present an up-to-date review of what is known about lymphocytes in one medium-sized volume. Starting with anatomy and physiology, he deals with circulation, lifespan, and production, then the lymphocyte's

role in inflammation and repair and in antibody production, and its role in transplantation immunity. Next, there are chapters on lymphocyte transformation and the possible function of lymphocytes as stem cells and trephocytes. Finally, there is a short and useful section entitled "Some Conclusions" in 16 brief paragraphs. The main text is followed by an extensive bibliography of 777 references, with titles, and an index.

Dr. Elves's book is well conceived and a brave attempt is made to present a critical review of a difficult subject. However, the book is not easy to read, and in places—and this is not Dr. Elves's fault—it reads like a catalogue of discordant results and false interpretations. All in all, however, of the two books now being discussed that of Dr. Elves would seem to be the more useful to a pathologist or physician who wishes to bring himself up to date in a difficult field. The book is illustrated rather sparingly with 43 figures, mostly line diagrams and photomicrographs. Some of the latter are of rather poor quality and the text is marred by occasional infelicities of style.

J. V. DACIE.

Girls Growing Up

Adolescent Gynecology. Edited by Felix P. Heald, M.D. (Pp. 163+x; illustrated. 72s.) Edinburgh and London: E. & S. Livingstone, 1966.

This attractive little volume reports the proceedings of a seminar supported by the Department of Health Education and Welfare of the United States. But when it was held, and where, is not revealed. It must have been a good meeting, since well-known and excellent speakers—including J. W. Goldzieher, R. B. Greenblatt, C. W. Lloyd, A. L. Southam, and S. H. Sturgis, invidiously perhaps to select but a few—took part. No doubt the papers all sounded well when given, but some read rather too colloquially and repetitively. More ruthless editing would have been advantageous, but one can well sympathize with the editor's difficult task in this situation.

The scope of the work is best indicated by the subjects covered: Janet McArthur on the reproductive endocrinology of adolescence; Lloyd on the biochemistry of steroids and hormones; Goldzieher on the identification of sex hormones by chemical and biological assays (a controversial and stimulating essay, this, emphasizing the necessity of regarding endocrine laboratory data with caution); Anna Southam on metropathia haemorrhagica and non-psychogenic amenorrhoea; Sturgis on the management of congenital defects; F. P. Heald on ovarian tumours during adolescence; V. B. Mahesh and R. B. Greenblatt on hirsutism; A. M. Burnett on vaginitis; W. J. Dougherty on public health aspects of venereal disease; A. E. Marans on the psychological impact of pregnancy on the adolescent girl; and S. L. Werkman on sex education in adolescence. There is an index, but it is somewhat sketchy and incomplete.

From a number of points of view the adolescent girl is requiring increasing attention from the doctor and since she fits neatly into neither the province of the paediatrician,

nor that of the gynaecologist it is obviously the family doctor to whom she ought most readily be able to turn for advice. This book could certainly provide him with a timely and useful refresher course.

G. I. M. SWYER.

International Council of Nurses

A History of the International Council of Nurses. 1899-1964. The First Sixty-Five Years. By Daisy Caroline Bridges, C.B.E., R.R.C., S.R.N., S.C.M., F.R.S.H. (Pp. 254 + xxi. 40s.) London: Pitman. 1967.

On 1 July 1899, at the annual conference of the Matrons' Council of Great Britain and Ireland, Mrs. Bedford Fenwick proposed "that steps be taken to organize an International Council of Nurses." The resolution was carried and a provisional committee appointed, which at its meeting next day authorized the English members to draw up a constitution and circulate it to interested

parties. A year later the constitution was adopted, Mrs. Bedford Fenwick elected the first president, and Miss Lavinia Dock honorary secretary. Between 1901 and 1912 congresses were held at Buffalo, Berlin, Paris, London, and Cologne, but we are told that "it was inevitable that with no established office or secretariat, and with the president and honorary secretary divided by the Atlantic Ocean, very little work could be undertaken between meetings."

The intervention of the war of 1914-18 made matters more difficult, but in 1922 changes were made, a full-time secretary was appointed, and an office established in Geneva. The new secretary, Miss Christiane Reimann, was a very capable hard-working officer who visited many European countries and greatly advanced the membership and influence of the council during her 12 years of office. She was succeeded by Miss Anna Schwarzenberg, whose ability to speak seven languages was of great assistance. The war of 1939-45 made it necessary to move the headquarters first to London and then to New York. After peace was declared the office was again established in London, and

the secretariat was increased and reorganized, so that when Miss Bridges was chosen as chief executive officer in 1948 she was able to do much more field work in different parts of the world, thus increasing the usefulness and influence of the International Council. Between 1948 and 1961 a conference was held at Stockholm and congresses in Petropolis (Brazil), Rome, and Melbourne, and membership of the I.C.N. was increased by the addition of over 30 countries. The present headquarters is again in Geneva, and the executive director is Miss Helen Nussbaum. At the congress held at Frankfurt in 1965 there was an assembly of 6,000 nurses from 63 countries—good evidence of a thriving organization.

The story is well told in a pleasing style, controversial points are gently dealt with, and credit given where credit is due. The illustrations are very good and tell a story of their own. The book should appeal to all nurses and to those medical practitioners who wish to keep themselves well informed about the achievements of a sister profession.

ZACHARY COPE.

Books Received

Review is not precluded by notice here of books recently received.

Transport und Funktion Intracellulärer Elektrolyte. Symposium in Schönen, 1967. Edited by F. Krück. (Pp. 299; illustrated. DM. 32.) Munich: Urban & Schwarzenberg. 1967.

Modern Trends in Pathology—2. Edited by T. Crawford, B.Sc., M.D.(Glasg.), F.R.C.P., F.R.C.P.(Glasg.), F.C.Path. (Pp. 323 + vii; illustrated 85s.) London: Butterworth. 1967.

Lecture Notes in Pharmacology and Therapeutics for Nurses. By James A. Boyle, M.D., M.R.C.P. (Pp. 228; illustrated. 25s.) Edinburgh and London: E. & S. Livingstone. 1967.

The Vitamins. Chemistry, Physiology, Pathology, Methods. 2nd edition. Vol. 1. Edited by W. H. Sebrell, jun., and Robert S. Harris. (Pp. 570 + xiii; illustrated. £10.) New York and London: Academic Press. 1967.

Viral and Rickettsial Infections of Animals. Vol. 1. Edited by A. O. Betts and C. J. York. (Pp. 388 + xi; illustrated. £6 8s.) New York and London: Academic Press. 1967.

Surgery of the Ear. 2nd edition. By George E. Shambaugh, jun., M.D. (Pp. 722 + xi; illustrated. £10 10s.) London: W. B. Saunders. 1967.

Radiology in Neuro-Ophthalmology. By Guido Lombardi, M.D. (Pp. 244 + viii; illustrated. £5 6s.) Edinburgh and London: E. & S. Livingstone. 1967.

Introduction to Psychotherapy. Its History and Modern Schools. By J. A. Hadfield. (Pp. 363. 50s.) London: George Allen & Unwin. 1967.

Medizinische Radiologie. By Professor Joachim Atndt. (Pp. 375; illustrated. No price given.) Jena: Gustav Fischer. 1967.

A Guide to the Identification of the Genera of Bacteria. With Methods and Digests of Generic Characteristics. 2nd edition. By V. B. D. Skerman. (Pp. 303 + xii; illustrated. 78s.) Edinburgh and London: E. & S. Livingstone. 1967.

Quantitative Problems in Biochemistry. 4th edition. By Edwin A. Dawes, Ph.D., D.Sc., F.R.I.C. (Pp. 351 + viii. 37s. 6d.) Edinburgh and London: E. & S. Livingstone. 1967.

Medicine in Medieval England. By C. H. Talbot. (Pp. 222. 35s.) London: Oldbourne. 1967.

New Trends in Basic Lymphology. Proceedings of a Symposium held at Charleroi, Belgium, 1966. Edited by J. M. Collette, G. Jantet, and E. Schoffeniels. (Pp. 235; illustrated. Fr. 48.) Basel and Stuttgart: Birkhäuser. 1967.

The McPherson Experiment. Expanding Community Hospital Services. By John R. Griffith, Lewis E. Weeks, Ph.D., and James H. Sullivan. (Pp. 337; illustrated. \$10.) Ann Arbor, Michigan: Bureau of Hospital Administration. 1967.

The Origins of the National Health Service. The Medical Services of the New Poor Law, 1834-1871. By Ruth G. Hodgkinson, Ph.D. (Pp. 714 + xvii. £6 6s.) London: Wellcome Historical Medical Library. 1967.

Ophthalmic Eponyms. An Encyclopedia of Named Signs, Syndromes, and Diseases in Ophthalmology. By Spencer P. Thornton, M.D. (Pp. 324 + ix. No price given.) Birmingham, Alabama: Aesculapius. 1967.

Functional Bandaging. Including Splints and Protective Dressings. By Seymour W. Meyer, M.D., F.A.C.S., D.S. (Pp. 294 + viii; illustrated. 75s.) Barking, Essex: Elsevier. 1967.

A Manual of Abdominal Operations. By R. M. Kirk, M.S., F.R.C.S. (Pp. 208 + xvi; illustrated. 30s.) London: Pitman. 1967.

Funktionelle Neurologische Diagnostik. Volume 3. Gehirn. Edited by Dr. Harri Joschko. (Pp. 332 + xxiii; illustrated. £5 2s. 5d.) Jena: Gustav Fischer. 1967.

Toxikologie-Fibel. By Professor Wolfgang Wirth. Professor Gerhard Hecht, and Dr. Christian Gloxhuber. (Pp. 391 + xiii. DM. 36.) Stuttgart: Georg Thieme. 1967.

Middle Age. Edited by Roger Owen. (Pp. 152. 8s.) London: British Broadcasting Corporation. 1967.

Organization and Handling of Bibliographic Records by Computer. Edited by Nigel S. M. Cox and Michael W. Grose. (Pp. 187 + ix; illustrated. 65s.) Newcastle upon Tyne: Oriel. 1967.

Studies on the Chemical Composition of Foods Commonly Used in Southern Africa. Collected by F. W. Fox, D.Sc.(Lond.). (Pp. 73 + xiv. 2.75 Rands.) Johannesburg: South African Institute for Medical Research. 1966.

The Principles of Medical Computing. By Thomas R. Taylor, M.B., Ch.B., M.R.C.P.G., M.R.C.P.Ed., D.P.M. (Pp. 154 + ix; illustrated. 35s.) Oxford: Blackwell. 1967.

The Facemaker. By Richard Gordon. (Pp. 244. 25s.) London: William Heinemann. 1967.

Ruthin: A Town with a Past. By Trevor Hughes. (Pp. 137; illustrated. 15s.) Ruthin: Dr. Trevor Hughes. 1967.

Concise Anatomy. By G. M. Wyburn, J. G. Warbrick, and Mary E. Todd. (Pp. 218 + x; illustrated. 35s.) London: Longmans, Green. 1967.

Tulburari Metabolice in Boli Neuro-Psihice. By Dr. V. Ionasescu. (Pp. 291. 21.50 Lei.) Bucarest: Editura Academiei Republicii Socialiste Romania. 1967.

Biologia Arsurilor. By Professor N. Nestorescu, Dr. Al. Gh. Ciplea, and Dr. C. Bona. (Pp. 184; illustrated. 12 Lei.) Bucarest: Editura Academiei Republicii Socialiste Romania. 1967.

A Dictionary of Pharaonic Medicine. First edition. By Dr. Hassan Kamal. (Pp. 509; illustrated. 2 Egyptian pounds, 500 milliemmes.) Cairo: Kawmiah Distributing Co. 1967.

Technique in Blood Grouping. 2nd edition. By Ivor Dunsford, Ph.D., M.M.Path., F.I.Biol., and C. Christopher Bowley, M.B., B.S., F.R.C.O.G., F.C.Path. (Vol. 1: pp. 264 + xviii. Vol. 2: pp. 265-534 + xi; illustrated. £5 5s. set of 2 volumes.) Edinburgh and London: Oliver & Boyd. 1967.

Advances in Reproductive Physiology. Vol. 2. Edited by Anne McLaren. (Pp. 347; illustrated. 75s.) London and New York: Academic Press. 1967.

Correspondence

Letters to the Editor should not exceed 500 words.

"Geriatric Emergencies"

SIR,—I suggest that the difficulties in Dr. D. F. C. Deacon's area, and in some others, may be partly ones of communication (7 October, p. 53).

The term "geriatric" carries too many meanings. Some speakers mean any patient over 65, but most exclude surgical cases; some mean any chronic illness; others only chronic illness of the elderly; some think only of confused or incontinent patients, or patients with social difficulties, or possibly both. I fear that our administration will never be rid of this word, once coined to describe certain new medical knowledge, but now applied to beds, chairs, wards, doctors, and anything else in need of an adjective. May I plead for caution when recommending patients for admission? Ambiguity at such times can be disastrous.

"Geriatric emergencies" are not always medical emergencies. They may prove to have chronic dementia, longstanding hemiplegia, or simply no home. Some small crisis, domestic or medical, has exacerbated long-standing difficulties. Admitted in haste, they block precious beds for months, for the longstay unit, geared carefully to an assessed

waiting-list, cannot suddenly take them over. Small wonder that "acute" wards try to exclude them.

Chronic dementia is a particularly serious problem. I hold strongly that these cases should be nursed apart from fully sane patients of any age and that they are as unsuitable for the acute geriatric wards as for the acute medical wards. Dr. Deacon's patients evidently agree with me. Confusion or delirium due to acute illness seems, however, to be tolerated by sane patients, who see the necessity for urgent physical treatment of so sick a man. Differential diagnosis may be difficult, but the relevant history helps greatly, and the general practitioner may know this best. If we are to separate these cases it is not enough to hold special beds empty for psychogeriatric emergencies. We must direct the right cases to these beds, and need a clear diagnosis on the telephone. The phrase "I have a geriatric emergency case" is too vague. Please can we avoid it?—I am, etc.,

G. DALAWELL WALKER.

Newsham General Hospital,
Anfield, Liverpool 6.

Anaemia in Elderly Housebound Patients

SIR,—A survey was made among patients over the age of 65 and known to be housebound in an N.H.S. practice situated two miles north of the centre of Birmingham during 1964.¹ Many of them had been visited regularly, or at intervals, during the previous two or three years. Fifteen patients in the sample lived alone and 31 lived with a relative; eight of the latter group were men and the rest were women. Results were obtained from 45 of the 46. The mean age of the whole group was 81 years. Where the patient had been treated for anaemia during the previous two years the level before treatment was the level included in the survey.

Of the whole group 41% had haemoglobin levels below 12.0 g./100 ml. They all had mean corpuscular haemoglobin concentration levels below 31% and were considered iron-deficient. Some of the patients were known to be taking aspirin or to have hiatus herniae and other conditions from which they might have bled, but no evidence of overt bleeding was encountered during the survey.²

At the same time as the elderly housebound were being examined a stratified random sample of the whole practice population was investigated.¹ In this random sample the men and women born in 1880 and 1890, and who were 74 and 84 years old at the time of the survey, showed an incidence of anaemia of 17%, a figure similar to those of French³ in Staffordshire and

Semmens⁴ in Yorkshire, but higher than that of Hobson's survey in Sheffield.⁵ This suggests that those who are housebound by age and infirmity are especially liable to become anaemic. Similar figures for the incidence of anaemia are found among entrants to old people's homes.

The fact that most of the housebound patients had been seen at intervals during the previous year supports the opinion that it is easy to overlook anaemia, especially in the elderly, if reliance is placed on clinical observation. This may be partly due to a stagnant peripheral circulation giving a false impression of health, and partly to an all-too-easy attribution of lassitude in the elderly to senile changes. Most general practitioners have a number of patients who are visited at intervals because they are known to be housebound. If the incidence of anaemia generally is as high as is suggested by the present survey then this section of the population warrants periodic checks by the general practitioner or health visitor so that the development of anaemia does not go unnoticed.—I am, etc.,

Cambridge.

R. H. MORGAN.

REFERENCES

- 1 Morgan, R. H., Cambridge M.D. thesis, 1965.
- 2 Bedford, P. D., and Wollner, L., *Lancet*, 1958, 1, 1144.
- 3 French, D. G., *British Encyclopaedia of Medical Practice Interim Supplement*, No. 190, 1958, p. 2.
- 4 Semmens, A., *Brit. med. J.*, 1959, 2, 1153.
- 5 Hobson, W., and Blackburn, E. K., *ibid.*, 1953, 1, 647.

Massive Overdose of Adrenaline

SIR,—I would like to comment on the case of adrenaline overdosage described by Dr. M. A. Lewis (7 October, p. 38).

The picture described is similar to, but more severe than, that seen in a phaeochromocytoma crisis. Initially, due to catecholamine release, there is intense vasoconstriction and hypertension. During this vasoconstrictive phase circulatory volume is depleted by loss of water, electrolytes, and plasma proteins into the tissue spaces. Following this phase, with return of more normal vascular tone, the patient may be found to be hypotensive, since he is by now hypovolaemic: the paradoxical hypotension of a phaeochromocytoma crisis. The use of vasopressors at this stage tends to prolong the vasoconstriction and prolong the hypovolaemia (? and hypotension). The adrenaline used may, by local vasoconstriction, have produced a "depot" anyway. Intravenous lactated Ringer solution, plus a longer-acting blocking agent such as phenoxybenzamine, is indicated here to convert the patient with a state reminiscent of acute peripheral circulatory failure with cold white skin to a warm, pink, vasodilated patient with adequate tissue perfusion and renal output.

It would be interesting to know whether haemoglobin estimations were done on the patient described. One would expect initial haemoconcentration, perhaps gross, with a gradual return to normal as the patient replenished a low circulatory volume.—I am, etc.,

M. C. CROCKER.

Department of Thoracic and
Cardiovascular Surgery,
Groby Road Hospital,
Leicester.

SIR,—Dr. M. A. Lewis is to be congratulated on successfully treating a patient who had received a subcutaneous injection of 16 mg. adrenaline by giving trimetaphan camsylate (7 October, p. 38).

He refers to my review of similar cases¹ in which I stated that the maximum tolerated dose of adrenaline was in the region of 7–8 mg. The patients who survived these doses had received no treatment and the figure of 7–8 mg. for the maximum tolerated dose accordingly still stands.—I am, etc.,

Dulwich Hospital, BERNARD J. FREEDMAN,
London S.E.22.

REFERENCE

- 1 Freedman, B. J., *Lancet*, 1955, 2, 575.

Bottle Cuts

SIR,—Over the past three weeks I have treated at least three severe lacerations—in these instances due to milk bottles, though no doubt beer bottles play an equally important part. The first involved the ulnar nerve in the arm, the second involved the radial nerve in the forearm, and the third involved the superficial palmar arterial arch in the hand. The arm and forearm lacerations also in-

volved the surrounding muscles, causing considerable damage. In each case an unfortunate milkman had slipped on a wet and slippery pavement or step and fallen heavily on a glass bottle, which had shattered and caused the injury. Altogether a total of about three hours was taken for treatment of these cases, the work involving up to three doctors at any one time, with a difficult exploration and nerve suture.

Our casualty department sees and treats between 80 and 120 new attendances daily from a large catchment area, including dock-yards and a motorway. There is one duty casualty officer, with orthopaedic and surgical firms on call, and a second casualty officer seeing reattendances for a few hours in the morning only, and such lacerations impose a severe strain, involving delay in treatment for many patients.

Prevention is always better than a cure, which often is incomplete in these cases. Little can be done about our English weather and wet slippery pavements, but surely in this age of plastics much time and expense would be saved to busy casualty departments and the public if milk distributors and brewers would supply their products in polyethylene bottles. Is there some objection to this or do these firms not realize the potential danger of their containers?—I am, etc.,

MALCOLM J. MCARTHUR.

St. Bartholomew's Hospital,
Rochester,
Kent.

Humidification of Oxygen

SIR,—Information supplied in the article "Is the Woulfe Bottle an Efficient Humidifier of Oxygen?" (29 July, p. 277) must not go uncriticized. The hair hygrometer is not constantly accurate over large ranges of humidity and if so used must be constantly recalibrated for the range in which it is being used. It is generally conceded that hygrometry gives constant and accurate results.

Method of delivery is not discussed, and this will determine the actual atmosphere inhaled by the patient. With nasal catheters there is a marked tendency for patients to breathe via the mouth, and this will negate somewhat the attempt at humidification, since mouth breathing will produce conditions in the trachea of 31° C. and 26 g./cu. m., much lower than those found when breathing via the nose (34° C. and 34 air humidity). The best results with this method, and these under the most unusual and artificial conditions, were 27.7 air humidity, still 5–12 below that found naturally, even in the oropharynx. The high levels of humidity reported do not obtain in practice. Even in Australia the average daily summer temperature is 22° C. with 12.9 air humidity. This does not take account of winter temperatures or cool nights, for oxygen therapy often must be continuous. One can assume that the gas issuing from the bottles is saturated with water vapour, and this certainly will be so with the modern diffuser. The statement that absolute humidity is dependent upon relative humidity and temperature is correct—not ambient temperature, but the temperature of the water bath. It is simple enough for anyone to fairly estimate the humidity being delivered, and this has been done using the information supplied in the text and the graph (Fig. 2) of the article.

Ambient temperature minus temperature drop in water below ambient equals temperature of water bath.

Flow l. per Minute	3	5	8
	g./cu. m.	g./cu. m.	g./cu. m.
Cool	6.5–7	5.5–6.5	6–6.5
Hot	22.9–26.9	18.9–22.9	16–20.0

These results are lower than that reported in the article and are those usually found in practice. The only worth-while results are those with low flows which will limit the application of the method, and these were obtained under unusual artificial conditions.

Without external heating this method at best prevents the inhalation of dry gas and does nothing to augment the humidification or produce high humidity which is required for some conditions—for example, tracheo-bronchitis; tracheostomy. The method is only indicated for oxygen therapy of short duration.—I am, etc.,

C. A. SARA.

Royal Alexandra Hospital for Children,
Sydney, Australia.

REFERENCES

- 1 Cole, P. J., *Laryngoscope*, 1953, 67, 449.
- 2 Sara, C. A., and Clifton, B. S., *Med. J. Aust.*, 1962, 2, 447.
- 3 Sara, C. A., *ibid.*, 1965, 1, 99.
- 4 — and Currie, T., *ibid.*, 1965, 1, 174.

Respiratory Distress Syndrome

SIR,—Because the oesophagus enters the stomach from behind it is difficult to belch while lying on the back; and if Dr. Mark Reid's babies (30 September, p. 863) are nursed supine this may account for their distension after bicarbonate.

Over the past two years, for ill newborn babies, I have turned increasingly from intravenous treatment to immediate hourly tube feeds of 20% dextrose and 1–2% sodium bicarbonate, alternating with milk. Babies tolerate this well if kept throughout on their bellies in a head-up position.—I am, etc.,

Downton,
Wiltshire.

T. H. HUGHES-DAVIES.

Anxiety State after "Sex Education"

SIR,—Dr. Louise F. W. Eickhoff (30 September, p. 865) must have realized that her 10-year-old boy patient attending "the excellent boarding school" was psychologically vulnerable from an early age as he had no father to initiate him in the male role. Presumably one of the reasons for sending such a boy to boarding school was just this. Perhaps Dr. Eickhoff had something to do with this recommendation and now regrets it, for in many ways a child with family social problems is better able to work through these at home. Residential schools may be a socially and an educationally expedient way of side-stepping certain emotional situations.

As a school doctor for some years, I am now much more hesitant about this traditional middle-class way of putting such problems into cold-storage (possibly to occur later in life or in the next generation). Those interested in developmental paediatrics are fascinated by the phasing of the several biological

rhythms that exist, but every child has to face his or her puberty at some time. Some children are by instinct better orientated towards somatic and autonomic phenomena than others. Some have to be taught. Who better to teach than teachers? School doctors, health visitors, or school nurses perhaps.

It should not be our medical concern to avoid all anxiety in 10-year-olds. A certain amount of anxiety shows a healthy awareness of life. Rather it is its absence, or its unsatisfactory resolution, that is prejudicial to the future mental health of the child. Had the whole class shown anxiety one might think something had gone amiss.—I am, etc.,

Chesham Bois,
Amersham, Bucks.

B. H. BURNE.

Hospital Admissions among Students

SIR,—Dr. Graham Grant (9 September, p. 674) does well to publicize the fact that students do suffer from serious as well as trivial disease, and that between 2% and 3% of them have to be admitted to hospital each year. The figures for students at the University College of Swansea for the same years as he studied (1963–5) show the same incidence (182 admissions affecting 170 out of a total of 7,110 students). The proportion of women students was at least as high as Dr. Grant's—namely, between 25% and 30%.

However, Dr. Grant emphasizes the high proportion of admissions for mental, psychoneurotic, and personality disorders, and also for conditions associated with pregnancy—respectively 21% and 9% of the total admissions. This is not universally true, however, and the corresponding figures at Swansea are 9% and 4%. So far as I can see this is not due to under-reporting of admissions due to these conditions here, and I think it important that the general impression held by many people, both doctors and others, that these conditions are so common among students should not be encouraged by the publication of figures from only one university.—I am, etc.,

University College of
Swansea.
Glam.

T. C. DANN.

Carcinogenic Properties of Ortho-dianisidine

SIR,—I refer to Dr. E. D. Acheson's letter (7 October, p. 51). It is true that Occultest and Hematest (Ames Company) contain ortho-tolidine as an indicator for occult blood. However, if these tablets are used in accordance with the manufacturer's instructions there is no risk whatsoever. Indeed, it would be more logical to indicate on packets of cigarettes that a noxious substance is contained therein.

I am most anxious that no taint of toxicity be attributed to such an excellent diagnostic method.—I am, etc.,

Edinburgh 10.

D. G. ILLINGWORTH.

SIR,—Carcinogenic aromatic amines have been used as chemical reagents in laboratories for many years (26 August, p. 557).

This Institute has drawn attention to the possible hazards from these in a pamphlet entitled "Precautions for Laboratory Workers

who Handle Carcinogenic Aromatic Amines."¹ Whereas a number of aromatic amines are known to induce cancer, no arylamino sulphonic acids have been found to be carcinogenic. There is no evidence that the sulphonic acid group is removed by metabolic processes.

In view of this it has been recommended that Cleve's acid (1-naphthylamine-7-sulphonic acid or 8-aminonaphthyl-2-sulphonic acid) should be used in the Griess-Ilosvay test for nitrite.^{2,3} The colours given in this test by 1-naphthylamine and Cleve's acid are similar, so that the same colour discs can be used in the estimations.—We are, etc.,

E. BOYLAND.

R. A. M. CASE.

Chester Beatty Research
Institute,
London S.W.3.

REFERENCES

- ¹ Chester Beatty Research Institute, *Precautions for Laboratory Workers who Handle Aromatic Amines*, 1966. London.
- ² Crosby, N. T., *Proceedings of the Society for Water Treatment and Examinations*, 1967, 16, Pt. 1, p. 51.
- ³ Taylor, E. W., *The Examination of Waters and Water Supplies* (Thresh, Beale, and Suckling), 1958, 7th ed., p. 216. London.

Melanoma, Halothane, and Liver Necrosis

SIR,—The letter by Mr. Geoffrey S. W. Organe and Dr. Gavin L. B. Thurston (7 October, p. 49) tends to give the impression that halothane is the only anaesthetic agent which, on repeated administration, may be followed by jaundice and liver necrosis. Such an impression would be misleading. It has been reported¹ that repeated administration of an intravenous barbiturate to 329 patients was followed by jaundice in 41 of them, 15 of whom died from liver necrosis. This unhappy event was investigated by medical officers responsible for the public health. After a careful study of all the relevant facts they concluded that the jaundice and the liver necrosis were caused by a virus transmitted during the intravenous injections.

It seems to me that the problem of unexpected postanaesthetic jaundice will not be solved until we provide ourselves with a reliable serological test for viral hepatitis.—I am, etc.,

MICHAEL JOHNSTONE.

The Royal Infirmary,
Manchester.

REFERENCE

- ¹ Dougherty, W. J., and Altman, R., *Amer. J. Med.*, 1962, 32, 704.

Adenomyoma of Stomach

SIR,—Following the interesting description of gastric adenomyoma given by Dr. J. G. McNulty (30 September, p. 843), we would like to report a case in which the lesion was viewed through a gastric fibroscope and its appearance recorded by intragastric photographs.

A 42-year-old woman presented with an eight-weeks history of recurrent epigastric pain which was unrelated to meals and incompletely relieved by alkali. She had lost 8 lb. (3.6 kg.) in weight. Two years previously she had experienced similar symptoms, which then resolved after a few weeks. At the time of her referral to hospital a barium-meal examination showed an abnormality on the lesser curve of the stomach, adjacent to the angulus. Endoscopy was performed with a

fibrescope incorporating a gastric camera. A circumscribed lesion was identified in the proximal antrum, but it did not manifest the features of simple peptic ulceration. It comprised a raised smooth area with rounded edges and in the centre was umbilication or shallow ulceration. The findings did not allow a confident endoscopic diagnosis; a neoplasm was suspected and a Bilroth I partial gastrectomy was carried out.

The gastrectomy specimen contained a raised lesion 2 cu. mm. in diameter, with a central irregular umbilicated area situated close to the lesser curve near the angulus. Section showed a partly cystic ill-defined mass in the muscle coats and slender channels could be seen passing up from the cysts to open into the base of the umbilicated area. Histological examination revealed a typical adenomyoma with areas of well-marked pancreatic differentiation and cyst formation. The channels, passing up from the cysts, were lined by a tall columnar epithelium which was in direct continuity with the gastric mucosa. There was no evidence of ulceration or malignancy.—We are, etc.,

I. D. O. FREW.

D. D. GIBBS.

P. L. BERGER.

Good Hope General Hospital,
Sutton Coldfield,
Warwickshire.

Operations on the Gall Bladder

SIR,—Your leading article (30 September, p. 811) is open to criticism. *The Registrar General's Statistical Review of 1962*¹ shows that if deaths from malignant disease of the biliary passages (Code No. 155a), from cholecystitis and cholangitis without mention of gallstones (Code No. 585), from cholelithiasis (584), and from other diseases of the gall bladder (586) are combined the death rates per million living are:

	At Ages 45-54	55-64
Males ...	17.5	61.5
Female ...	19	91

On the assumption that 5-10% of the population have gallstones by the age of 60, 50-100,000 operations per million will be needed to eliminate them; and besides disorganizing the N.H.S. these will give (at your suggested operation mortality of 1%) an increased mortality from gall-bladder disease of 500-1,000 per million. The "careful studies" which you quote as providing "factual information" seem to neglect clinical common-sense arithmetic.

It is more speculative, but fairer to your argument, to consider the equilibrium state when a policy of removing silent stones has been followed for some time. At present it looks as if about 750,000 persons out of the present annual total of births will survive to the age of 60. If every gallstone carrier is operated on by this age it will cost 400-700 premature deaths to make a clean start with a virtually gallstone-free population at this age. Unfortunately most gallstones develop after 60, and we cannot expect deaths from this cause at ages over 70 to be more than halved. In 1962 exactly 700 deaths were certified as due to cholelithiasis, 470 of them in patients over 70. This number will obviously increase as the elderly population increases (? to about 600). It is possible, therefore, that early operation would lessen the total number of deaths ascribed to various

forms of gall-bladder disease, but only at the cost of a lessened expectation of life.—I am, etc.,

Budleigh Salterton,
Devon.

DENYS JENNING.

REFERENCE

- ¹ *The Registrar General's Statistical Review of England and Wales, 1962*. H.M.S.O.

Phenobarbitone and the Shoulder-Hand Syndrome

SIR,—Recently a woman of 35 years, upon whom we performed a stereotaxic thalamotomy for Parkinsonism with predominant rigidity, developed a contralateral shoulder-hand syndrome with oedema of the wrist on the fourth day after operation. Phenobarbitone was administered to her for the first time from the day of operation onwards in the dose of 30 mg. thrice daily. Within a few days she experienced similar pain, though to a lesser degree, in the opposite upper limb and both lower limbs. The pain was confined to the region of her joints but was not sufficient to restrict their mobility. She could not recall ever having suffered from such pains before or during the course of her illness, nor was she subject to epileptic seizures, thereby precluding shoulder trauma. Salicylates were tried for a few days, but proved ineffective. It was then that one of us recalled your leading article (15 April, 1967, p. 130) on the subject and phenobarbitone was discontinued, with the result that pain and oedema rapidly subsided. We are, etc.,

ANIL D. DESAI.

H. M. DASTUR.

Department of Neurosurgery,
K.E.M. Hospital,
Parel, Bombay, India.

Aspirin and Gastric Bleeding

SIR,—The leading article on aspirin and gastric bleeding (30 September, p. 810) is on a timely subject but fails to present the broad and basic aspects of the problem. While aspirin may occasionally produce gastric haemorrhage by direct action on the gastric mucosa, it seems certain that this is not the *modus operandi* responsible for most of the occult gastrointestinal bleeding nor for the massive haemorrhages. As I have recently pointed out, aspirin causes occult bleeding to varying degrees even in normal subjects,¹ whereas sodium salicylate does not. Obviously, aspirin induces haemorrhage by virtue of its acetyl linkage.

Without going into theoretical considerations, two practical facts concerning aspirin should be stressed. Certain normal subjects and many with a bleeding tendency, particularly those with the Minot/von Willebrand syndrome, will have a prolonged bleeding time after ingesting a small dose of aspirin and occasionally have an accentuation of their bleeding tendency. By means of the aspirin tolerance test such subjects can readily be detected.

The second cogent fact, which is often overlooked, is that aspirin has two pharmacological activities: through its acetyl group it is an effective analgesic, and through its salicylate content it is an anti-inflammatory agent. It is the latter action that explains

its therapeutic effectiveness in rheumatic fever and rheumatoid arthritis. In these conditions a high concentration of salicylate in the blood must be maintained. This can be accomplished by either sodium salicylate or aspirin. The latter is completely hydrolysed in a few hours after ingestion, and thus furnishes salicylate ions. There is no evidence that aspirin itself has any anti-inflammatory action. Since large doses of aspirin may induce gastrointestinal bleeding, even in patients with no evidence of a bleeding disease, it seems logical to use sodium salicylate to maintain a high level of salicylate in the blood. Recent studies in my laboratory indicate that this drug, unlike aspirin, does not cause the diapedetic or mucous membrane bleeding.—I am, etc.,

Marquette Medical School,
Milwaukee,
Wisconsin, U.S.A.

A. J. QUICK.

REFERENCE

Quick, A. J., *Wisconsin med. J.*, 1967, 66, 365.

Children with Myelomeningocele

SIR,—As an offshoot of our research into the assessment of gait in cerebral palsied children we designed a hip level "polyplanar" joint for use with callipers of the type described in Mr. E. H. Strach's article (23 September, p. 791). Our object was to reproduce a walking pattern as near normal as possible. The joint illustrated (Fig. 1) ensures external rotation with hip flexion and internal rotation with extension which gives pelvic rotation, thus allowing normal weight transference on to the forward leg.¹

By interconnecting the two joints on either side stability can be gained without the loss of mobility, since only reciprocal hip movements are possible. We have used inflatable splints for stabilizing the limbs of children with cerebral palsy,² and we first fitted a pneumatic system to the callipers, accepting that a more expensive hydraulic system would give less "back lash." Now we are trying a cheap twin cable system which can be preloaded to take up all excess movement (Fig.

2). Although it is still in the development stage, we have been encouraged by the remark of a parent, who said (of his child with myelomeningocele), on seeing the callipers in use, "But this is ordinary walking!"

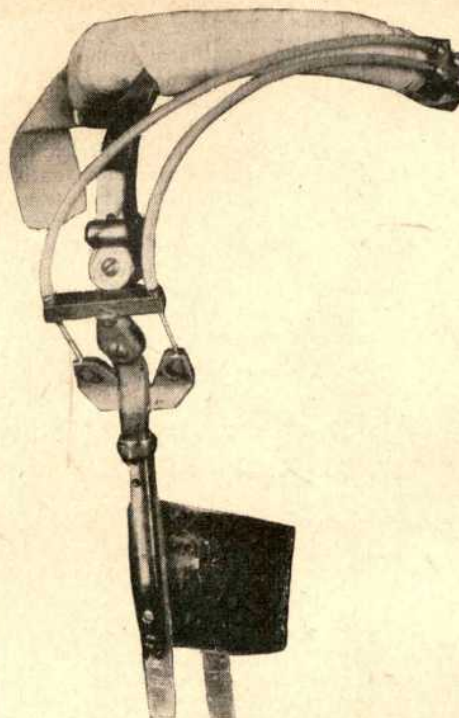


FIG. 2

Recent engineering advances have influenced other appliances, but the humble calliper has, through its dependability, ceased to evolve. The resultant gait is accepted as inevitable—but need it really be so? Perhaps the motor problems of the child with a myelomeningocele will form the environmental background for the next evolutionary stage of the full-length calliper.—We are, etc.,

PETER ROBSON,

Deputy Director.

DAVID SCRUTTON,

Research Physiotherapist.

Paediatric Research Unit,
Guy's Hospital Medical School,
London S.E.1.

REFERENCES

- Scrutton, D. R., Robson, P., and Davies, R. M., *Nature (Lond.)*, 1967, 213, 950.
- Robson, P., and Scrutton, D. R., *Phys. Ther. Rev.*, 1967, 47, 219.

SIR,—In Mr. E. H. Strach's very interesting and comprehensive article on myelomeningocele (23 September, p. 791) he does me the honour to recommend for hip complications my simple splint, originally designed for congenital hip dislocations in infants, which was widely popularized in Europe (unfortunately excluding Britain) and in South America by Professor Putti, the pioneer of early diagnosis of congenital dislocation of the hip. I am tempted to recommend another simple apparatus for the early treatment of meningocele when conditions do not permit radical operation immediately after birth, which gives such good results in the hands of highly skilled surgeons, and for which some cases have no access or are unfit.

What I refer to is a protective dome of perspex, or other plastic, well perforated to allow evaporation and large enough to avoid all contact with the surface of the swelling, but supported by a flange resting on the normal surrounding skin and held in place by tapes round the axillae and groins. The surface of the swelling is dusted with an inert powder and no dressing applied. If the child is very small the perspex may be shaped as a cylinder along the whole spine.

During my years working in the Bath and Wessex area I had many opportunities of using this method, though not a series comparable with Mr. Strach's large one. It was surprising how, within a few days, the tumour steadily shrank and normal skin grew in over the remainder from the edges. A few cases died suddenly and unexpectedly within a matter of days, or weeks, probably from cerebral complications, but those that survived had no degree of paraplegia, nor lack of sphincter control.

Many unfortunate cases reached me who had had a belated excision, before the modern technique had developed, and they uniformly had paraplegia with incontinence of bowel and bladder, and provided difficult problems to get them ambulatory.—I am, etc.,

Edinburgh.

M. FORRESTER-BROWN.

Psychotropic Drugs

SIR,—I would be grateful for the opportunity to add my comments on the Dunlop Committee's report on psychotropic drugs.¹

The immediate and obvious conclusion is the remarkable safety of these drugs. Taking the general-practice figures only, the adverse reactions approximate to something like 0.003% of each prescription, and the fatal reactions to one-fourteenth of this figure. There is no doubt that these drugs have transformed psychiatric treatment and relieved much suffering in both psychotic and neurotic illnesses. Contrary to the widely held lay belief that psychiatric patients become dependent on these drugs, the general experience is that most of them tend to stop the drugs too early, as soon as they feel better. It is therefore all the more unfortunate that such wide publicity should be given in the press to the Dunlop Committee's report. Already several of my patients, not appreciating the remarkably small number of adverse reactions, have expressed anxieties about being on psychotropic drugs, and a few actually stopped them for a time.

The Committee's reports are most helpful to the doctor in advising him of possible adverse reactions to any drug, but I cannot see that the wide promulgation of its findings and suggestions in the press can have any value to the general public, and can only promote anxiety in any patient who should happen to be on that drug.

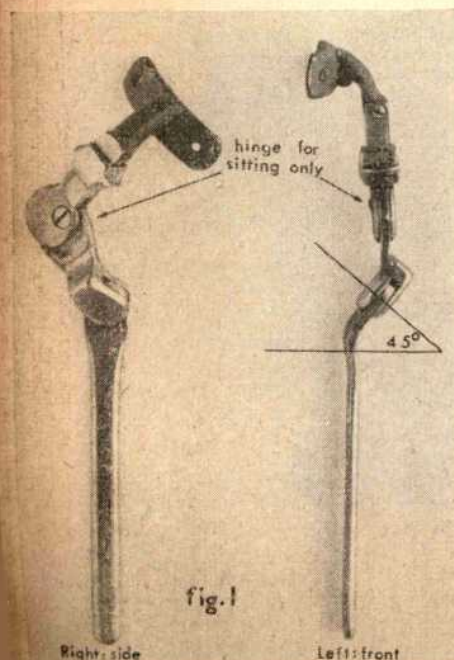
I would therefore make a strong plea that consideration should be given to distributing future reports of the Dunlop Committee on a strictly confidential basis to doctors only.—I am, etc.,

R. WALLACE SIMPSON.

Old Manor Hospital,
Salisbury,
Wilts.

REFERENCE

- Psychotropic Drugs*, Committee on Safety of Drugs, Adverse Reaction Series, No. 6, September 1967.



Stress Incontinence

SIR,—I was very interested in the correspondence from Mr. T. Moore (16 September, p. 740) and Mr. S. A. Vincent (19 August, p. 498) about the treatment of stress incontinence by electrical stimulation.

In this unit we have for some years been treating such patients by "maximal" electrical stimulation, but using this term time-rather than current-wise. We have been treating them with an implant with the electrodes placed on the anterior fibres of the levator, the implant being activated by a radio-frequency linkage through the small external unit worn by the patient. We have observed a "lift forward" of the bladder neck on stimulation, and this fits in well with the theories of continence put forward by Jeffcoate and the Liverpool school.¹ We have found that sometimes stimulation gives rise to an increased urethral pressure, but sometimes this is not observed.

The advantage of this treatment is that although the patient has a small operation she does not then need to attend the physiotherapy or other department except for routine checks on her equipment. The patient will notice a deterioration of the equipment because she becomes wet. This work was described in my Hunterian lecture (December 1966; to be published), although since then improvements in technique have been developed.

In two cases we have used "Hopkinson's plug"² successfully. In one case because there had been so many retro-pubic interventions that it was impossible to use this approach again, and in the second case because it was felt that the patient was too senile for an operation.—I am, etc.,

K. P. S. CALDWELL.

Sphincter Research Unit,
Royal Devon and Exeter Hospital,
Exeter.

REFERENCES

- 1 Jeffcoate, T. N. A., and Roberts, H., *Amer. J. Obstet. Gynec.*, 1952, 64, 721.
- 2 Hopkinson, B. R., and Lightwood, R., *Brit. J. Surg.*, 1967, 54, 802.

SIR,—Having read in your correspondence columns of the interesting results achieved by Mr. S. A. Vincent (19 August, p. 498) and by Mr. T. Moore (16 September, p. 740) by electrical stimulation of the perineal muscles, I beg to state that I cured one young woman who was sorely afflicted by ordering her to take riding lessons.

Before this is dismissed as a successful case of psychotherapy I should like to make two points:

(1) That she informed me that during the first few rides her saddle became soaking wet, and that over a period of weeks she got progressively drier and finally achieved complete control.

(2) That anyone who has attempted to remain in the saddle on an excitable animal by gripping with the knees and who has never ridden before, or not for many years, will know next day from their aching perineal and adductor muscles that every available fibre has been brought into vigorous action out of sheer terror.

This approach has a very limited application, but I have put it forward as I believe it might help in suitable cases.—I am, etc.,

York. J. K. WILLSON-PEPPER

Early Discharge of Maternity Patients

SIR,—May we reply to comments made on our papers (26 August, pp. 517 and 520).

We would endorse the view expressed by Dr. S. E. Browne (16 September, p. 739) and agree that the penultimate paragraph of the discussion of our second paper might have been more explicit. Although we agree in principle that children should be allowed to visit their mothers in maternity units, we submit that the facilities are inadequate to permit this in many units, including our own. We feel that Dr. R. S. Saxton's problem (16 September, p. 739) should receive sympathetic consideration by his local maternity liaison committee.

While agreeing with Dr. E. D. McEwan (23 September, p. 801) that the results of our survey agree with those mentioned in his most interesting paper,¹ of which we were aware, we wish to comment on two points. Firstly, only 101 of the 1,044 babies in his series were discharged within 72 hours of birth. We consider this a small sample from which to draw firm conclusions regarding the safety of discharging babies so early. Secondly, since in Bradford the breast-feeding habits of immigrants appear to be influenced by the length of their stay in this country, only European mothers were included in the breast-feeding survey. We regret this point was not clarified in our first paper.—We are, etc.,

M. W. ARTHURTON.

F. N. BAMFORD.

G. A. CRAIG.

JESSIE M. B. MUIRHEAD.

St. Luke's Hospital,
Bradford 5, Yorks.

REFERENCE

- 1 McEwan, E. D., *Lancet*, 1964, 2, 744.

Carpal Tunnel Syndrome Associated with a Scribner Shunt

SIR,—Various symptoms and signs resulting from median nerve compression at the wrist have been described.¹⁻⁵ This is a report of the carpal tunnel syndrome complicating an arteriovenous Teflon-silastic shunt⁶ at the wrist of a patient in terminal renal failure.

A 40-year-old patient with a 17-year history of recurrent pyelonephritis associated with bladder-neck obstruction was admitted in terminal renal failure for haemodialysis and ultimately renal transplantation. No clinical evidence of peripheral neuropathy was found.

A Teflon-silastic arteriovenous shunt was implanted in the left forearm near the wrist. The left radial artery and cephalic vein were cannulated under 1% lignocaine local anaesthesia. After four weeks, owing to recurrent clotting, this shunt had to be removed and another implanted in the right forearm. A week later the patient complained of numbness and tingling in the thumb, forefinger, and middle finger of the left hand, and weakness was noted in the left abductor pollicis brevis. No symptoms were present in the right hand. Three weeks later wasting became visible on the lateral border of the left thenar eminence, and paraesthesiae continued. There was also diminution in appreciation of light, and painful sensation over the left thumb, forefinger, and lateral half of the middle finger, and percussion over the flexor aspect of the left wrist stimulated paraesthesiae in the fingers already mentioned. At no time was the patient in heart failure, and x-rays of the wrist were normal.

Damage to the median nerve at the wrist incurred by the implantation or removal of a Scribner shunt has not hitherto been described. It seems unlikely that injury to the nerve occurred during the insertion of the shunt. It may, however, be accounted for by one of the following explanations:

Ligation of the distal end of the radial artery may have jeopardized the blood supply to the digital vessels and median nerve.

During the time that the curved portion of the arterial shunt lay in the subcutaneous tissues of the flexor aspect of the forearm pressure on the flexor retinaculum and median nerve may have resulted. Damage to the median nerve may have occurred as a result of direct pressure or by occlusion of the vasa nervorum.

During the removal of the clotted shunt trauma to the nerve or to its blood supply may have resulted from the measures taken to secure haemostasis.

I am grateful to Professor R. Y. Calne for permission to publish this case.

—I am, etc.,

Addenbrooke's Hospital,
Cambridge.

D. B. EVANS.

REFERENCES

- 1 Garland, H., Bradshaw, J. P. P., and Clark, J. M. P., *Brit. med. J.*, 1957, 1, 730.
- 2 Sumner, D., and Clark, J. M. P., *ibid.*, 1963, 1, 581.
- 3 Cseuz, K. A., Thomas, J. E., Lambert, R. H., Love, J. G., and Lipscomb, P. R., *Proc. Mayo Clin.*, 1966, 41, 282.
- 4 Phalen, G. S., *J. Bone Jt. Surg.*, 1966, 48A, 211.
- 5 *Brit. med. J.*, 1966, 2, 1339.
- 6 Quinton, W., Dillard, D., and Scribner, B. H., *Trans. Amer. Soc. artif. Internal organs*, 1960, 6, 104.

Sodium Chlorate Poisoning

SIR,—We agree with Dr. A. C. Kennedy and Dr. R. G. Luke (23 September, p. 801) that the incidence of acute renal failure due to chlorate ingestion is much greater than the reported cases would indicate. We must apologize for having failed to notice their patients, but a more serious omission is the paper of Jackson, Elder, and McDonnell,¹ which deals entirely with the subject of acute renal failure and chlorate poisoning illustrated by three cases.

For the review of the recent literature we relied on the very comprehensive review of "The Clinical Dialysis of Poisons" in the *Transactions of the American Society for Artificial Internal Organs*.² This check list has been MEDLARS assisted since 1963 but is clearly deficient before this date.—We are, etc.,

R. K. KNIGHT.

J. R. TROUNCE.

J. S. CAMERON.

Guy's Hospital,
London S.E.1.

REFERENCES

- 1 Jackson, R. C., Elder, W. J., McDonnell, H., *Lancet*, 1961, 2, 1381.
- 2 *Transactions of the American Society for Artificial Internal Organs*, 1965, 2, 349.

Headlight Glare

SIR,—The case of polarization to eliminate dazzle as suggested by Dr. S. J. Lines (30 September, p. 867) has been considered impracticable because cambering, banking, and surface irregularities of roads prevent 90° cross-polarization from being maintained.

The headlamps of an approaching vehicle would thus fluctuate in apparent brilliance.

The dazzle problem is admittedly serious, particularly in this country, where every motorist feels free to express his personality by festooning his car with extra lamps and other decorations. The position could be materially improved by enforcement of the Vehicle Lighting Regulations.

A dangerous and illegal practice which seems to be growing is the use of rear-mounted spotlamps to dazzle motorists behind. In one recent case known to me the victim was first harassed by close pursuit with undipped headlamps, then passed and blinded by the rear-spots until the aggressor became bored and disappeared into the night. The circumstances prevent the victim from reading the registration number of the offending vehicle, but prevention should be simple—in daylight the illegal lamps can be seen just as easily by the police and traffic wardens as by anyone else.—I am, etc.,

University of Glasgow.

N. R. GRIST.

Fluoridation of Water Supplies

SIR,—Fluoridation of water supplies is official B.M.A. policy, and one gathers that the Ministry of Health is trying to persuade local authorities to put this policy into effect.

One also gathers that as time goes by increasing numbers of eminent doctors and scientists, too numerous to list here, are coming to have grave doubts about the wisdom of this policy. Few who study the case against fluoridation (and most do not) can also fail to have grave doubts. Surely it is time that the whole question of fluoridation of water supplies was reassessed.

Fluoridation has been practised in parts of the United States for some years, and there is evidence that fluoridation postpones but does not prevent the onset of caries,^{1,2} and that when caries does come conservative dentistry is rendered more difficult.³⁻⁵ There is also evidence that fluoridation is definitely harmful to a proportion of the population, particularly those with damaged kidneys, and that others become allergic to it.⁶⁻⁸ Even if the percentage of these people is small, no one has the right to poison them through the public water supply. (It is not everyone who can dig a well in the back yard, as the lady in Andover had to do in 1956 when Andover fluoridated its water.)

In fluoridating water supplies the dose to the individual cannot be regulated. Fluoride may be put into the water supply at 1 p.p.m. but does not necessarily get evenly distributed, and samples have been found to vary from 0.4 to 1.4 p.p.m. (for example, in Wilmingtan, Mass.). And of course some drink more water than others. The undiagnosed diabetic and those whose job makes them perspire freely may drink as much as 30 pints (17 l.) a day; this gives an intake of 17 mg. of fluoride, which, with 2 or 3 more from other foods such as tea and fish, brings it up to the chronic toxic dose of 20 mg.

Fluoridation of public water supplies amounts to compulsory mass medication and is morally quite unjustifiable. It infringes human freedom—the freedom of a doctor to treat his patients as he thinks best, and the freedom of the patient to choose whether to accept or reject the medication advised. Any doctor can now treat his young patients with

fluoride if he thinks it desirable. And every child can have it in accurate dosage if his doctors and parents wish it, but there is no need to force the rest of the population to ingest a toxic substance every day of their lives in uncontrollable doses, knowing that it will quite certainly harm some people, and having no idea whatever what the effect will be on the rest.

Anyway the proper way to control dental caries is to educate women not to stuff their children with sweets, white sugar, and sweet biscuits, and to see that they clean their teeth after meals.—I am, etc.,

Peaslake, Surrey.

RONALD KERR.

REFERENCES

- 1 Weaver, R., *Proc. roy. Soc. Med.*, 1948, 41, 284.
- 2 Sutton, P. R. N., *Fluoridation, Errors and Omissions in Experimental Trials*, 1959. Melbourne.
- 3 Black, G. V., and McKay, F. S., *Dent. Cosmos*, 1916, 5, 129.
- 4 Smith, M. C., and Smith H. V., *Amer. J. publ. Hlth*, 1940, 30, 1050.
- 5 Dillon, C., *Dent. Dig.*, 1956, 62, 362.
- 6 Waldbott, G. L., *A Struggle with Titans*, 1965. New York.
- 7 *Fluoridation of Domestic Water Supplies in North America as Means of Controlling Dental Caries*, Report of United Kingdom Mission, Ministry of Health, H.M.S.O., 1953.
- 8 Feltman, R., and Kosel, G., *J. dent. Med.*, 1961, 16, 190.
- 9 Shea, J. J., Gillaspie, S. M., and Waldbott, G. L., *Ann. Allergy*, 1967, 25, 388.

Mortality of Bereavement

SIR,—It is always refreshing to see someone take up a popular belief and put it to the test of science. Dr. W. D. Rees and Miss Sylvia G. Lutkins (7 October, p. 13) have presented a well-documented study of the mortality of bereavement. To illustrate their statistical material a case report might be in point.

Some time ago I had occasion to treat an old childless couple over a period of five years. Two other specialists were also involved in the care of these patients, whom we got to know

very well. Champion tennis players and hole-in-one golfers, the devoted couple kept active, doing everything jointly, and invariably came to the surgery together. It is significant that each time any of the three doctors exchanged opinion about the couple the feeling was expressed that if one spouse died the other would follow very soon. Admitted as an emergency to hospital, the woman died of peritonitis from perforated diverticulitis. Three months after his bereavement the widower died of acute coronary occlusion, while heart disease had not till then been a major complaint.

Those with close feelings toward canine friends take it as a fact that dogs can die of a broken heart. Indeed, recent references show that this term might not be out of place after all. Perhaps research on the above laboratory animal could answer some of the questions regarding the pathology of grief raised in your leading article.—I am, etc.,

Denens,
Switzerland.

S. W. A. GUNN.

Intestinal Spirochaetosis

SIR,—In reference to the communication by Dr. W. A. Harland and Dr. F. D. Lee on this subject (16 September, p. 718) I feel it should be recalled that in the early 1950s Dr. A. G. Shera, then pathologist to the Eastbourne Hospital, presented to a meeting of the Association of Clinical Pathologists a description of this condition fully illustrated by microscopical preparations and with clinical details of several cases. A précis of Dr. Shera's presentation appeared in the *Journal of Clinical Pathology*.¹

It has always been my opinion that Dr. Shera's observations failed to attract the attention they deserved.—I am, etc.,

Wolverhampton,
Staffs.

S. C. DYKE.

REFERENCE

- 1 Shera, A. G., *J. clin. Path.*, 1953, 6, 327.

Approval of Emergency Treatment Service

SIR,—The reported statement of the chairman of the Inner London Executive Council (*Supplement*, 7 October, p. 3) that his council was not to blame for the temporary abandonment of the British Medical Association Emergency Treatment Service in London is interesting. The Inner London Executive Council has never been so blamed, the suggestion in the letter sent to London doctors being that the slow response from practitioners there might partly be due to the long delay in giving approval to the service. And, whatever the reason for the chairman's hastening to don this particular cap, there can be no argument that a period of some nine months' waiting could fairly be described as a delay, a delay in this case in the provision of a service to patients which could only have been of considerable benefit to them—an aspect which has apparently been quietly ignored in all this time except perhaps by one national newspaper.

But the reasons given by the chairman for this delay are even more interesting, not to say alarming. The council, though "satisfied that the service sponsored by the B.M.A. would be of high quality," concerned itself with other matters, "in the interests of the doctors who would use the service"—in short, with the company structure, which was being changed, of the operating company,

with a booklet issued by the B.M.A., and with the contract forms, in use throughout the country, to be used by subscribing doctors wishing to join the service. These forms were found to be quite unacceptable—by the executive council, need I say. Obviously doctors who had already signed these contracts had not found them so.

Sir, it would seem to me that it is time that all members of the executive council, and particularly the relevant subcommittees, should read the E.C.N.s 415 and 573 and the E.C.L. 103/66 and learn or remind themselves of the instructions and guidance on deputizing services offered therein by the Minister.

It is the duty of an executive council to give permission to an individual doctor to use a deputizing service, to refuse this permission, or to modify or qualify his use of such a service, and to do so the council must obviously have first-hand knowledge of the efficiency and method of working of the service. The council freely admitted the high quality of the B.M.A.-sponsored deputizing scheme, which is the limit of its remit so far as the organization as opposed to the individual practitioner is concerned.

Nowhere have I seen a suggestion that an executive council should concern itself with the private contractual arrangements of a

Whatever its origin...



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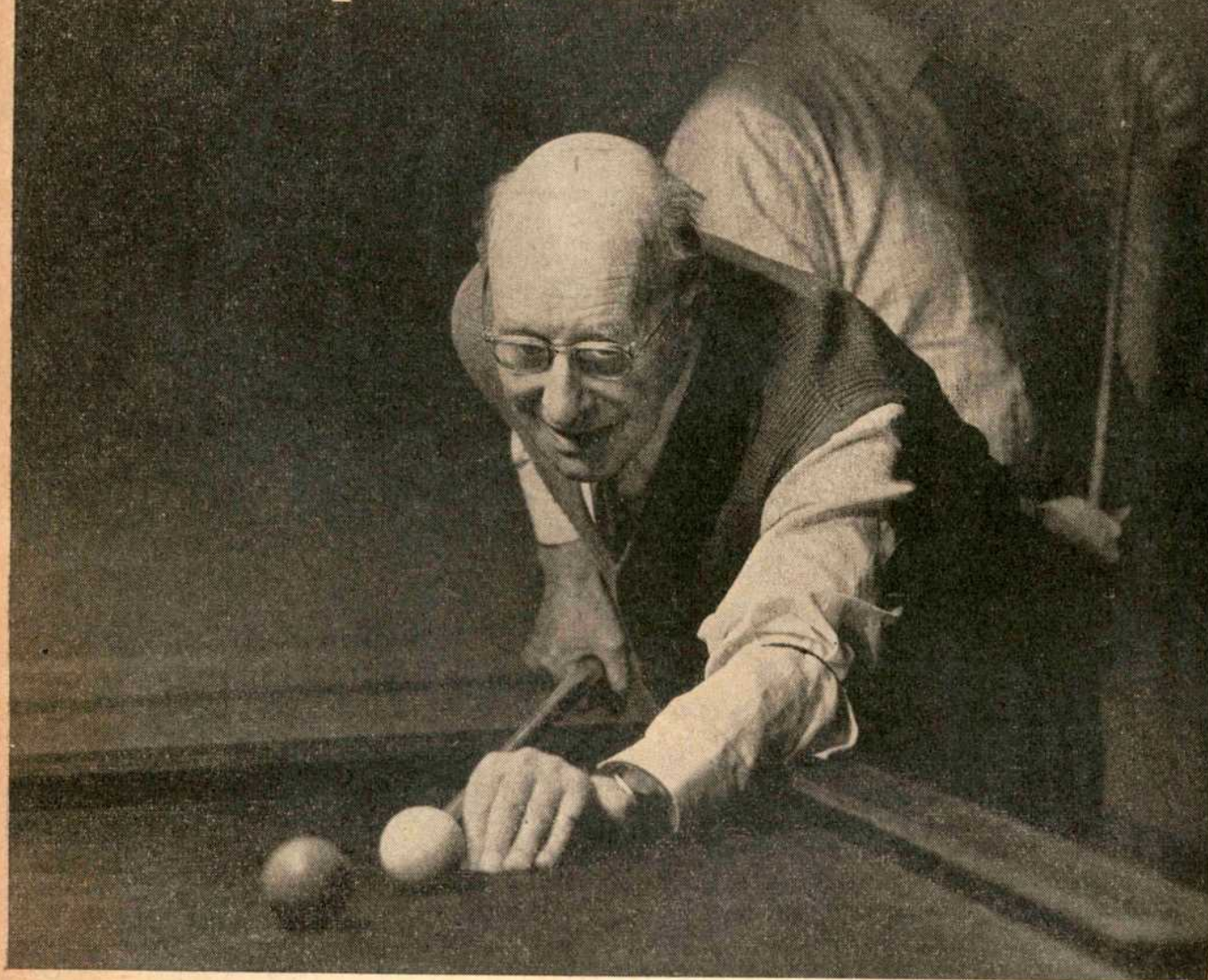
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Senokot restores natural rhythm to the constipated colon



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BASIC NHS COST: From the dispensing packs, the cost of a teaspoonful of granules or two tablets is about a halfpenny.

Granules: 56, 170 and 900 grammes.

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re-educates the bowel

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general practitioner unless there is a possibility of a breach of the regulations. Nowhere have I seen it suggested that an executive council should concern itself with literature issued by the B.M.A.—God forbid! Nowhere have I seen a suggestion that an executive council should concern itself with the internal intricacies of company formation once the efficiency of the organization has been established.

Whether inspired by fatherly interest or big-brotherly determination, executive councils must be sharply reminded that their interference in contractual or other arrangements made by general practitioners with other parties, and in the absence of any breach of the regulations, will be deeply resented and utterly repudiated, not only by the individual doctors who have their liberty of action once again questioned, but by the B.M.A., G.P.A., M.P.U., and any other professional organization.

Finally, I would recommend to the Inner London Executive Council a long, cool look at their own "contracts" with general practitioners, unilaterally signed, in the hope that it might stimulate some thought on the standing, the legality, the value, and the fairness of this piece of paper which every practitioner must sign when joining an executive council list as a principal.—I am, etc.,

Sheffield.

W. P. LAMBIE.

Dependent Relatives

SIR,—There will be many who were surprised by Dr. A. Youatt's letter (30 September, p. 868). I myself am not wholly able to follow the last part of his argument about "tax having been paid" on his estimated collective value of relatives' services. But the one incontrovertible fact which emerges is that he has paid, and has had accepted by his local tax inspector, the charge for the services of a dependent relative as a secretary/receptionist in his practice at a figure of £1,200 per annum. This may sound a startling sum to some doctors. However, this is no surprise to me.

In 1963 I took an appeal to the Special Commissioners over the vexed question of charges for the services of dependent relatives. At that time my wife was responsible for secretarial duties, largely at week-ends and in the evenings. For these services the Commissioners agreed that a sum of £520 per annum (plus £120 for her relief during sickness) was commercially justified on the facts. Clearly, on this basis, any dependent relatives who are giving services, as many do 24 hours a day, seven days a week, will be worth commercially upwards of twice this amount; particularly if, as is frequently the case, they possess qualifications making them specially suitable for the services given.

Following this appeal it became apparent to me that, if this pattern were to be followed by all G.P.s, it would have a profound effect on their own gross remuneration, which was then governed by the "Pool" system; this itself was determined in part by a Government sampling of tax returns. The position today is different in some respects. But the Review Body is dependent for guidance in pricing gross remuneration on similar tax sampling. Therefore, if all general practitioners were to show similarly realistic

though widely differing sums for the services of their relatives (where relevant), this would be reflected in the gross remuneration paid to general practitioners in respect of overheads or running costs of their practices.

In order, however, to justify proper charges for the services of related staff certain requirements have to be fulfilled:

(a) The facts in each individual case must be established, preferably using a standard fact-finding technique.

(b) The valuation of the services should be the result of the application of standard objective criteria to the established facts.

(c) There should be clear evidence that the related supplier of the services on the one hand and the doctor to whom they are being supplied on the other hand have put such services on a formal contractual basis.

(d) That there is proof that services have actually been paid for.

It will be seen from this that doctors may experience some difficulty (as I did) in establishing that the changes have been valued on an objective commercial basis rather than on a purely subjective one decided upon between the doctor and the related staff, with little or no relation to their commercial worth. It was for this reason that I formed a company, Medical Management Services Ltd. The company commissioned a leading firm of management consultants to conduct a "job specification and evaluation" for certain administrative services common to most practices. As a result M.M.S. Ltd. has evolved, with the firm of chartered accountants who administer it, its own method of evaluation for ancillary services. This has proved acceptable to the Revenue in actual practice in widely separated parts of the country.

The object of this is not to save tax—any tax saving is incidental—but to demonstrate incontrovertibly the realistic cost of running a medical practice.—I am, etc.,

Poole, Dorset.

G. C. PRICE.

Vocational Training for General Practice

SIR,—In the *Supplement* of 23 September (p. 135) you report Mr. D. C. Bowie as saying, "If young men and women were trained in scientific medicine it would be a waste and a failure if they could not practise that kind of medicine. Therefore it was very important that conditions should be created in general practice in which young graduates could continue in the way in which they had been trained." I cannot believe that you have correctly reported my old friend Mr. Bowie in making him put forward a proposition which is really declaring that, instead of doctors being trained to treat the complaints which patients present, patients in general practice should be trained to present the complaints which doctors are capable of treating.

Surely one of the greatest troubles in general practice is that doctors have been trained in hospital by people who know nothing about general practice and are therefore quite incapable of teaching it. The way to stop the "waste" is to have less training in the so-called "scientific" medicine, and more encouragement for general intelligence and humanity.—I am, etc.,

Newick, Sussex.

F. GRAY.

Mileage Allowances

SIR,—We now see the results of the long-awaited interim mileage allowances negotiated between the B.M.A. and the Ministry (19 August, *Supplement*, p. 121). A reduction of 3d. a mile for cars under 1200. This new system excludes all cars in the popular range, which previously qualified as over 10 h.p.—for example, Cortina, Anglia, Viva, Morris 1000, and 1100.

It is obvious that those who can ill afford it are being penalized at the expense of their richer colleagues. No wonder the junior medical staff have no faith in the B.M.A., and why large numbers of senior medical staff see no reason for returning to the fold.—I am, etc.,

Stoke Poges, Bucks.

D. L. BENNETT.

SIR,—Concerning the recent change in mileage allowances, it appears that in fact anyone now acquiring a car of 1000–1199 c.c. capacity will qualify for a smaller allowance than before. As most popular small cars are of this size, the saving to the Health Service must be almost as much as the increase for other cars. Has it suddenly become less expensive to run a car of this size? Surely the willingness of doctors and dentists to use their cars on official business at a substantial loss is being sorely tried by this change.—I am, etc.,

Eaton, Norwich.

R. J. PURNELL.

Post-registration Nurses

SIR,—I find it rather incredible that Dr. A. Paton should refer to the post-registration nurse as "a relatively new educational phenomenon" (23 September, p. 788). Perhaps he is unaware that as far back as 1918 the Royal College of Nursing was holding a course for sister tutors and in 1921 held an international students' course in collaboration with Bedford College, London.

During the last few decades there has been a worldwide increase in the number and variety of courses offered to those who have completed their training. This is so not only in the professional world but also in the business world, which frequently is ahead of the professions in their vision of future needs.—I am, etc.,

Wimbledon,
London S.W.19.

MARGARET F. YOUNG.

Points from Letters

Safer Dental Anaesthesia

Mr. S. L. DRUMMOND-JACKSON (London W.1) writes: Few who have studied the subject deny that it is the "milling anaesthetic practice" run by those who would be least likely to take post-graduate instruction which is the best candidate for the highest proportion of anaesthetic hazards. No legislation can improve safety until the measures by which safer practice can be achieved are freely available. These measures, let us hope, will progressively increase, but they will start with courses of but a few days, whether we like it or not, and it will be at least ten years before we can reasonably expect that every man who administers an anaesthetic should have taken some form of approved instruction within the last x years. This may be restrictive, but so are many safety rules, and there are few alternatives which seem possible.

Obituary Notices

Sir ARCHIBALD GRAY, K.C.V.O., C.B.E., T.D., LL.D., M.D., F.R.C.P., F.R.C.S.

Sir Archibald Gray, consulting physician for diseases of the skin to University College Hospital and to the Hospital for Sick Children, Great Ormond Street, died at his home in London on 13 October. He was 87.

Not many men attain eminence in two fields as different as a specialized branch of medicine on the one hand and hospital and university administration on the other, but



[Bassano & Vandy]

Sir Archibald Gray was distinguished in both. For as long as 37 years he had charge of the skin department of University College Hospital, and there and elsewhere he built up a reputation which made his name familiar in dermatological circles all over the world. His gifts in the field of academic administration were evidenced in the succession of posts he held, up to that of Deputy Vice-Chancellor of the University of London.

Archibald Montague Henry Gray was born on 1 February 1880 at Ottery St. Mary, South Devon, the son of a general practitioner. He was educated at Cheltenham College, and he entered University College and Hospital, London. He also later studied in the University of Berne. He took the M.B. London with honours in 1903, and the B.S., again with honours, the following year. He proceeded M.D., with the University Medal, in 1905, took the F.R.C.S. in 1908, was elected F.R.C.P. in 1918, and was appointed C.B.E. the following year. During the first world war he was attached to the general staff at the War Office and was consulting dermatologist in the Army Zone, British Expeditionary Force, holding the rank of lieutenant-colonel, R.A.M.C. (T.A.). After the war he returned to a full life of activity in Gower Street, where he was physician to the skin department and lecturer in dermatology to the medical school. He had charge also of the skin department at the Great Ormond Street Hospital for Sick Children from 1920 to 1924, and was consulting dermatologist for many years to the Royal Air Force and adviser in dermatology to the Ministry of Health and to the L.C.C. special hospitals.

Gray early began to take an interest in university affairs. He was a member of the Senate of the University of London from 1929 to 1950, a member of the Court from 1947 to 1958, and Deputy Vice-Chancellor in 1938-9. In his own school he was Dean from 1926 to 1935, and Dean of the Faculty of Medicine of London University from 1932 to 1936. He also represented his university on the General Medical Council. He was an excellent committee man and was made a member of the Government committee on the

medical services of the Navy, Army, and Air Force, which sat from 1931 to 1933, and of the inter-departmental committee on the organization of medical schools (better known as the Goodenough Committee), which sat from 1942 to 1944. In the Royal Society of Medicine he was a prominent figure. For many years he was a member of the Council of the Section of Dermatology and became its president. From 1919 to 1924 he was honorary secretary of the society, its honorary treasurer from 1926 to 1932, and in the difficult early years of the second world war its president.

In 1941 the Ministry of Health instituted a survey of hospital services, dividing England and Wales into 10 areas for the purpose, and appointing persons experienced in the clinical and administrative work of hospitals as surveying officers. Each report made a Blue Book and the whole was a kind of hospital Domesday. Sir Archibald Gray was responsible with Dr. Andrew Topping for the information relating to hospital services in London and the surrounding area. He had been before the war vice-chairman of the London Voluntary Hospitals Committee.

Sir Archibald Gray's achievements in the field of dermatology were widely recognized. His work was characterized by the scrupulous attention to detail demanded by the dermatologist, and by prolonged and careful study of the problem presented by the individual case. So long ago as 1913 he was chosen as honorary secretary of the Section of Dermatology at the 17th International Congress of Medicine in that year. He was vice-president of the International Congress of Dermatology in 1930 and its president in 1952. He was president of the British Association of Dermatology and Syphilology in 1938-9, honorary member of the Polish Academy of Science and Letters, the American Dermatological Association, the Spanish Academy of Dermatology, the Austrian Dermatological Society, and the Australian Dermatological Association, and he was corresponding member of the dermatological societies of France, Denmark, and Hungary. From 1948 to 1962 he was adviser in dermatology to the Ministry of Health, and from 1951 to 1961 chairman of the board of management of the London School of Hygiene and Tropical Medicine. He was knighted in 1946 and appointed K.C.V.O. in 1959. The honorary degree of LL.D. was conferred on him in 1958 by the University of London.

As Harveian Orator to the Royal College of Physicians in 1951 he gave a learned discourse on the history of dermatology since the time of Harvey, and ended by pointing out some of the problems remaining to be solved in the dermatological field, reminding his audience that the skin might respond to conditions affecting the organism as a whole or might act as an entirely independent organ, producing in itself its own toxins which might affect any part of the skin and leave the rest unaffected. He

was editor for some years of the *British Journal of Dermatology and Syphilology*, and author of the section on skin diseases in Price's *Textbook of the Practice of Medicine* and of articles on the subject in the *Medical Annual* and in the *Official Medical History of the [First World] War*.

In 1919 he married Elsie, daughter of the late Mr. F. B. Cooper, of Newcastle-under-Lyme, and they had one son and one daughter.

W. N. G. writes: It is just 45 years ago that I presented myself to Sir Archibald Gray (as he was to become) and was accepted as his clinical assistant at University College Hospital. Thenceforth he was my unfailing counsellor, friend, and supporter. Professionally I owe almost everything to him. The breadth of his knowledge and the exactness of his observation made his teaching lucid and convincing, and he had an almost photographic memory of clinical cases. Influence and power came to him naturally because of his exceptional competence and his interest in professional politics and college and university affairs. He did not seek the limelight, but did enjoy holding the reins of government. When he spoke in public it was with an authority that compelled attention, and this was aided by his splendidly clear voice and enunciation.

Sir Archibald arrived at his conclusions logically, and held his opinions so strongly that he could be impatient at times with those who had other views. But differences were always amicably composed, and he never harboured any rancour, and was essentially friendly. His friendships indeed were worldwide, and one of his proudest achievements was the organizing, under his presidency in London, of the first International Dermatological Congress to be held after the second world war. It was a most successful and happy event. For a man with such an active mind, vividly interested in all that was going on, his long incapacitating illness must have been a grievous trial. But it was always a pleasure to visit him, and one came away inspired by his cheerfulness, patience, and courage. He was happy and fortunate in his family circle, and drew great satisfaction from the attainments of his son, Professor John Gray, and from having a grandson a medical student at University College Hospital. To all his family I express my sympathy in their great loss, and especially to Lady Gray, who tended him so devotedly. I shall always remember Sir Archibald Gray with gratitude and affection.

A. G. TIMBRELL FISHER, M.C.
M.B., CH.B., F.R.C.S., F.A.C.S.

Mr. A. G. Timbrell Fisher, a former orthopaedic specialist at the Rheumatism Unit, St. Stephen's Hospital, and the Charterhouse Rheumatism Clinic, died on 10 October. He was 79.

Alfred George Timbrell Fisher, second son of Canon W. H. Fisher, was born in Bristol on 1 November 1887. He was edu-

cated at Clifton College, Bristol, and at Bristol University and St. Bartholomew's Hospital, London, qualifying with the Conjoint diploma in 1911 and graduating M.B., Ch.B. a year later. After early resident posts at the General Hospital, Bristol, he became demonstrator of anatomy, and of surgical applied anatomy, at Bristol University. During the first world war he served in France and Belgium as a surgical specialist with the R.A.M.C. and was awarded the



L. SURZYNSKI

Military Cross and mentioned in dispatches. After demobilization with the rank of major he took the F.R.C.S. in 1919, later holding the appointments of assistant surgeon in the orthopaedic department of St. Bartholomew's Hospital and in the surgical unit of University College Hospital. He was appointed surgeon in charge of out-patients at the Dreadnought Seamen's Hospital, Greenwich, and consulting surgeon to the Ministry of Pensions. In 1919-20, and again in 1921-2, he was Hunterian professor of the Royal College of Surgeons of England. A member of the British Medical Association, he was vice-president of the Section of Orthopaedics at the Annual Meeting in 1936. In 1948 he became a Fellow of the American College of Surgeons; he was also a Commander of the Order of St. John of Jerusalem. He was consulting surgeon to the St. John Clinic and Institute of Physical Medicine, and until he reached the age of retirement was orthopaedic surgeon to the Rheumatic Unit, St. Stephen's Hospital, Chelsea. He continued his work as a medical member of the medical and pensions appeal tribunal.

His books included *Internal Derangements of the Knee-Joint*, and *Treatment by Manipulation*, both of which went through several editions.

F.B. writes: Timbrell Fisher was a member of the *ad hoc* committee nominated by Lord Dawson of Penn to discuss the proposed terms of reference for the British committee on chronic rheumatic diseases which was to be appointed by the Royal College of Physicians. On its creation he was elected a member of both the subcommittee on classification and nomenclature and the editorial and literature subcommittee, to both of which he gave valuable service. His ideas were original; he marshalled his facts and wrote them down in clear and simple English. He based his writings on his careful pathological studies and his very successful treatment by manipulation in addition to the more orthodox orthopaedic measures practised at that time.

Timbrell Fisher was one who not only realized the importance of integration and communication to the proper study of the rheumatic diseases but what is even more important the need to apply what was being learned to the treatment not only of the individual patient who came under his care but to the management of all those who

attended the rheumatic unit at St. Stephen's Hospital. Timbrell Fisher's studies on the pathology of arthritic joints, combined with his clinical ability as a manipulator and orthopaedic surgeon, his personal humility, and his willingness to co-operate with the other members of the team, made him a valuable and delightful colleague as well as a first-class postgraduate teacher. Although he realized his own ability, and fought for what he wanted, he was a shy man.

He had few interests outside his work. He had a deep love of the countryside, and enjoyed long walks on Exmoor and in the Quantocks. His first wife, by whom he had two sons and a daughter, died in 1953. Later he remarried, and continued in consulting practice up to the time of the death of his second wife in July of this year. We will miss a good companion, a conscientious, friendly man, and one who had a full and useful life.

L. SURZYNSKI, M.D.

Dr. L. Surzynski, general practitioner in Maida Vale, London, and president of the Polish Medical Association in Great Britain since 1949, died on 28 September. He was 75.

Leon Surzynski was born in Inowroclaw, Poland, on 8 April 1891, which at the time was under the German partition. He received his primary and secondary education in Inowroclaw, and completed his medical studies at Leipzig and Munich Universities, graduating M.D. at Leipzig in 1917. During his undergraduate years he took an active part in the Polish independence movement. Between the years 1918 and 1922 he served initially in the German Army, and subsequently in the newly formed Polish Army under the leadership of Jozef Pilsudski. Jozef Pilsudski later became Marshal of Poland, and Dr. Surzynski was always a fervent supporter of his ideals. During the years of Poland's independence he took an increasing interest in politics, at the same time maintaining his private practice in Poznan. This political interest led him to become a member of the Polish Diet in 1928; and in the last sitting of the House between 1935 and 1939 he was elected deputy leader. In the Diet he represented the part of Poland known as Wielkopolska, and for a period of time was a city councillor of Poznan—his home town. In appreciation of his services to Poland he was awarded the Polonia Restituta, the highest Polish civil order, and the high military order of the Cross of the Valiant.

Apart from his chosen fields of medicine and politics, Dr. Surzynski was a very talented musician. He was president of many musical societies, but devoted most of his time to the Polish choirs. He was president of the Choral Society of Poland, and of the Slavonic Choral Society. During the last 20 years of his life spent in London he further pursued his interest in Polish choral music, and was the leader and organizer of the Polish choirs in Great Britain. During the second world war he was the chief medical officer for the Y.M.C.A. in Bucharest between 1939 and 1940. In 1941-2 he was the president of the Polish Red Cross in Jerusalem. From 1943 to 1946 he was liai-

son medical officer to the British Mission of Johannesburg.

After the war he came to London, where he spent the remainder of his life. He was always deeply concerned about the welfare of the Polish refugees in Britain. He maintained an interest in the Polish Army hospitals, and as president of the Polish Medical Association he was associated with the Polish medical school attached to Edinburgh University. He was separated from his wife and family, who had remained in Poland until 1958, when his wife joined him in London. In the last years of his life he was primarily concerned with the running of his practice in Maida Vale. His hospitality knew no bounds, and his guests could be certain of a warm welcome, with entertaining conversation and excellent music provided by the host. In him we have lost a great Pole, a fine doctor, and a man with a keen social conscience. Dr. Surzynski had an extremely amiable and dynamic personality, and will be remembered and loved by friends and patients alike.

We extend our deepest sympathy to his widow, two daughters—one of whom has followed him into the medical profession—and grandchildren in Poland.—J. T. L. and J. K.

K. J. L. SCOTT, M.D., M.R.C.P.

Dr. K. J. L. Scott, a general practitioner in Woking, died in the Nuffield Nursing Home on 26 September. He was 69.

Kenneth James Langlands Scott was born in Waimate, New Zealand, on 6 October 1897, and received his medical education at Otago University, graduating M.B., Ch.B. in 1922; two years later he proceeded M.D. That same year he was offered a post at the Mayo Clinic, but decided to come to Britain, where he took the M.R.C.P. shortly after his arrival. His early interest was in cardiology; he studied under Sir James Mackenzie, and was appointed Patterson research scholar in cardiology at the London Hospital. On the death of Sir James he settled in practice in Woking. During the second world war he served in the Indian Medical Service in the Middle East, attaining the rank of lieutenant-colonel. After demobilization he returned to his practice, but still maintained his particular interest in cardiology, giving his patients the benefit of his considerable experience. He was closely connected with the Woking Victoria General Hospital, and was for many years its medical director and senior physician.

Kenneth Scott pursued his hobbies with boundless enthusiasm and considerable success. As a philatelist his collection of early New Zealand stamps and postmarks earned him a reputation in this field. From his own vineyard he produced up to 200 bottles of wine a year, and was honoured by being made a Chevalier du Tastevin de Bourgogne. In his practice he never spared himself. Despite failing health latterly, he insisted on giving his patients the same care and attention he had always done. To his wife and four daughters go the sympathy and affection of his patients and friends.—F. M. L.

A memorial service will be held for Professor H. A. Magnus at King's College Hospital in the Hospital Chapel at Denmark Hill, London S.E.5, on 26 October at 3 p.m.

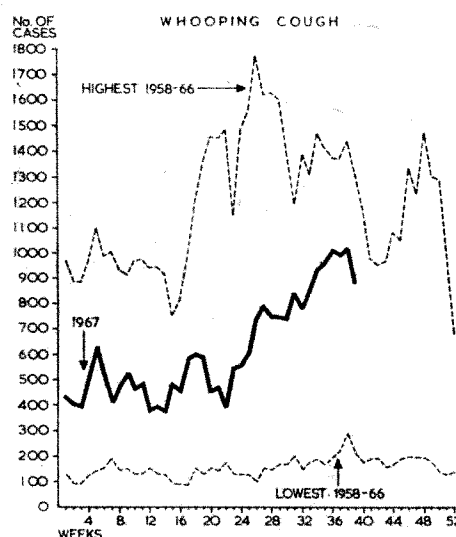
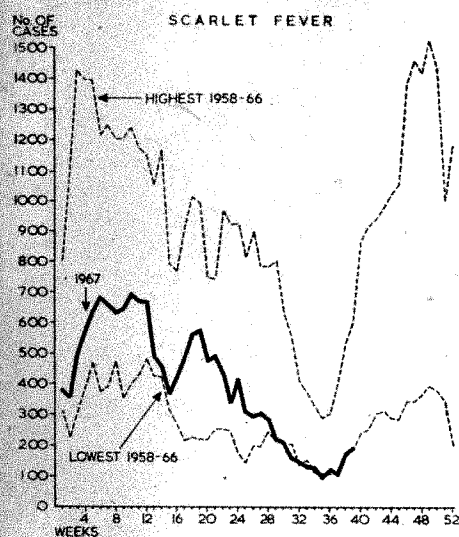
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of scarlet-fever and whooping-cough in England and Wales.

Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

			Week Ending 29 Sept. 6 Oct.	
Dysentery				
Greater London ...	...	...	45	43
Kent ...	...	...	0	11
Lancashire ...	...	...	44	34
Warwickshire ...	...	...	21	37
Yorkshire East Riding ...	...	...	6	15
Yorkshire North Riding ...	...	...	6	14
Yorkshire West Riding ...	...	...	25	17
Glasgow ...	...	...	38	67
Edinburgh ...	...	...	8	14
Paratyphoid Fever				
Greater London (Islington) ...	...	...	5	2
Typhoid Fever				
Ealing (London) ...	...	...	0	1
Hillingdon (London) ...	...	...	0	1
Waltham Forest (London) ...	...	...	0	1
Liverpool C.B. ...	...	...	0	1
Sheffield C.B. ...	...	...	0	1
Goole M.B. (Y.W.R.) ...	...	...	0	1

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 30 September (No. 39) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included) Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

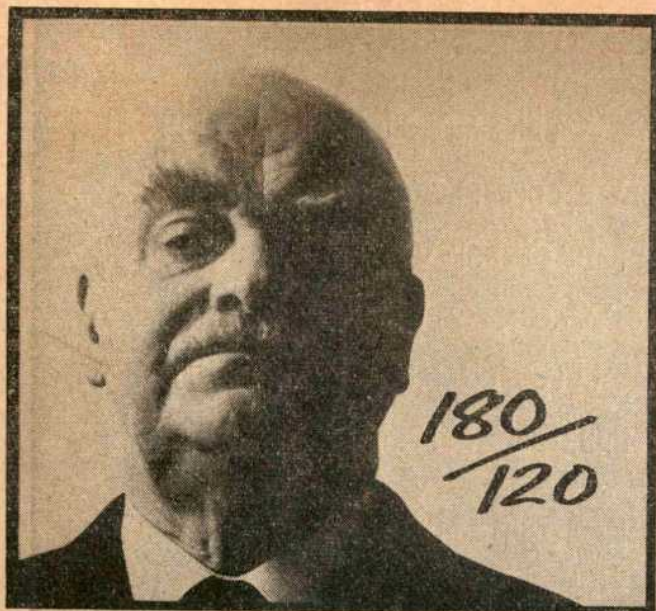
The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	1	0	0	1	0	
Dysentery ..	225	45	97	2		299	59	82	10	12
Encephalitis, acute ..	5	0		0		3	0		0	
Enteric fever: Typhoid ..	6	1	0	0		3	1	0	0	
Paratyphoid ..	9	6	0	0		2	0	1B	0	
Food-poisoning ..	232	41	9	12		146	24	5	3	
Infective enteritis or diarrhoea under 2 years ..				30	40				14	50
Measles* ..	871	79	15	18	34	3,260	344	128	48	39
Meningococcal infection ..	7	1	1	1	1	6	0	4	1	
Ophthalmia neonatorum ..	11	2	1	0		12	0	2	0	
Pneumonia† ..	67	11	56	7	2	74	7	68	0	
Poliomyelitis, acute: Paralytic ..	0	0	0	0		1	0	0	0	
Non-paralytic ..	0	0	0	0		0	0	0	0	
Puerperal fever‡ ..	103	21	2	1		80	21	15	0	
Scarlet fever ..	199	28	26	11	10	243	26	22	4	6
Tuberculosis: Respiratory ..	168	44	37	13		199	46	36	10	
Non-respiratory ..	41	9	13	4		56	11	6	0	
Whooping-cough ..	874	135	59	12	23	617	90	52	9	11
DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute ..				0						0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	8	1	1	0	0	6	2	2	0	1
Influenza ..	2	0	2	0	0	3	0	0	0	1
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	622	112	17	16	8	500	91	24	14	4
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	36	7	2	2	0	31	1	4	0	6
Non-respiratory ..				0	0				0	0
Whooping-cough ..	2	0	0	0	0	1	0	0	0	0
Deaths 0-1 year ..	278	55	15	8	7	278	53	23	9	11
Deaths (excluding stillbirths) ..	9,718	1604	545	137	168	9,043	1480	562	113	170
LIVE BIRTHS ..	16,069	2586	858	259	466	16,720	2840	864	316	396
STILLBIRTHS ..	220	32	9			250	49	22		

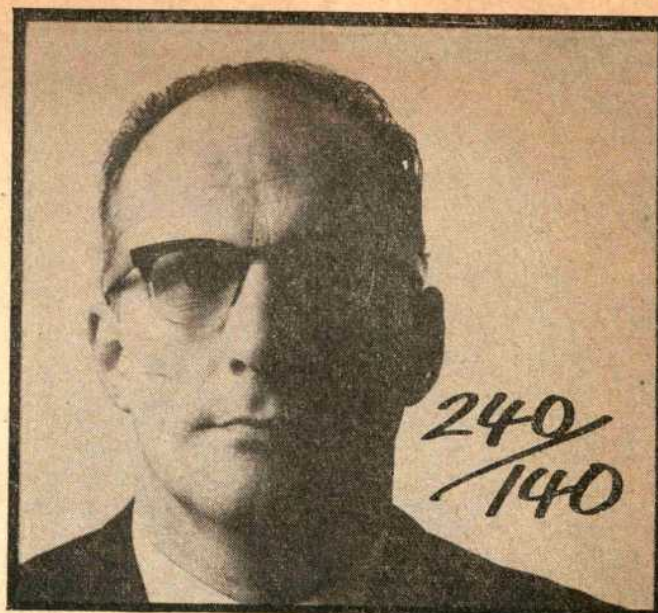
* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonias.

‡ Includes puerperal pyrexia.



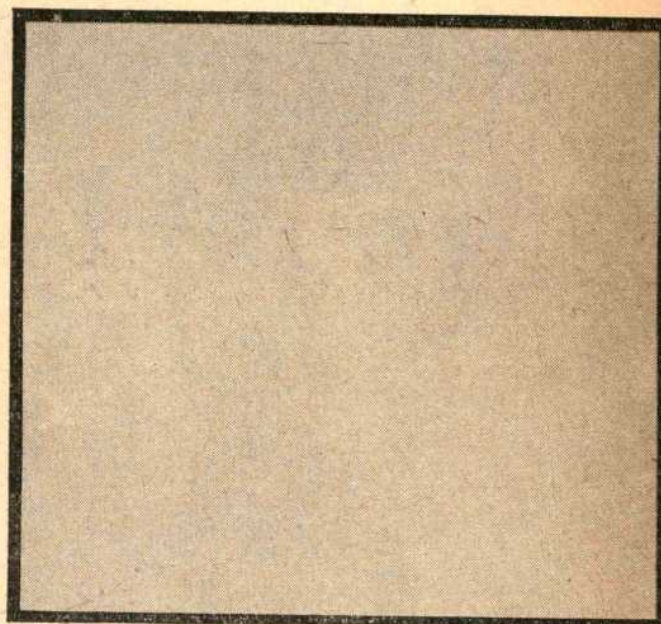
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REFERENCES

- 1 J Lancet, (1965) 85:7
- 2 Calif Med, (1965) 103:109
- 3 Maryland Med J, (1966) February
- 4 Antibiot Ann, (1959-60) p. 614
- 5 West Med, (1964) 5:62
- 6 Obstet and Gynec, (1964) 24:921.

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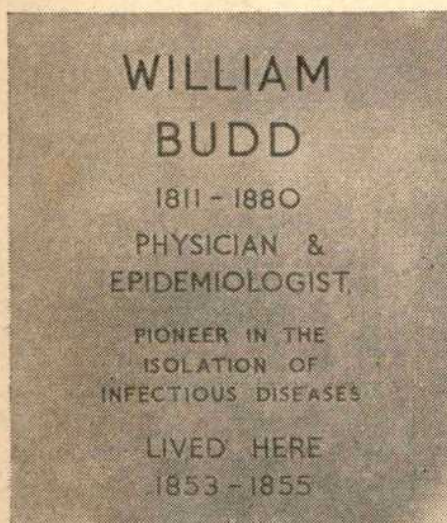
MEDICAL NEWS

Sir Arthur and Lady Porritt

The British Medical Association gave a dinner on 10 October in honour of Sir ARTHUR PORRITT, Governor General Designate of New Zealand, and Lady PORRITT, at B.M.A. House. Among those present were the following Past-Presidents: Lord COHEN OF BIRKENHEAD, Sir IAN FRASER, Sir JOHN MCNEE, Sir CLEMENT PRICE THOMAS, Sir TUDOR THOMAS, Sir ARTHUR THOMSON, Dr. E. A. GERRARD, and Dr. ALEXANDER H. HALL. The guests were accompanied by their ladies. Mr. R. V. COOKE, President, presented Sir Arthur with an inscribed silver cigarette box and Lady Porritt with a cut-glass and silver powder bowl. Sir ARTHUR presented the B.M.A. with a silver condiment set. He is expected to leave for New Zealand on 26 October.

William Budd Memorial Tablet

On 16 October Mr. R. V. COOKE, President of the British Medical Association, unveiled a plaque to the memory of William Budd at George's bookshop, Bristol, the house



(Photo Prints (Bristol))

in which he lived from 1853 to 1855. The unveiling was preceded by a meeting in the Alfred Marshall Building at which Mr. JOHN TOTTERDILL described life in Bristol in Budd's time and Professor R. C. WOFINDEN spoke about Budd and his career. Professor T. F. HEWER, professor of pathology at Bristol University, presided. The ceremony was held under the auspices of the West of England Branch of the Society of Medical Officers of Health in association with the Bristol Division of the British Medical Association, Bristol Medico-Chirurgical Society, Bristol Civic Society, and George's bookshop.

Sheffield University

Professor R. KILPATRICK has been appointed head of the department of pharmacology and therapeutics at Sheffield University.

The title of Sir Ernest Finch Visiting Professor has been conferred on Sir HEDLEY ATKINS, P.R.C.S., and on Sir EDWARD WAYNE for the period of their respective visits to Sheffield during 1967-8.

Chair of Anatomy, Tasmania

Dr. COLIN PETER WENDELL SMITH has been appointed to the chair of anatomy in the University of Tasmania. Dr. Wendell Smith, who is 40, was educated in Derbyshire and at Watford Grammar School, qualifying from St. Bartholomew's Medical College in 1951. He joined the staff of Guy's Hospital Medical School in 1956 as junior lecturer in anatomy, and had been lecturer in anatomy there for three years when in 1961 he was appointed associate professor of anatomy in the University of New South Wales. He is at present working at Guy's Hospital Medical School as a Commonwealth Medical Fellow under the Commonwealth Scholarship and Fellowship Plan. His principal research interest is in the relationship between the neuron and its satellite cells, and earlier studies in this field have been followed up by investigations into the structure and function of neuroglia.



(Photographia Ltd.)

Minister Opens Hospital Extensions

The Minister of Health, Mr. KENNETH ROBINSON, officially opened last week a new operating-theatre suite and extensions to the outpatient and other departments at St. Helier Hospital, Carshalton. Similar improvements to hospital efficiency, he said, could be seen all over the country. It was not only in the development of new district general hospitals or in the provision of additional beds that the hospital service was making progress but also in the modernization of specialist departments such as pharmacies, physiotherapy departments, and outpatient departments. The provision of a modern hospital service lay largely in the upgrading and re-equipping of specialist departments. By improving them the best use could be made of existing beds. The Minister was introduced by LORD ADDISON, chairman of the South-west Metropolitan Regional Hospital Board.

Gift to Glasgow University

Glasgow University has been given £30,000 by Mr. ALEXANDER STONE, chairman of the British Bank of Commerce, towards the building of an advanced microbiology research unit at Garscube, Glasgow. The unit will be in the charge of Professor Iwo R. W. LOMINSKI, head of the department of microbiology.

Butterworth Gold Medal

The winner of the Butterworth Gold Medal for this year's essay, the subject of which was "The Manifestations of Senility and their Management," is Dr. M. K. THOMPSON, of Croydon, Surrey.

Accidents at Work

Speaking in London last week at a conference on industrial safety, Mr. RAY GUNTER, Minister of Labour, pointed out that the time lost over a 12-month period through industrial injury and industrial

disease was more than 23m. days, compared with about 2m. days lost in disputes. Of 372 fatal accidents in factories last year 100 might have been prevented by reasonable foresight on the part of the employer or occupier. In 91 instances the deceased was considered to have been primarily responsible. Attention to safety, he said, should be brought home to employees by effective safety policies, especially in regard to sound training and competent supervision. A safe work-place and a safety conscious work-force were the ultimate objectives.

Broadmoor Hospital to be Rebuilt

The MINISTER OF HEALTH has decided in principle that the special hospital at Broadmoor should be rebuilt on its present site. It is intended to reduce the number of male patients, at present about 680, to a maximum of 500. The remainder will be transferred to a new hospital to be built, possibly on land adjacent to the special hospital at Moss Side, Maghull, Liverpool.

Harveian Oration

LORD PLATT delivered the Harveian Oration on 18 October at the Royal College of Physicians of London. His subject was "Medical Science: Master or Servant?" The Oration will shortly be published in the *British Medical Journal*.

Coming Events

Glasgow University Club, London.—Annual dinner, 2 November, 7 p.m. for 7.30 p.m., Cumberland Hotel, London W.1. LORD TODD, F.R.S., will preside. Details from Dr. J. F. HEGGIE, North Middlesex Hospital, London N.18.

King Edward's Hospital Fund for London.—Conference on ward housekeeping experiments at Whittington Hospital and Greenwich District Hospital, 1963-7, 9 November, Hospital Centre, 24 Nutford Place, London W.1. Details from Miss J. B. CRAIG.

Royal College of Obstetricians and Gynaecologists.—Scientific meeting, 17 November, Newcastle upon Tyne.

Leeds School of Medicine.—Annual dinner, 17 November, 7 p.m. for 7.30 p.m., Griffin Hotel, Boar Lane, Leeds 1. Tickets (35s.) from Honorary Secretary, Dinner Committee, Medical School, Leeds 1.

Institute of Religion and Medicine.—Open meeting, 17 November, 5.30 p.m., Friends' House, Euston Road, London N.W.1. Dr. MARGARET MEAD will speak on "Reward and Punishment."

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 23 October

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Dr. G. Simon: Radiology in the Patient with Dyspnoea.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., (1) Dr. A. Karen (Brno): Some Problems of Atrophic Rhinitis, Scleroma and Ozaena; (2) combined staff consultation clinical meeting.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. B. W. Meade: Pathology of Trauma—Metabolic Consequences; 6.30 p.m., Dr. T. L. Dormandy: Aspects of Homeostasis—Osmolality. ●

MANCHESTER MEDICAL SOCIETY: SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Manchester University Medical School, 9 p.m., Dr. G. M. Komrower: Early Diagnosis of Mental Retardation with particular reference to Detection of Biochemical Upsets giving rise to Mental Handicap.

MANCHESTER MEDICAL SOCIETY: SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital, 5.30 p.m., presidential address by Professor J. L. Hardwick: Trace Elements and Dental Caries.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Professor Sheila Sherlock: Hepatic Reactions to Drugs.

Tuesday, 24 October

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. J. M. Barnes: Toxic Substances and the Nervous System.

EDINBURGH UNIVERSITY MEDICAL STUDENTS COUNCIL.—At Lecture Hall "A," Hume Tower, George Square, Edinburgh, 5 p.m., B.M.A. lecture by Dr. Alex Comfort: "The Control of Ageing."

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. D. D. Munro: Biology of Hair Growth.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammesmith Hospital, 2 p.m., Mr. C. K. Vartan: Breech Presentation. (Admission by ticket only, obtainable from Secretary, Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, London S.W.)

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University Medical School, 4.30 p.m., university lecture on the history of medicine by Dr. W. Brockbank: The Early History of Our Medical School.

NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., Dr. R. Howell: cases and discussion.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. D. J. Waterson: Surgical Paediatric Problems in the Services.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian lecture by Professor M. H. Irving: The Sympatho-adrenal Factor in Haemorrhagic Shock.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. W. J. Dempster: Symptomatology of Rejecting Kidney Homotransplants.

SOCIETY OF CLINICAL PSYCHIATRISTS.—At Royal Society of Medicine, 6.30 p.m., discussion by Dr. H. V. Dicks, Professor W. Linford Rees, Dr. D. Williams: The Role of the Psychiatrist in Contemporary Society.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. G. A. D. Gordon: Ultrasonic Techniques in Neurology and Neurosurgery.

WESTMINSTER HOSPITAL MEDICAL SCHOOL.—8 p.m., Dr. R. M. A. McClelland: Information Retrieval.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, 1 p.m., clinical meeting.

Wednesday, 25 October

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. L. Szur: Principles of Dermatological Radiotherapy—II.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Peppy: Pulmonary Hypersensitivity Disease due to Inhaled Organic Dusts.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 3 p.m., Mr. A. M. Sutherland: Pelvic Tuberculosis. (Admission by ticket only, obtainable from Secretary, Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, London S.W.)

INSTITUTE OF UROLOGY.—5 p.m., Dr. C. S. Ogg: Blood and Urine Changes in Renal Disease.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—At X-ray Department, Kingston Hospital, 1.30 p.m., demonstration of radiographs by Dr. M. A. Hewett: Some Common Upper Abdominal Conditions.

OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Dr. K. D. Bardhan: Intrinsic Factor.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Arnott demonstration by Mr. E. H. Cornelius: Some Presidents of the College and their Contribution to the Museum and Library.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. C. Leevy New Jersey: Liver Disease of the Alcoholic.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conference by Professor J. F. Goodwin, Dr. E. Olsen: Cardiomyopathy. (2) 2 p.m., Dr. J. S. Cameron: Proteinuria.

STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., films: Jugular Venous Pulse; Cardiac Output in Man. (2) 6 p.m., lecture by Mrs. C. Pepler.

WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Professor T. A. J. Pranker: Management of Anaemia.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, course for general practitioners, 2 p.m., Dr. J. E. M. Glancy: Sexual Deviation; 3 p.m., Dr. W. Walther: Use of the Autoanalyser for Multiple Analyses.

WHITTINGTON HOSPITAL.—At Academic Centre, Archway Wing, London N., 11.30 a.m., Dr. Deborah Doniach: Autoimmunity in Liver Disease.

Thursday, 26 October

ABERDEEN UNIVERSITY FACULTY OF MEDICINE.—At Large Lecture Theatre, University Medical Buildings, Foresterhill, 5 p.m., Dr. J. M. Walshe: Wilson's Disease—a Triumph of Hope over Experience.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. D. B. Hope: Storage of Polypeptide Hormones.

CHADWICK TRUST.—At 90 Buckingham Palace Road, London S.W., 5 p.m., paper by Surgeon Captain F. P. Ellis: Health of the Navy—the Changing Pattern.

DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Dr. J. A. R. Lenman: Applied Physiology in Neuromuscular Disease.

GALENICALS, UNIVERSITY OF BRISTOL MEDICAL STUDENTS' SOCIETY.—At Lecture Theatre (E.29), New Medical School, Bristol, 5.15 p.m., B.M.A. lecture by Professor R. S. Illingworth: "Bad Treatment."

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. P. D. Samman: Principles of Dermatological Treatment.

LONDON HOSPITAL MEDICAL COLLEGE.—At the College Hall, Ashfield Street, 4.30 p.m., Schorstein memorial lecture by Sir Reginald Watson-Jones: Amputations of Body and Mind.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Thomas Vicary lecture by Sir Clifford Naunton Morgan: Surgery and Surgeons in 18th Century London.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 4 p.m., Mr. J. I. Burn: Management of Early Cancer of the Breast. (2) 5 p.m., lecture on medical history by Dr. E. S. Clarke: Disease in pre-Greek Antiquity.

RUNWELL HOSPITAL.—At Wickford, Essex, 8 p.m., Dr. T. M. Caine: A Five-year Follow-up of Treated Neurotics, Assessing Changes in Symptoms, Attitudes and Personality Tests.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Mr. R. G. Law: Standards of Obstetric Care.

Friday, 27 October

BROOK GENERAL HOSPITAL.—2 p.m., Mr. A. Howarth: Globus Hystericus.

NORTH STAFFS MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—At Hartshill, Stoke-on-Trent, 8 p.m., Dr. D. W. Liddell: Temporal Lobe Epilepsy.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—5.30 p.m., clinicopathological conference with cases from St. Mary's Hospital.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. J. Lorber: Current Problems in the Treatment of Hydrocephalus, and Long-term Results of Treatment.

Saturday, 28 October

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Postgraduate Lecture Theatre, Addenbrooke's Hospital, 10.30 a.m., all-day symposium: Old Age and Anaesthesia.

NUTRITION SOCIETY: SCOTTISH GROUP.—At University Medical Buildings, Foresterhill, Aberdeen, 11.15 a.m., symposium: Diet and the Central Nervous System.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, 10.30 a.m., Dr. K. W. G. Heathfield: neurological ward round.

Sunday, 29 October

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—10.15 a.m., seminar for general practitioners by Mr. R. F. McNab Jones.

ROYAL NORTHERN HOSPITAL, LONDON.—10 a.m., clinical conference by Dr. W. E. Clarke.

Universities and Colleges

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council held on 12 October, with Sir Hedley Atkins, president, in the chair, Mr. R. V. Cooke was readmitted as a member of the Council of the College.

Dr. J. T. Priestley was admitted to the Honorary Fellowship of the College.

Lord Cohen of Birkenhead was appointed Thomas Vicary lecturer for 1968.

The death of Sir James Learmonth, Honorary Fellow, was reported with deep regret.

Colonel S. H. Janikoun was admitted as the professor of military surgery.

The Lady Cade medal was presented to Air Vice-Marshall G. H. Morley.

The Hallett prize was presented to Dr. Solomon Victor (Madras Medical College).

Mr. G. L. Scott, of Merchant Taylors' School, Crosby, Liverpool and Guy's Hospital Medical School was admitted as the Macloghlin scholar for 1967.

Mr. M. Bewick was appointed as the Johnson and Johnson research fellow on wound healing in the department of physiology of the College. Diplomas of Membership were granted to D. F. Abbott, J. R. O. Collin, S. I. Lewis, and J. L. Watts.

Diplomas of Fellowship were granted to M. Bewick and V. K. Kak.

Diplomas of Fellowship in the Faculty of Anaesthetists were granted to the following:

R. S. Peachey, D. I. Hughes-Davies, W. H. Morton, B. Hayes, Abigail E. E. Mensah, Margaret L. Shaw, J. F. Murray, Gillian M. Davies, T. I. Cash, G. W. Gamlen, I. P. Unsworth, R. A. Spilsbury, Valerie A. Codman, C. M. A. Bell, Elizabeth A. Binsted, D. G. Lewis, J. B. Williams, R. Loveday, D. G. Nancekivell, D. W. M. West, I. Ul Haq, P. L. Mulrooney, M. K. Sen, W. T. Fothergill, Norma E. Davies, R. W. Hall, T. R. Austin, S. J. Lines, Margaret E. Beveridge, T. A. Fraser, L. A. G. Jayasekera, A. A. Khawaja, H. Padmanabhan, J. K. G. Pigott, M. S. Y. Khalil, S. K. Mitra, S. K. H. Desai, J. Restall, S. H. Tan, Margaret D. Tyrrell, R. S. Ahearn, J. M. Anderton, W. W. Biggs, J. A. Bushman, B. R. S. McClements, W. Németh, C. M. Bowkett, S. de Lange, Isobel R. Mackay, J. B. H. Magner, Judith A. Radcliffe, D. M. Ross, R. I. R. Sinton, D. J. Turner, J. R. B. Young, R. A. Bond, Audrey Clarke, J. B. Dyson, A. I. Gurubatham, A. E. Heenan, B. M. Jones, P. R. Pridaux, Tri-Ratna M. Tuladhar, Ann V. Beaugie, Carole A. Brown, D. N. Davies, H. A. Edwards, W. Fitch, P. F. Reilly, Rehana Shafi, D. P. Winder, Ann B. Brown, J. H. Kerr, D. Leivers, S. W. Lim, J. McV. Loudon, J. Swinney, R. J. N. Turner, P. L. Jones.

Diplomas were granted, jointly with the Royal College of Physicians of London, to the following:

DIPLOMA IN OPHTHALMOLOGY.—E. El T. A. Abdalla, N. Ahmad, A. R. M. Al-Saleh, D. R. Amies, Than Aung, I. A. Ayesh, K. I. Badli, E. H. Barnout, M. H. Bhimani, M. Boossia, R. W. Bors, R. M. Brown, S. P. Brumley, L. Condons, M. S. Davies, S. C. Debnath, R. S. Dhillion, D. G. Emery, Helen M. Evans, V. H. Gandhi, M. G. Glasspool, N. Gregoratos, Abdul-Munim A. Hamid, G. C. Hipwell, M. A. Hosain, J. M. Hudson, M. Hussain, Khiaie Myo, T. H. Kirkham, A. Kyaw, Seck-Kee Leong, M. K. J. Lim, W. E. McCready, A. K. Mathur, A. R. Menezes, D. Millington, Rachel E. Need, V. R. Patel, R. P. Pokhrel, A. K. Prasad, K. Rajaratnam, V. V. Rao, A. E. A. Ridgway, J. H. Sandford-Smith, M. A. Sattar, F. Suleiman, A. H. Taj, F. Tappouni, Mary M. Walshe, Y. M. Wan, R. G. Wilson.

DIPLOMA IN LARYNGOLOGY AND OTOTOLOGY.—S. M. S. Rahman.

DIPLOMA IN ANAESTHETICS.—L. R. Green.

DIPLOMA IN PHYSICAL MEDICINE.—J. B. Baggott, H. C. Burry, J. V. Forner Valero, Jessie K. M. Easton, M. A. Fouda, Doreen V. Jayamaha, F. L. Johnson, R. W. Tinsley.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—J. M. Goodburn.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—S. H. Abraham, H. A. Addy, R. Andersen, P. G. Atkinson, N. K. Biswas, S. M. Budhdeo, S. Chan, G. Cust, N. D. Dhabuwala, B. Dumavibha, P. R. A. Gaffney, A. K. Ghosh, J. J. Gilbert, A. Howis, P. U. Isichei, Md. R. Islam, M. Jamal, T. D. Jones, C. K. Kaufman, A. N. Khan, A. Y. Khogali, Z. A. Lins, Hee-Tak Mak, M. Misherghi, K. N. Murray, J. Mutemurana, S. G. Ng, R. W. Okach, C. T. Oon, S. Prasad, J. L. Pretorius, G. D. Qureshi, B. D. Reid, S. C. Roy, Lydia Schellekens, R. R. Shah, J. A. Sheikh, B. I. Syed, S. W. Tarlton, D. E. Taylor, S. Tin Tun, Taw D. C. Weeks, F. J. Wilson, J. C. Wilson, R. P. Yadava, W. Zylstra.

DIPLOMA IN PATHOLOGY.—Ruth M. Perinpanayagam.

After the meeting the Gordon-Watson lecture was delivered by Brigadier J. M. Matheson on "Infection in Missile Wounds."

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387-4499. TELEGRAMS: *Atiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated. Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. ADVERTISEMENTS AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia. MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 28 OCTOBER 1967

Pointers

Intrauterine Transfusion: Workers in Newcastle concluded from their studies that in spite of the hazard this procedure has an important role in the management of some cases of Rh-haemolytic disease (p. 189).

Transepidermal Water Loss: Is greatly increased in patients with erythroderma, psoriasis, and ichthyosis compared with normal subjects. This may explain the hypothermia and increased B.M.R. found in some of these patients (p. 195).

Emergency Intracardiac Pacemaking: Discussion of bedside method of placement using intracavitary electrocardiogram picked up by pacemaker electrode as a guide in patients with Adams-Stokes attacks (p. 199).

Oxygen Therapy: In paediatric use knowledge of exact concentration of oxygen is important. Studies show that incubators generally fulfil manufacturers' specifications, and that the Oxyginaire Humidaire Tent was the most efficient of the tents tested (p. 201).

Colitis in India: Ulcerative variety is not rare, but diagnosed less often than in the West because of the frequency of infectious conditions of the bowel, lack of facilities for precise diagnosis, and lack of long-term follow-up (p. 204).

Congenital Cyanotic Heart Disease: Retinal vascular changes initially present revert to normal after surgical correction of cardiac lesion, but E.E.G. defects do not change because they are not due to simple cerebrovascular disturbance (p. 207).

Electrophoretic Studies and Cancer: Study of survival of radioiodine-labelled serum γ G-globulin showed that the different fractions broke down at different rates, and were different in a patient with cancer from a normal subject (p. 210).

Case Reports: Enzyme variant in congenital methaemoglobinemia (p. 212); Anaphylactic reaction after soap enema (p. 215); Fatality after phenformin overdose (p. 216); New wave in E.C.G. complex (p. 217).

Conferences: Chemotherapy of tuberculosis in developing countries (p. 230). European Association for Study of the Liver (p. 232).

Dyspepsia: Symptoms, diagnosis, and management of gastro-oesophageal reflux due to hiatus hernia (p. 218).

Clinicopathological Conference: Crohn's disease in patient with treated adult coeliac disease (p. 222).

Nobel Prizes: Leader (p. 185). Photographs (p. 247).

Abortion Bill: Debate in House of Lords (p. 245).

Joint Annual Meeting in Australia: Provisional programme (*Supplement*, p. 25).

Public Health Committee: Report of meeting (*Supplement*, p. 27).

Retirement Pensions: *Supplement*, p. 26.

Prophylaxis in Rubella

Since the recognition of the teratogenic properties of rubella virus a quarter of a century ago many attempts have been made to prevent the disease during the early months of pregnancy. Until recently the only practical method of prevention has been by passive immunization. The results of 25 years' experience with either convalescent plasma or serum, pooled gammaglobulin, or convalescent rubella gammaglobulin have recently been reviewed by R. Lundström.¹ In experimentally induced infections gammaglobulin was surprisingly ineffective,² while in clinical trials the degree of protection afforded by this form of prophylaxis showed wide variation, though in a number of studies a substantial degree of protection was shown.³⁻⁶

Several factors probably contribute to the disappointing results reported with gammaglobulin in the prevention of rubella compared with its more obvious effect against measles. It is clear from the data reviewed by Lundström that the results were in many instances based on a small number of individuals, of different age and sex, living under widely differing environmental conditions and subjected to varying degrees of exposure to rubella. From 1954 to 1963 there was no practical method of assaying the content of rubella antibody in the prophylactics. Dosage could be an important factor in determining the outcome, as it is known that the antibody content can vary from batch to batch.^{7,8} The time of administration is probably even more important in view of the newly discovered details of the pathogenesis of rubella and in particular the prolonged period of infectivity and presence of viraemia, both of which occur for several days before the onset of the rash. More important, however, is the fact that the assessment of the efficacy of gammaglobulin in rubella on the basis of clinical attack-rates is not very meaningful when so many infections are atypical or subclinical. Subclinical infection may be associated with viraemia and foetal damage,⁹ and the trials so far reported have not established whether gammaglobulin, which has been shown to reduce the clinical attack-rate, protects the foetus, or what is the true rate of infection in immunized persons who do not develop symptoms. Some of the answers to these problems were contained in two papers in the *B.M.J.* of 9 September.^{10,11}

Since 1954 gammaglobulin has been available to general practitioners in this country. In an earlier report J. C. McDonald⁵ showed that the clinical attack-rate in family contacts given 750 mg. or 1,500 mg. of gammaglobulin was 1.27%. In a group of untreated women observed at about the same time the attack-rate was 3.7%.¹² This suggested that the gammaglobulin had a protective effect, but the attack-rates were low in both groups and the two were not strictly comparable. Now McDonald and C. S. Peckham¹⁰ report a further study on the use of gammaglobulin and its possible protective effect on the foetus. During the period 1954-62 gammaglobulin was issued to 36,577 rubella contacts. The dosage varied from 750 mg. to 1,500 mg., depending on the availability of supplies.

Data were finally obtained on 30,764 contacts, of whom 370 (1.2%) developed rubella within 28 days of inoculation and a further 0.3% at intervals thereafter. Later in the epidemic the attack-rate rose from 1.2% to 2.5% and then to 3.25%. The overall attack-rate in 15,173 women exposed to family contacts was 1.95%. As with the earlier survey this seems a low figure, but it is not possible to tell what it would have been without gammaglobulin. Attack-rates of 12% to 30% in unprotected women have been reported in surveys elsewhere. The observations on the incidence of defects, however, are more enlightening. Six hundred and ten women developed rubella and 424 (70%) came to term, including 319 cases of failure of prophylaxis and 105 cases in which the mothers had been treated with gammaglobulin after the appearance of the rash. Of the 424 liveborn children observed at the first postnatal inquiry at 3-9 months of age, 13% were found to have defects, of which 9.2% were of the rubella syndrome type. At the second postnatal inquiry at 2 years of age the rates increased to 18% for total defects and 13.6% for rubella defects, mainly heart disease and deafness in various combinations. No cataracts were observed, but only 14% of the 424 women were exposed in the first eight weeks of gestation.

The incidence of defects in the 30,297 women who were in contact with rubella, but who escaped infection was very different. Information was obtained from all but 13%. At the first postnatal inquiry 2.6% were found to have congenital defects, of which 0.4% were of the rubella type, with 3.6% and 0.6% at the second inquiry. The type of defects were very different from those observed in the offspring whose mothers had had rubella. They consisted in the main of malformations of the central nervous system and the musculo-skeletal and cardiovascular systems—malformations that are to be expected in the normal course of events. Comparatively few cases of deafness were encountered and a difference was also noted in the incidence of patent ductus arteriosus in the two groups. This latter manifestation is commonly associated with congenital rubella and is usually found together with other rubella-type defects. Eleven cases of patent ductus were observed out of 93 (11%) cases of congenital heart disease in the group who escaped infection, compared with 8 out of 13 cases (62%) in the group whose mothers had had rubella. Thus there was no excess of rubella-type defects in this group as a whole. This in itself is an important finding; but what could not be determined was the actual number of women in contact with rubella who did not develop clinical disease and who escaped infection altogether. This, after all, is the real test of the prophylactic value of gammaglobulin.

Antibody tests for rubella have recently been developed, and these have been used by members of the Public Health Laboratory Service to study the matter in more detail. In a report prepared by D. N. Hutchinson and his colleagues¹¹ it was found that only 4.9% of pregnant women in the Manchester area did not possess rubella neutralizing antibody. This is a low figure, but it is known that the incidence of rubella antibody varies considerably from one population group to another.^{13 14} In further studies in six different areas in the Midlands and north-west the proportion of non-immune subjects was found to vary from 6% to 21%. In 30 non-immune contacts given 750 mg. of gammaglobulin, 26.7% showed evidence of infection with production of anti-

body (seroconversion), and in 29 contacts given an additional 1,500 mg. between 8 and 12 days after contact 31% showed seroconversion. All but one of the patients showing evidence of infection received an initial dose of gammaglobulin within three days of contact. This study also showed once again the very much higher risk from contact in the home than elsewhere. A quite marked variation in antibody titre was detected among the 16 batches of gammaglobulin, but the numbers of susceptibles receiving material from any one batch was too small for differences in protection to be determined. These results indicate that the true attack or infection rate is around 30%.

Despite the obvious shortcomings of gammaglobulin revealed by these studies it still has a role as a prophylactic, limited though it may be. With the development of the haemagglutinin-inhibition test for rubella,¹⁵ which is quicker and more sensitive than the neutralization test, it should be possible to study the problem further by concentrating on the use of gammaglobulin of high titre given to non-immune contacts with the minimum delay after exposure. The main difficulty in studying rubella is inherent in the natural history of the disease. Infected individuals can be shedding virus for such a long and variable time before the onset of symptoms—and for a comparable time in subclinical infections—that it is difficult to determine when first contact has occurred. These and other results point to the need for the development of a rubella vaccine. Progress has already been made in this direction. P. D. Parkman and his colleagues¹⁶ have reported preliminary findings with an attenuated rubella vaccine prepared in monkey kidney-cell cultures which produced seroconversion without symptoms of infection in vaccinated children, though a number were found to be excreting virus from the oropharynx, albeit in low titre. Since this report further vaccines have been developed and are now on trial in several areas.¹⁷ Special problems of safety and antigenicity have to be considered in the development of a rubella vaccine, and it is likely to be several years before such a vaccine could be put into general use. Nevertheless, great progress has been made in a very short time.

¹ Lundström, R., *Archivvirusforsch.*, 1965, 16, 506.

² Krugman, S., and Ward, R., *New Engl. J. Med.*, 1958, 259, 16.

³ Bass, M., Davidson, H. B., Foote, F., Muckenfuss, R., and Landon, J. F., *N.Y. Med.*, 1949, 5, No. 23, p. 21.

⁴ Grayston, J. T., and Watten, R. H., *New Engl. J. Med.*, 1959, 261, 1145.

⁵ McDonald, J. C., *Brit. med. J.*, 1963, 2, 416.

⁶ Brody, J. A., Sever, J. L., and Schiff, G. M., *New Engl. J. Med.*, 1965, 272, 127.

⁷ Korn, R. F., *J. Infect. Dis.*, 1952, 90, 183.

⁸ Schiff, G. M., Sever, J. L., and Huebner, R. J., *Science*, 1963, 142, 58.

⁹ Avery, G. B., Monif, G. R. G., Sever, J. L., and Leikin, S. L., *Amer. J. Dis. Child.*, 1965, 110, 444.

¹⁰ McDonald, J. C., and Peckham, C. S., *Brit. med. J.*, 1967, 3, 633.

¹¹ Report to the Public Health Laboratory Service Rubella Working Party, *ibid.*, 1967, 3, 638.

¹² Watson, G. I., and McDonald, J. C., *ibid.*, 1963, 2, 419.

¹³ Sever, J. L., Schiff, G. M., and Huebner, R. J., *Obstet. and Gynec.*, 1964, 23, 153.

¹⁴ Lundström, R., Svedmyr, A., Hagbard, L., and Kayser, K., *Acta paediat. scand.*, 1967, in press.

¹⁵ Stewart, G. L., Parkman, P. D., Hopps, H. E., Douglas, R. D., Hamilton, J. P., and Meyer, H. M., *New Engl. J. Med.*, 1967, 276, 554.

¹⁶ Parkman, P. D., Meyer, H. M., Kirschstein, R. L., and Hopps, H. E., *ibid.*, 1966, 275, 569.

¹⁷ Meyer, H. M., Parkman, P. D., Panos, T. C., Stewart, G. L., Hobbins, T. E., and Ennis, F. A., in *First International Conference on Vaccines Against Viral and Rickettsial Diseases*, Washington, 1967, p. 390.

Men of Vision

The Nobel prize for medicine for 1967 is shared by Professor R. A. Granit, of the Karolinska Institute, Stockholm, Professor H. K. Hartline, of the Rockefeller Institute, New York, and Professor G. Wald, of Harvard University, Massachusetts, the feature common to their work being the analysis of the mechanism of vision.

Granit's analysis of the relatively slow electrical changes that take place when the eye is exposed to light—the electroretinogram, or E.R.G.—was the work that first brought him fame in the field of visual physiology. As with the electrocardiogram, the E.R.G. could be resolved into a number of components, so that the electrical events recorded from the cornea were the algebraic sum of both positive and negative variations.

Subsequent work has largely confirmed his basic postulates, though more precise and localized recording has revealed many instructive complications. From the E.R.G. Granit progressed to the study of the action potentials in single fibres of the optic nerve, studies that culminated in his “dominator-modulator” theory of colour vision. Thus certain fibres appeared to be carrying messages indicating the general luminosity of the stimulus while others, the modulators, appeared to indicate its chromatic quality. The modulators tended to group into three regions of the spectrum, and thus gave an electrophysiological basis to the Young-Helmholtz trichromatic theory. Granit's great achievements in electrophysiology spring from his realization that the retina is, indeed, merely an outgrowth of the fore-brain, so that the properties of the synapses within the retina, and the organization of its neurones, are by no means peculiar to this sensory system. His analyses of retinal electrophysiology were thus generalized, and nowhere is this better seen than in his classical book *Receptors and Sensory Perception*, published in 1955. Furthermore, this realization led him to expand his field of investigation so that the electrophysiology of the proprioceptors of muscles has now become his field of main interest. Thanks largely to Granit's studies and those of younger men from all over the world who gained their early experience in his laboratory, the importance of the spindle in the control of muscular contraction is being realized, while the complex control exerted on muscular action through the spindle by cerebellar and other motor centres is being elucidated.

Hartline, like Granit, made the vertebrate E.R.G. one of his earliest studies in retinal physiology, but very soon moved to a more simply organized eye—namely, that of the horseshoe crab, *Limulus*. This, like the insect eye, consists of an aggregate of “micro-eyes” or ommatidia, each with its own refracting apparatus, photosensitive cells, and sensory nerve cell. Study of a single ommatidium, with the single group of fibres emerging from it and running to the central nervous system, provided an opportunity to study clearly the electrical events following illumination. A single fibre of the optic nerve of the vertebrate eye is the axon of a ganglion cell of the retina—that is, of a second-order sensory neurone—but the fibre leading from the ommatidium is the axon of a primary sensory neurone (the eccentric cell), and thus the message should be much simpler. The results of Hartline's studies on this system, carried out with ever-improving techniques, form the solid foundation for present-day theories of sensory processes. Thus the concept of the “generator potential,” the slow non-propagated negative variation developing in the receptor cell, has received ample justification from his

records obtained with micro-electrodes inserted into individual eccentric cells.

Perhaps one of the most interesting discoveries was the mutual inhibition between ommatidia. For a long time it was considered that the responses in fibres emerging from adjacent ommatidia were independent of each other, since there was no clear-cut synapse on the visual pathway where interaction could occur. In fact, however, interaction has been detected, and is thought to occur in the plexus of fibres just outside the ommatidia. It probably represents a crude form of synaptic action, but this awaits elucidation. The importance of this particular aspect is the opportunity it gives to study quantitative aspects of inhibition, since it is becoming clearer, as the study of sensory physiology is pressed further forwards to the sensory and integrating areas of the cerebral cortex, that inhibition is far more important than excitation. Thus uniform illumination of the retina, which excites presumably every rod and cone, produces little or no response in the vast majority of neurones in the visual cortex. Only when the retina is excited by certain patterns of light and dark will these cortical neurones respond; and the mechanism by which this discrimination is achieved is by way of inhibitory processes taking place at successive levels of the ascending pathway.

Wald has devoted his energies to the elucidation of the chemical events taking place in the receptor following exposure to light and the reversal of these effects during dark-adaptation. The amounts of material available for analysis that can be obtained from a single retina are very small, so that special methods must be used to identify them. Wald's initial achievement, which brought him world-wide recognition, was the demonstration that one of the later products of decomposition is retinene, which proved to be a simple derivative of vitamin A, thus providing, incidentally, a rationale of the long-recognized relation between night-blindness and vitamin-A deficiency. Thus rhodopsin, the photopigment of the rods of most vertebrates, could be described as a protein molecule, opsin, with a prosthetic group, retinene. Subsequent studies showed the successive steps in the breakdown of the rhodopsin molecule that culminated in the splitting off of retinene and its conversion to vitamin A in the retina during exposure to light. These changes were “dark reactions” in the sense that, once the first change had taken place in response to light, the succeeding ones occurred on their own; they were the result of thermal, rather than photochemical, reactions. The question that interested the physiologist was the nature of the initial photochemical event that triggered off these later reactions, since it seemed likely that the electrophysiological event would be most closely related to this. Wald showed that one of the earliest events was the “change in shape” of the retinene molecule while it was still attached to the protein, opsin. The retinene molecule, by virtue of having several conjugated double bonds, could adopt a variety of *cis-trans*-isomeric forms; and it was shown that only when the molecule had two of these forms could it remain in stable association with the opsin molecule. In the so-called 11-*cis*-form it united to give the photopigment rhodopsin, while in the 9-*cis*-form it gave another pigment, isorhodopsin. It would seem, then, that the primary effect of light is to make the linkage between retinene and opsin “uncomfortable,” in the sense that the retinene is now no longer able to fit snugly into the opsin carrier. Because of this, the opsin may undergo some strain, and this strain leads to electrical changes, from which changes follow in the neurone associated with the rod—that is, in the bipolar

cell. Thus Wald's analysis of the chemical events resulting from the impingement of a quantum of light in the rod has carried us very close indeed to the recognition of the real nature of the photochemical stimulus.

These studies have been confined to the photopigments concerned with night vision—namely, rhodopsin, found in the rods of the great majority of vertebrates, and porphyropsin, found in the rods of fresh-water fishes. The two pigments mediate night vision and are apparently not concerned in the more complex daylight, or cone, vision, by virtue of which not only is light appreciated as such but also its qualitative variations are appreciated as colours. In recent years the investigation of the nature of the photopigments in the receptors concerned with daylight and colour vision, the cones, has been pursued in many laboratories. Wald long ago extracted a pigment from the chicken retina, which contains mainly cones, which he called iodopsin. It was entirely different in its light-absorption characteristics from rhodopsin, but like rhodopsin it contained retinene, and it underwent a similar series of chemical changes on illumination. This was only one pigment, however, and the trichromatic theory of colour vision demanded three pigments, contained in separate cones, as the basis for colour discrimination. It would seem that the methods of extraction that were adequate for the study of night-vision pigments were inadequate for extraction and separation of these three hypothetical pigments. And we owe to W. A. H. Rushton, of Cambridge, and R. A. Weale, of London, the detection of several daylight pigments in the mammalian retina. Their studies indicated the presence of red- and green-sensitive pigments; the presence of a blue-sensitive pigment was not demonstrated, probably because of the technical difficulties. The Japanese workers Hanoaka and Fujimoto measured the absorption of light by single fish cones, and found characteristic differences corresponding to what might well have been red-, green-, and blue-sensitive cones; fish cones were chosen because they were big enough to permit this type of measurement. Essentially similar results have been reported in the primate from the laboratories of Marks and of Wald, blue-, green-, and red-sensitive pigments having been described by Wald, for example. Thus the trichromatic theory of Young and Helmholtz has been unequivocally substantiated by modern physiological research.

Fall-out from Space Travel

The Russians' safe landing of a space ship on Venus is surely one of the most astonishing technical feats so far achieved by man. The skill and resources that have been devoted to it are of necessity immense. While the ultimate goal of space travel still remains a fairly remote possibility, enthusiasts for it, when challenged to justify the vast sums of money they manage to extract from governments, are apt to shelter behind something called "fall-out." This is the expression used when an invention or discovery made for one purpose turns out unexpectedly useful for a different purpose. Something spills over the side of the bandwagon, and a watchful backroom boy rushes in to catch it as it falls.

Many items of space fall-out are listed by Albert H. Schwichtenberg in a recent article,¹ one of three forming an "Aerospace Medical Symposium" in the *Journal of the American Medical Association*. Unlike a room or a factory,

a spacecraft cabin is hermetically sealed; moreover, airborne particles cannot "fall" to the floor. So contamination is far less tolerated. Consequently, methods of reducing it have been developed which can be beneficially applied to industry.

Violent oscillations can arise during take-off of a spacecraft under power, so in the interests of astronauts the frequencies which set up resonance in various parts of the body have had to be investigated. The results are applicable also to motor vehicles and industrial machinery. "Instrument packages" for monitoring the various physiological systems of astronauts have been developed to a high pitch never before attained, and Schwichtenberg mentions a bolometer, fixed near the carotid artery in the neighbourhood of the ear drum, which records minute changes of temperature to an accuracy between 1/100 and 1/1,000 C°. Research already done on the effects of radiation and on shielding and protective drugs could, the author points out, be useful in connexion with nuclear weapons. But it is to be hoped that this particular item of fall-out will be denied the opportunity to justify itself.

Research into weightlessness, which cannot be experienced on earth for more than a fraction of a minute at a time, would hardly be expected to provide fall-out. Yet it belies its name, for fall-out there is. So anxious are the space medicine men to establish the effects of weightlessness over far longer periods than astronauts have yet had to endure that they have experimented with the next best thing—almost total immersion in water. A notable fall-out from this research is the "dry water immersion bed," used for the treatment of intractable trophic ulcers.

So far 19 astronauts have spent a total of some 2,000 weightless hours in 25 flights, writes Charles A. Berry.² The longest flights have lasted 4, 8, and 14 days, and in these the blood of the pilots in command has shown deficits in red cell mass of 5%, 20%, and 19% respectively.³ However, this phenomenon, due to a haemolytic process, was not attributed to weightlessness but to the cabin atmosphere being 100% oxygen. The reason for the pure oxygen is that air pressure inside the cabin is kept at only one-third of the atmospheric pressure on the earth's surface, and the reason for this, in turn, is that experience with pressurized aircraft convinced the engineers that a higher internal pressure would be difficult to maintain.

The forecast, made before space flight actually began, that an atmosphere of 100% oxygen at low pressure would be harmful was only one of several that proved too pessimistic, and Berry mentions many others. The suits of the "space-walkers," for instance, showed no sign of the impact of micro-meteorites while they floated outside the ship, and still less of any puncture of the suits, inside which a pressure of a quarter of an atmosphere was maintained. But the first space-walker encountered unexpected difficulty which had not been foreseen even by the pessimists: his attempts to complete his "tasks" led to excessive heat and sweat, and he had to hurry back inside. Berry attributes this trouble to the combined effect of "the basic laws of physics producing action and reaction and the need to stop an action, the difficulty in trying to maintain position to do a task, the problems of mobility in a 3.5 lb./sq. in. (242 millibars) suit, some amount of heat

¹ Schwichtenberg, A. H., *J. Amer. med. Ass.*, 1967, 201, 247.

² Berry, C. A., *ibid.*, 1967, 201, 232.

³ See *Brit. med. J.*, 1967, 3, 388.

⁴ Kidera, G. J., *J. Amer. med. Ass.*, 1967, 201, 242.

load in the space suit and the carbon dioxide level in the helmet." Another false prophecy, derived from experiments in aeroplanes, was that a period of weightlessness would reduce tolerance to subsequent violent deceleration on re-entry into the atmosphere, but though it reached a maximum of 8.2 g it was well tolerated.

The remaining article, by George J. Kidera,⁴ shows that the most frequent medical causes of commercial pilots being grounded are cardiovascular (52%) and psychiatric (17%).

Plan for Hospitals

A working party set up jointly in 1965 by the King Edward's Hospital Fund and the Institute of Hospital Administrators was asked "to consider how, if at all, the present pattern of hospital administration might need alteration in the light of the changes that have taken place since 1948 and of further changes that may be brought about during the next fifteen years by the development of District Hospitals." Its twelve members included one medical man, Professor John Anderson, of King's College Medical School, and two hospital matrons, the others being lay hospital administrators. The working party set themselves the task of considering existing systems of management of hospitals at district level, suggesting changes that might be required in these systems, and considering a management pattern for the future, bearing in mind the advent of district hospitals.

In its report,¹ recently published, the working party identified three features of the existing arrangements which it regards as unsatisfactory and tending to hamper efficient and economic management. They are, firstly, over-use and misuse of the committee system; secondly, the absence of a clear definition of the roles and responsibilities of the various senior officials and of their relationship one to another; and, thirdly, the absence in the organization of any one official holding overall responsibility and authority. The working party's recommendations are designed to overcome these defects and also to provide for the closer association which it foresees will develop between the hospital and the other health and welfare services in the community. Its proposals rest on "two basic assumptions about the hospital service 15 years hence." The first is that the Ministry or some other central authority will continue to administer the service, the district hospital remaining the lowest tier of a three-tier structure, and the second that the best management structure for a district hospital will be "that which extracts from scarce resources of money, labour, and equipment the maximum possible benefit for the patient."

It is proposed that the hospital management committee should be replaced by a district hospital board. This would still be appointed by "the regional agent of the central health authority," but would have far fewer members, consisting of an appointed chairman and seven other members, three of whom would be on it *ex officio*. There would be two community advisory committees, one concerned with general medical matters and co-operation with other health and welfare services, the other with the interests of patients and co-operation with the local community. The chairman of each of these committees would be *ex officio* a member of the board.

The task of the board is seen as "to administer the moneys allotted to it and formulate the necessary policy to run the District Hospital." Executive function would be delegated to a general manager responsible for running the hospital, who would also be an *ex-officio* member of the hospital board. The general manager would be assisted by four directors of service in charge of medical and paramedical services, nursing services, finance and statistical services, and general services. These posts would be full-time appointments, though the director of medical and paramedical services might initially need to be part-time. A hospital medical services committee would be appointed by the senior clinical staff to advise the director of medical and paramedical services.

The late Professor J. M. Mackintosh, who contributed much to the study of medical administration, often claimed that there were only two countries in which the head of the medical services was not a doctor—the United Kingdom and Abyssinia. Whether this is so or not, it is certainly true that in Britain—more particularly the southern half of it—there is a body of opinion which holds that in hospitals at all events the doctor's place is in the ward and the operating-theatre, not the board-room. Most doctors are in no doubt that the primary function of a hospital is to deploy certain forms of investigation and treatment in the most effective way. The notion that they are really specialized institutions to be run by appropriately qualified managers with the help of doctors is not true. Undoubtedly lay officials have an essential role in the successful management of hospitals, but it should not be the dominant one.

The working party's report, though presented as a contribution to long-term planning, is essentially a presentation of the case for lay administration of hospitals. As such, it ought to serve a useful purpose in stimulating the medical profession to clarify its thinking on the shape of things to come.

Health Education of Asian Immigrants

Hazards to which newly arrived Asian immigrants are prone include pulmonary tuberculosis^{1, 2} and venereal disease,³ the effects of intestinal parasites—in particular anaemia from hookworm infestation⁴—and accidents due to unfamiliar surroundings.⁵ Thus health education⁶ could make a valuable contribution to the wellbeing of these people.

The newly arrived immigrant may be seen by his own countrymen, by a family doctor with whom he is urged to register shortly after arrival, by local-authority medical, social, or educational workers, and by staff of the Ministries of Labour or Social Security. If all bear in mind the risk he may be running, they can offer preventive measures or treatment by the appropriate services. A recent symposium held by the Health Education Section of the Royal Society of Health in Bradford showed that during three years of keeping specific records the infant mortality rate among children born locally to Asian immigrants had fallen to that of the English population of similar housing and employment background; and numbers of new notifications of pulmonary tuberculosis and venereal disease were declining rapidly. This had been achieved in part by special attention to the organiza-

¹ *The Shape of Hospital Management in 1980*. King Edward's Hospital Fund for London, 1967. London.

tion of medical and social services and by education in their use.⁷

Evidence from Bradford itself, discussed at the symposium, suggests that after the first few months of life in Britain the health problems of immigrants become little different from those of our own population. Dr. F. N. Bamford showed that the main causes of death of infants born in this country of Asian parents, such as prematurity and bronchopneumonia, had the same incidence as in the general population. Serious forms of malnutrition were rare, but suboptimal nutrition might still be a problem, though improving with economic circumstances and possibly with the impact of education. For example, he noted that the number of days on which meat was eaten had risen substantially after stay in this country. Only 3% of a sample of 1,442 Asian schoolchildren had a haemoglobin level of less than 10 g. per 100 ml. Out of more than 2,000 bacterial cultures of the stools of immigrants no significant excess of intestinal infections had been found. There were no general problems of inadequate cleanliness or personal hygiene.

The lack of knowledge among the immigrant population of the interpretation of signs and symptoms of disease, particularly in paediatric practice, has led to some difficulties in general practice. It is only the family doctor who can effectively educate his own patients to assess those symptoms which require medical attention and to appreciate the degree of urgency with which it might be needed.

Thus the main problems of health education for immigrants, other than those who are newly arrived, are related not so much to its content as to the techniques required to put it across. The cultural, social, and religious patterns of immigrants need understanding, for they have to be taken into account when advising patients on questions of diet, family planning, and mental health.

To help overcome the language barrier local authorities can appoint Indian and Pakistani liaison officers. Spoken communication in simple matters may be possible, and a mixture of Urdu and English is often understood. Written communication may need translation into four or five languages. Printing of simple documents of instruction—for example, directions on the use of drugs or attendance at surgeries and clinics—is not difficult and requires only a translator and access to photo-lithographical processes, both of which are available in most large towns. But not all immigrants are literate. Suitably staffed infant welfare clinics of the traditional pattern perform vital educational work.

At present the pattern of immigration is changing. Male workers are no longer arriving in large numbers, but their families are making a great impact. Children of school age rapidly become proficient in English, particularly where special instructional centres are provided. These educational methods frequently allow an emphasis on social instruction and prove invaluable in everyday matters of hygiene, clothing, and nutrition. School medical officers can play a valuable

part in co-operation with the staffs of schools in promoting health education.

As the way of life of the Asian immigrant becomes more settled, his health problems and so the health education he needs approximate to those of our own population. It would therefore be a mistake, both educationally and in the wider context of integration, for the basic aims of the community programmes intended for him to differ from those for the native of this country. What is especially needed is patience to give help and advice against the background of different cultures and languages and experiment in developing techniques for this purpose.

Students Abroad

Not all travellers abroad are swirling down the brain drain. Many in fact are enriching their experience in a way that will be greatly to the benefit of their countrymen, and if they can begin to do so while they are still students so much the better. With this in mind the British Medical Students' Trust was founded in 1958 by undergraduates for undergraduate education. It is a legally constituted charity now independent of the British Medical Students' Association, which established it, but with links through its board of trustees with both the B.M.S.A. and the B.M.A. The president is Lord Cohen of Birkenhead and the chairman of the trustees Mr. A. M. A. Moore. Through the generosity of industry—mainly pharmaceutical firms—and charitable foundations, as well as of individuals, the trust is able to finance visits abroad for about 30 to 50 medical students a year, some to advanced centres of study, others to exceedingly out-of-the-way places. In learning to help tackle unusual problems in strange conditions, often in the developing countries, the fortunate students chosen to go on these trips get the opportunity of helping people who need help and of discovering early on how much more there is to medicine than the textbooks contain. The trust has now launched a national appeal for funds, and it may be commended as a thoroughly worth-while cause. The address is British Medical Students' Trust, B.M.A. House, Tavistock Square, London W.C.1.

Meeting in Australia

Next year's Annual Meeting of the B.M.A. will be held jointly with the Australian Medical Association in August. The provisional programme appears in the *Supplement* this week to tempt readers in Britain to start making arrangements as soon as possible for a trip round the world. The theme, "A Review of Australian Medicine as at 1968," is aptly chosen, for British doctors cannot fail to be drawn to a country where independence of mind is highly esteemed and medical research in a lively condition. As well as the opportunity to see medicine afresh through Australian eyes, visitors are offered some suggestions for stopping off at places of interest on the way. Further details will be published when they are available, but it is not too soon to begin making arrangements for what will undoubtedly be a delightful and memorable occasion.

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Papers and Originals

Intrauterine Transfusion in Rh-isoimmunization

D. V. I. FAIRWEATHER,*|| M.D., F.R.C.O.G.; D. TACCHI,* M.D., F.R.C.O.G.; A. COXON,† M.B., M.R.C.O.G.
M. I. HUGHES,‡ M.B., CH.B.; S. MURRAY,‡ M.D., M.R.C.P., F.C.PATH.; W. WALKER,§ M.D., M.R.C.P., M.C.PATH.

Brit. med. J., 1967, 4, 189-194

Fifteen per cent. of all cases of Rh-isoimmunization end in stillbirth. Until 1963 the only available means of preventing this outcome in cases with a high risk of stillbirth was to deliver the foetus prematurely before intrauterine death had occurred. The value of this was limited, because many intrauterine deaths due to haemolytic disease of the newborn occur early in pregnancy, and because in the event of a live birth prematurity is a serious danger.

The introduction of intrauterine transfusion (Liley, 1963) offered the possibility that intrauterine life could be prolonged to a stage where premature induction could be more successfully employed, but implicit for its success and justification is a reliable forecast of the possible stillbirth and of the probable time of intrauterine death.

The present communication describes our selection of patients for intrauterine transfusion and our experience of the procedure as employed in the Newcastle hospitals during 1965 and 1966.

Selection of Patients

The final decision to carry out intrauterine transfusion depends on the level of bile pigment in the liquor amnii. Amniocentesis, however, involves risks, and to discriminate those patients in whom this procedure is justified use is made in the first place of the previous obstetric history.

Selection of Patients for Liquor Examination

At the first visit a patient can be placed in one of four categories:

(1) Patients currently developing antibodies—that is, first affected cases. The risk of stillbirth is only 8%, but this group comprises 60% of all cases. In these, intrauterine death tends to occur late in pregnancy, only 30% occurring before 37 weeks' gestation.

(2) Patients who have already had an affected infant who required no treatment. These families represent 10% of the total and carry no greater risk of stillbirth than pregnancy generally.

(3) Patients who have already had an affected infant who required transfusion. These families constitute 20% of the total; the risk of stillbirth is increased to 20%, but 40% of the stillbirths occur before 37 weeks' gestation.

(4) Patients who have already had a liveborn hydropic infant or a stillbirth due to haemolytic disease. This is the history in 10% of cases; the risk of a subsequent stillbirth if the foetus is Rh-positive exceeds 50%, and early intrauterine death often occurs. Walker (1960) estimated that after one previous stillbirth 50% of subsequent stillbirths occur in utero before 35 weeks, but after more than one stillbirth 50% die before 32 weeks' gestation.

If allowance is made for the size of and risk of stillbirth in each group it is calculated that the three groups carrying a significant risk of stillbirth contribute equally to the total stillbirths.

In 1965 and 1966 amniocentesis was carried out initially at approximately 22 weeks where previous stillbirth or very severe disease had occurred, at 32 weeks when there had been previous moderate disease, but at 35 weeks in first affected cases and only if the antibody titre exceeded 1/16 by indirect Coombs test. Liquor examination was usually repeated at intervals of two to three weeks.

Selection of Patients for Intrauterine Transfusion

There are many methods for estimating bilirubin in liquor, but we (Knox *et al.*, 1965; Savage *et al.*, 1966) have found that for predicting stillbirth at 34-36 weeks' gestation the critical liquor ratio transmission 520 $m\mu$ is 1.06. As the bilirubin level in liquor tends to fall as pregnancy advances it was appreciated that a higher ratio would have to be adopted earlier in pregnancy, and a level of 1.1 was arbitrarily chosen.

To assess the reliability of this criterion and the value of intrauterine transfusion we decided to carry out a controlled trial in 1965. Patients were admitted to the trial if the liquor ratio exceeded 1.1 early in pregnancy, but final selection for or against intrauterine transfusion was random.

In 1966 we discontinued the trial and were able to improve selection for intrauterine transfusion to include only those cases where the liquor ratio early in pregnancy was 1.1 or higher on two consecutive occasions and was not falling.

Our experience also enabled a second group of patients to be included for intrauterine transfusion—namely, those with a single ratio exceeding 1.1 at about 32 weeks. Previous to intrauterine transfusion such patients would probably have been induced at 32 weeks' gestation, but combining such serious prematurity with severe haemolytic disease had resulted in almost a 40% neonatal mortality. In comparison, in patients induced at 35 weeks the neonatal mortality is under 20% and after spontaneous delivery at term just over 2%. It was also appreciated that the technique of intrauterine transfusion is much easier at 32 than at 22 weeks' gestation.

Material

In 1965 16 patients were admitted to the trial and in seven intrauterine transfusion was carried out within two weeks of the initial liquor examination. Provided the foetus survived, intrauterine transfusion was repeated at intervals of two to three

* Princess Mary Maternity Hospital, Newcastle upon Tyne.

† Newcastle General Hospital, Newcastle upon Tyne.

‡ Regional Blood Transfusion Centre, Newcastle upon Tyne.

§ Reader in Paediatric Haematology, University of Newcastle upon Tyne.

|| Present address: University College Hospital, London W.C.1.

weeks until delivery, which in all cases was induced prematurely. The nine patients not selected for intrauterine transfusion also had repeated liquor examinations until delivery, which was also induced prematurely.

In 1966 28 patients with a high and rising bilirubin level were selected for intrauterine transfusion, which was carried out within three weeks of the initial examination. Intrauterine transfusion was repeated at intervals of two to three weeks until delivery by premature induction. Another 17 patients also had amniocentesis, but, either because the bilirubin level did not meet the criteria or very early intrauterine death occurred, they were excluded from intrauterine transfusion. Liquor examination in these also was repeated at intervals of two to three weeks where appropriate until delivery.

Technique of Intrauterine Transfusion

Before the initial amniocentesis placental location is carried out by percutaneous femoral arteriography (or by radioisotope scanning) to reduce the risk of placental damage.

We feel it is important to extend to the mother in advance an adequate explanation of the programme to be followed and of the technique. One hour before the transfusion she is sedated with Omnopon 1/3 gr. (22 mg.) and scopolamine 1/120 gr. (0.5 mg.) and is then transferred to the x-ray department, where the operation is carried out under local anaesthesia. By using an image intensifier and television screen radiation is kept to a minimum and a Videotape recorder allows playback for reassessment without adding to screening time. The detailed steps are as follows:

(1) We find it a valuable aid, especially for the earlier transfusions—that is, at 24 and 26 weeks' gestation—to take a flat x-ray picture, by means of an under-couch tube, of the mother's abdomen with a marker on the umbilicus, when she is positioned for the transfusion. Within five minutes, after automatic processing, the dry film can be placed over the abdomen like a map, helping accurate palpation of a small foetus and enabling site and direction of puncture to be marked on the skin.

(2) With full aseptic technique, and after local anaesthesia, the Tuohy needle is introduced into the amniotic sac and a specimen of liquor is taken. The needle is then advanced until the foetal peritoneal cavity is entered.

(3) To ensure that the needle is not in solid tissue 1 ml. of saline is injected, then 2–5 ml. of Hypaque 45% (sodium diatrizoate) is injected. Sometimes the classical pattern of demilunes is seen, confirming the correct siting of the needle, but we have found the outline of the foetal diaphragm to be more helpful, though it often takes longer to develop.

(4) When we feel certain that the peritoneal cavity has been entered, a fine epidural catheter is introduced through the Tuohy needle and the latter is withdrawn. Before any transfusion aspiration is carried out to remove as much of the radiopaque material as possible, but also to remove any ascites or residual blood that may be present. Ascitic fluid, being clear and bright yellow, can usually be distinguished from liquor, which tends to be paler and cloudy. If necessary the nature of the fluid is confirmed by estimating the protein content by a sulphosalicylic acid method.

(5) A three-way tap is connected to the epidural catheter and donor blood, which is connected to the tap by a Baxter disposable giving set, can be drawn into a 10-ml. syringe and slowly injected into the foetus. Because concentrated red cells are used and the catheter is fine, we have found it necessary to compress the syringe by means of a modified screw clamp. The closed circuit minimizes risk of infection.

(6) Liley (1963) originally recommended injection of 100 ml. of blood, but we attributed three deaths, at 26 weeks' gestation, which occurred shortly after the procedure to the injection of too large a volume, and have now found the following routine more satisfactory: 24 weeks 30 ml., 26 weeks 45 ml., 28 weeks 60 ml., 30 weeks 80 ml., 32 weeks and later 100 ml. Approximately five minutes is taken to inject 10 ml. of blood.

(7) On completion of the transfusion 50,000 units of crystalline penicillin and 100 mg. of streptomycin mixture in 2 ml. is injected

down the catheter and into the needle track as the catheter is withdrawn. We do not undertake routine antibiotic administration to the mother subsequently, and we have not as yet left catheters in situ between transfusions. No case of infection occurred.

Technique has been kept as simple as possible, and we have not found it necessary to inject radiopaque substance into the liquor in order that it may be swallowed to outline the foetal alimentary tract; nor do we think it wise to inject dye into foetal soft tissues to act as a marker.

We have not adopted Liggins's (1966) method of using a second needle to impale and steady the foetus during puncture of the foetal abdomen.

Selection of Blood for Intrauterine Transfusion

Appreciating that erythrocytes might be damaged by injecting through a fine catheter and by contact with radiopaque dyes, two preliminary experiments were carried out:

(1) Both time-expired and fresh blood concentrated to have a haematocrit of 80% was injected through the catheter at rates varying from 30 seconds to 10 minutes per 10 ml. The injected blood was then mixed with an equal volume of saline, and after centrifugation haemolysis in the supernatant was measured. Significant haemolysis occurred at all rates exceeding three minutes per 10-ml. injection. The potassium levels predictably were higher in rapidly injected blood, being on average 9 mEq when injected at the rate of three to seven minutes per 10 ml., compared with 18.4 mEq at 30 to 45 seconds per 10 ml.

(2) The blood having been injected through the catheter was mixed with radiopaque dyes in varying dilutions, and incubated at 37° C. for 2, 12, 24, and 72 hours. The amount of haemolysis in the mixture was estimated and the sample examined for spontaneous agglutination and assessed for reliability of ABO grouping. One part dye to 60 of blood was anticipated in the peritoneal cavity at intrauterine transfusion and at this dilution Myodil (iopendylate injection) caused 90% haemolysis in 72 hours and the remaining cells showed abnormal ABO grouping. Neo-Hydriol (iodized oil injection) gave similar results but is not recommended by the makers for intrauterine transfusion. Conray 480 (sodium iothalamate) caused spontaneous agglutination, false ABO grouping, and some haemolysis after as little as two hours' incubation. With Hypaque 45%, however, there was only a small amount of haemolysis even at 72 hours with a 1/60 or 1/30 dilution, but in higher concentration, particularly with Hypaque 66%, agglutination and some haemolysis did occur.

We have therefore used Hypaque 45% in minimal quantity, and before injecting blood have aspirated as much of the dye as possible. Like Liley (1965) we have found little evidence that Hypaque causes serious peritoneal reaction, though in two cases where it was accidentally injected into the thigh pronounced tissue necrosis occurred possibly causing temporary partial femoral artery occlusion in one infant. Deliberate injection of dye into soft tissue should be avoided.

Because delivery was not anticipated for several weeks after transfusion red cells not older than 48 hours have been used. To avoid the theoretical risk of injecting large numbers of viable lymphocytes red cells have been recovered from the bottom of bottles, avoiding the buffy layer, and we have preferred blood collected into acid citrate dextrose rather than into heparin. Concentrated red cells (haematocrit about 80%) minimize risks to the anaemic infant, including the injection of excess potassium or citrate.

Group O cde/cde blood was used for all cases, and care was taken to exclude donors with anti-A or anti-B haemolysins. Full compatibility tests with the mother's serum were performed, and in a number of patients selection has been difficult because of the presence of multiple antibodies.

By taking into account the ABO, Rh, and MNSs groups of the mother and father, it has usually been possible to select blood distinguishable from that of the parents, and sometimes from another donor used for a subsequent transfusion. We have thus, and by the Kleihauer *et al.* (1957) technique, been

able to identify and quantitate donor blood in the foetus at delivery and also in blood that may have escaped into the liquor or been retained in the peritoneal cavity or other sites in the foetus.

Accidents

Accidents with the procedure, despite careful technique, do occur, though these decrease as the operator becomes more experienced. Sites other than the peritoneal cavity may be entered, and in this series of 77 intrauterine transfusions the pleural cavity has been entered on two occasions, the pericardium once, the gastrointestinal tract twice, and the bladder three times. In no instance did this appear to cause any immediate trouble, and six of these eight infants were subsequently born alive with no apparent sequelae.

On one occasion we think the liver was punctured, and on resiting the needle in the peritoneal cavity 25 ml. of foetal blood was aspirated previous to the intrauterine transfusion. The infant was born 10 days later and survived. There was a puncture wound over the liver with extensive skin bruising. Extensive haemorrhage from the liver has been described (Gordon *et al.*, 1966), and may prove fatal.

On one occasion the spleen was probably entered, and though the foetus was stillborn it did not appear that the accident was responsible for the intrauterine death.

On seven occasions a small amount of foetal blood was obtained at the time of intrauterine transfusion, but only on the one occasion referred to did it exceed 1 ml.

The possibility that injection of blood into the peritoneal cavity might lead to adhesions and subsequent intestinal obstruction would seem plausible, and in two infants born alive after intrauterine transfusion there was evidence of partial intestinal obstruction in the neonatal period, but this responded to conservative treatment and did not result in permanent sequelae. In one stillborn foetus small adhesions between loops of bowel were shown at necropsy.

In three instances large collections—up to 50 ml.—of donor blood have been found in the musculature of the abdominal wall, which may have resulted from leakage from the peritoneal cavity, foetal bleeding, or because of the oedematous state of the foetus the injection being actually made into the abdominal wall.

Results in 1965

Though eight cases were selected for intrauterine transfusion, in one case the procedure was withheld because of a steadily falling liquor ratio after the 24th week, and an Rh-negative infant was born. Ten intrauterine transfusions were performed on the remaining seven patients, four receiving a single transfusion and three receiving two transfusions.

Table I shows 28% survival in the transfused group compared with 66% in those not transfused. The erroneous impression that intrauterine transfusion is of no value was brought about in two ways. The cases selected for intrauterine

TABLE I.—Intrauterine Transfusion 1965 Trial*—Newcastle

	Intrauterine Transfusion	
	Yes	No
Stillborn	4	2
Liveborn haemolytic disease of newborn	1	1
Coombs negative	2	4
	0	2
Total	7 (10 transfusions)	9
Survival	28%	66%

* All patients included where previous history of stillbirth or very severe disease and liquor ratio > 1.1 at 24–32 weeks.

transfusion were, by chance, much more severely affected than those not selected, based on the retrospective observations that the first liquor ratios were higher in the treated group (average ratio 1.37) than in the untreated cases (average ratio 1.18). Also, in the untreated group were the two patients with Rh-negative infants and two infants with only moderate disease. Secondly, early difficulties encountered with the technique probably contributed to some of the deaths in the treated cases. However, valuable information accrued from the trial. Thus experience with the technique seemed to lead to better results, and an important point learnt was that the injection of 100 ml. of packed cells into a small foetus may precipitate death. Further, liquor findings showed that in all cases where a normal or only a moderately affected infant resulted there had been a fall in liquor ratio between the first and second test; whereas almost without exception pregnancies resulting in stillbirth or very severe disease showed an increase in ratio between the two tests.

That a normal infant may be associated with a high liquor ratio in early pregnancy is illustrated in Fig. 1, which shows cases resulting in Rh-negative infants and where at least three observations were carried out. In normal pregnancy the liquor ratio before 24 weeks may exceed 1.1; up to 30 weeks it may exceed 1.06, but after 33/34 weeks the ratio is usually below 1.04.

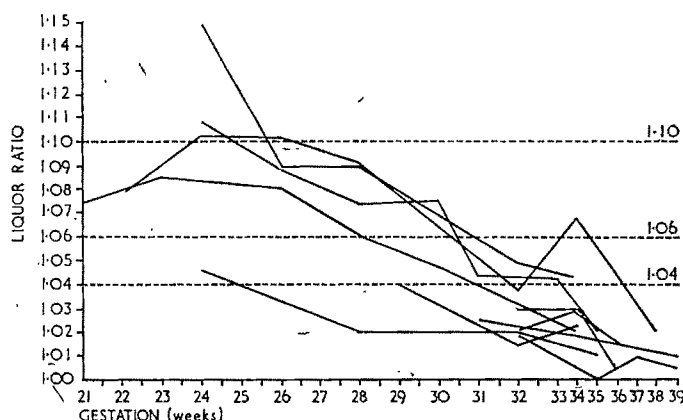


FIG. 1.—Repeated liquor examinations in Rh-negative pregnancies.

Results in 1966

The 28 patients selected under the revised criteria received 67 intrauterine transfusions (Table II). The overall survival rate was 54%. In 9 of the 11 stillborn cases death occurred very shortly after the first intrauterine transfusion, and in each case ascites had been detected at the transfusion. However, ascites was also present on at least one occasion in 12 of the 16 liveborn infants. Two of these infants had ascites tapped on two occasions, one on three, and one infant on no fewer than four occasions, a total of 160 ml. being removed. This infant was not hydropic at birth and survived.

TABLE II.—Intrauterine Transfusion 1966—Newcastle

Stillborn	11	10 with ascites found at I.U.T.
Liveborn haemolytic disease of newborn	2 (1)	12 with ascites found at I.U.T.
Coombs negative	14 (4)	1 (1)
Total	28 (67 transfusions)	
Survival	54%	

Numbers in parentheses are of cases where first transfusion was after 31 weeks.

Only six of the patients were selected for intrauterine transfusion after 30 weeks' gestation, and of particular interest is one infant who at operation had 110 ml. of ascites withdrawn before transfusion was carried out. Ten days later the infant was born alive; no donor cells were detected in the circulation; the cord haemoglobin was 38%, and though the infant had generalized oedema no significant ascites was present.

The one Rh-negative foetus transfused was wrongly selected, but it is probable that the calculated E.D.D. was incorrect and that liquor examination had been at 28 rather than at 32 weeks' gestation; allowance for this would have excluded selection. At birth the cord haemoglobin was 140% and 50% of the cord cells were donor cells. The infant (weight 4 lb. 6 oz.; 1,980 g.) developed hyperbilirubinaemia of prematurity requiring exchange transfusion, also respiratory distress, but survived.

Sixteen of the 17 patients producing liveborn infants in 1966 had labour induced between 35 and 37 weeks' gestation. One patient came into spontaneous premature labour at 35 weeks—16 days after the last (fourth) intrauterine transfusion. In the

haemoglobin value in unselected cases of haemolytic disease is 100%. We failed to rationalize the amount of donor blood present at birth, even taking into account the size of the foetus and the number of donor cells injected, and allowing for estimated red cell survival. While this probably represented a failure of absorption in certain cases, several times donor blood has been recovered from the liquor. We think that occasionally a leakage back from the foetal peritoneal cavity occurs.

Eight infants were severely affected and treated within half an hour of birth, one having a cord haemoglobin of 18%, all of which was donor blood. Nine infants were moderately affected and were treated within nine hours and two, though



FIG. 2.—Direct Coombs test on (1) weakly Coombs positive infant; (2) strongly Coombs positive infant; and (3) infants after intrauterine transfusions with 20% foetal cells.

present series only one patient (3.6%) went into premature labour as a result of the procedure. In this case there was technical difficulty with the third intrauterine transfusion; the foetal bowel was entered, and when the catheter was finally properly sited, the needle having been removed, it was found to be blocked. The procedure was then abandoned. The next day the foetal heart was absent, and two days later labour began and a stillborn macerated infant was delivered.

During 1966 a further 19 patients were considered but not selected for intrauterine transfusion. In six the foetus had already died by 24 weeks' gestation. Of the remaining 13, excluded on liquor examination, five infants were Rh-negative and five were born alive between 36 and 42 weeks. Three were stillborn, two from causes other than haemolytic disease (one with placental insufficiency and cord prolapse, the other was an intrauterine death showing no obvious cause). The third stillbirth occurred where the mother's serum contained multiple antibodies (anti-D, anti-A₁, anti-Fy^a, anti-E, and a weak unspecified antibody). Though compatible blood for mother or infant was eventually found, it was thought expedient to reserve this for this time of delivery.

Severity of Disease in the Liveborn Infant

Nineteen affected infants were born alive after intrauterine transfusions. Some of the infants, owing to the presence of almost 100% Rh-negative donor cells, failed to show a positive direct Coombs test, while others gave a weak result. However, in these latter, where a few Rh-positive foetal cells—for example, 5% of the sample—are coated with a strong antibody, the pattern of Coombs test is quite different from the weak positive test due to many Rh-positive foetal cells being coated with a weak Rh antibody (see Fig. 2).

Cord haemoglobin values varied from 18 to 140%, and the proportions of adult and foetal blood are shown in Fig. 3.

It will be seen that the donor blood contribution to the cord haemoglobin at birth varied from 0 to 100%. The average cord haemoglobin was 66%, with 40% donor blood and 26% foetal blood. This represents severe disease, for the mean cord

not meeting our criteria for exchange transfusion, required simple transfusion later.

Cord bilirubin levels also indicate increased severity in these infants after intrauterine transfusion, with a range of 1.9 to 7.1 mg., and a mean of 4.2 mg., compared with a mean of 3 mg. in unselected material.

All of these infants were delivered prematurely, usually at about 35 weeks' gestation, and this policy is reflected in the

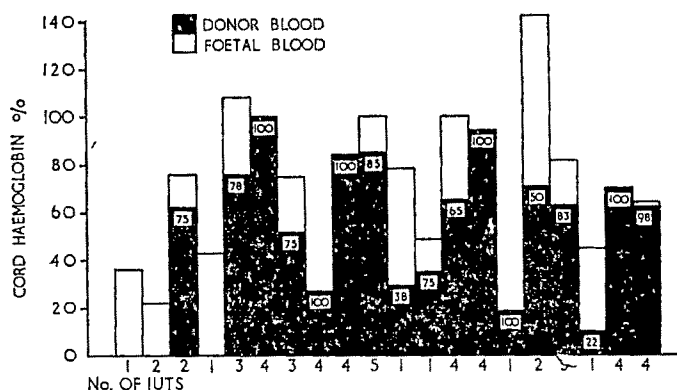


FIG. 3.—Cord haemoglobin values and percentage of donor cells in intrauterine transfusion cases.

birth weights, which ranged from 3 lb. 12 oz. (1,700 g.) to 7 lb. 5 oz. (3,315 g.), with a mean of 5 lb. 4 oz. (2,380 g.). Four infants were delivered by caesarean section because of failed induction, and a further three were delivered by caesarean section for other reasons (placenta praevia, foetal distress, unfavourable cervix). Six infants required resuscitation, though in only two was there prolonged difficulty in establishing respiration. Five infants developed respiratory distress, which was severe in two.

Six infants required two exchange transfusions, while one required four. We did not find, as has been reported in the literature (Bowman, 1966; Work *et al.*, 1966), that exchange transfusion was required frequently in cases treated by intra-

uterine transfusion. In such reports, however, many patients came into premature labour shortly after intrauterine transfusion, and possibly continued absorption, after birth, of donor cells from the peritoneal cavity aggravated the hyperbilirubinaemia (Fong, 1966):

Simple transfusion was required in 10 cases, a much higher incidence than in haemolytic disease of similar severity not treated by intrauterine transfusion. The prolonged anaemia may be due to depression of the bone marrow consequent on intrauterine transfusion. One infant with a cord haemoglobin of 28%, nearly all of which was donor blood, had a reticulocyte count of only 1%; and another with a cord haemoglobin of 18%, all donor blood, had a reticulocyte count of only 2%. One infant, who after five intrauterine transfusions required two simple transfusions, did not show an appreciable reticulocytosis until 14 weeks of life, and the Rh-negative infant, incorrectly selected, had a cord haemoglobin value of 140%, but the haemoglobin value in infant's cells was only 70%.

Three infants died. The cord haemoglobin values were 18%, 21%, and 26%. Cardiac arrest at the start of a second exchange transfusion was responsible in one case, pulmonary haemorrhage at 18 hours in another, and pulmonary haemorrhage and kernicterus on the fourth day in the third infant.

All surviving infants have been followed up at three-monthly intervals. At the time of writing the eldest was 18 months and the youngest 5 months. Developmental milestones, weight gain, and physical examination were normal in all but two. These exceptions are:

(1) An infant with severe haemolytic disease, heart failure, thrombocytopenia, and mild respiratory distress who was noticed to have a patent ductus arteriosus. At 6 months the ductus was still patent, and, though developmentally and physically normal, he was underweight.

(2) An infant with a cord haemoglobin of 38% with no donor cells demonstrable at birth suffered very severe respiratory distress, requiring 90% oxygen for 12 days with dextrose and intravenous nikethamide. At 1 year he was somewhat retarded and there was radiological evidence suggesting cerebral atrophy.

Congenital abnormalities were not a feature as in some reported series (Charles *et al.*, 1966). The only congenital defects observed, apart from the patent ductus, were two cases of squint. There have been no cases of deafness, even on audiometric examination, and there was no increase in the incidence of infection (Gordon *et al.*, 1966). Apart from the partial intestinal obstruction and partial femoral artery occlusion mentioned earlier, no complications in this series were attributable to the technique of intrauterine transfusion.

Discussion

Previous to any consideration of intrauterine transfusion it is well to remember that with conservative treatment 80% of all cases of Rh-isoinmunization will result in a living infant. In first affected pregnancies 90% will result in surviving infants.

Stillbirth occurs in 15% of cases overall and 50% of the stillbirths occur before 35 weeks' gestation. Those occurring late in pregnancy, if able to be identified, could be prevented by premature induction, but for those occurring early in pregnancy only intrauterine transfusion offers some prospect of help. The difficulties and dangers of the procedure, however, call for the most accurate possible selection of patients. In all published series the final selection has been based on liquor examination, but this necessitates amniocentesis, which is potentially dangerous. The majority of patients in whom early intrauterine death occurs are in the 10% of those who have a history of previous stillbirth or very severe disease. For these patients we recommend amniocentesis as early as 20 weeks' gestation. This is repeated, with or without intrauterine transfusion, at intervals of two to three weeks throughout pregnancy.

It should be remembered that the neonatal mortality in infants with severe haemolytic disease induced at 32 weeks is as high as 40%, compared with 20% in those induced at 35 weeks and 2% at term. Practically, intrauterine transfusion has done away with the need to carry out premature induction at 32 weeks, but though theoretically it should obviate entirely the need for premature induction in Rh-isoinmunization most workers still prefer, in the present state of knowledge, to induce labour when they think that the risks of prematurity are no longer overwhelming.

A second group of patients suitable for intrauterine transfusion can also be identified. We advocate amniocentesis at 32 weeks when a previous infant has been severely enough affected as to require any form of treatment. In this second group only one intrauterine transfusion should be needed. Subsequent refinements may select a small proportion of this group where amniocentesis earlier in pregnancy could be justified.

Because liquor bilirubin levels fall as pregnancy advances and because levels can be quite high at early stages of gestation even in normal pregnancy, very careful interpretation of the liquor results is necessary and there is need for accurate assessment of the stage of gestation (Walker, 1967). Our present criteria of bilirubin levels in liquor appear to be relatively satisfactory. We now carry out "early" intrauterine transfusion only if two consecutive values are higher than 1.1 and preferably showing a rise. However, in cases where the initial amniocentesis is made at 32 weeks intrauterine transfusion is performed if the ratio at that time exceeds 1.1.

The difficulties of the technique of intrauterine transfusion and the accidents that can occur have been covered in this report, but some points require special emphasis. We believe that the amount of blood injected, particularly into a small foetus, is important. Theoretically, exchange transfusion in utero (Adamsons, 1966) should be safer, but the greater dangers involved must restrict its use, and its contribution to the problem of intrauterine death can only be minimal. Liley (1964) originally regarded the presence of ascites as a contraindication to intrauterine transfusion, but 12 of our survivors had ascites removed on at least one occasion and Bowman (1966) has also reported survival in similar circumstances. It is desirable to avoid injecting large numbers of lymphocytes at intrauterine transfusion, for it appears that immunologically competent lymphocytes may occasionally colonize the reticuloendothelial system and produce complications (Cohen *et al.*, 1965; Kadowaki *et al.*, 1965; Githens, 1966; Naiman *et al.*, 1966).

Of course the later in pregnancy that patients are selected for intrauterine transfusion the better the results will appear; for not only is the operation technically more simple at later gestations but many of the very severe cases where intrauterine transfusion is especially applicable will already have resulted in stillbirth. In our 1966 series 21 cases initially treated before 30 weeks' gestation resulted in 11 stillbirths and 10 live births, whereas all seven treated after 30 weeks' resulted in live births. This point should be considered when evaluating published series.

In Table III we have summarized the three large English series. Though overall the survival rates were similar, the first point of difference is the time at which the initial intrauterine transfusion was carried out. Thus 75% of Newcastle cases were treated before 30 weeks' gestation, compared with 60%

TABLE III.—Time of Intrauterine Transfusion and Survival in Three Reported English Series

Gestation at First I.U.T.	Karnicki and Holman (1966) Lewisham		Gordon <i>et al.</i> (1966) Hammersmith		Present Series. Newcastle, 1966	
	Total	Survived	Total	Survived	Total	Survived
Before 30 weeks ..	19	3 (15.8%)	12	4 (33.3%)	21	9 (42.9%)
After 30 " ..	35	24 (68.6%)	8	6 (75%)	7	6 (85.7%)
All cases ..	54	27 (50%)	20	10 (50%)	28	15 (53.6%)

of Hammersmith cases and only 35% in the Lewisham series. The survival rate with these early transfusions was 43% in the Newcastle cases, 33% in the Hammersmith cases, and 16% in the Lewisham cases, but in each of the series the mortality rate was much higher in those cases treated before 30 weeks' gestation than in those treated later (with 70–85% survival).

Another point of difference was the onset of premature labour after intrauterine transfusion. This occurred within nine days of operation in 4% of the Newcastle cases, in 24% of the Lewisham cases, but in 65% of the Hammersmith cases. The reason for the difference is unknown but may be related to trauma or to leaving the catheter in situ between transfusions. Obviously if labour occurs early in pregnancy survival is jeopardized, and if later it is doubtful whether the foetus can have benefited significantly from the intrauterine transfusion. Indeed if large quantities of donor blood are still present in the peritoneal cavity after birth, continued absorption may contribute to the development of hyperbilirubinaemia (Fong, 1966).

Allowing for the severity of haemolytic disease and the degree of prematurity in the infants after intrauterine transfusion, we have not found particular problems in management except in one respect. The reticulocyte count on cord blood is often much lower than one would expect in relation to the haemoglobin level, and this erythroid hypoplasia persists longer and simple transfusion is required more often. Long-term follow-up, however, does not suggest any permanent defect. The leucocyte and platelet counts were not abnormal though increases in certain immunoglobulins have been noted (to be published). In the follow up of these cases, however, there has proved to be no difference in infection rates.

Though some of the deaths occurring immediately after intrauterine transfusion may have been due to technical difficulties, and certainly such cases have been recorded (Gordon *et al.*, 1966), no permanent sequelae have resulted in our surviving infants.

As regards neonatal death after intrauterine transfusion, we find that 3 out of 20 (15%) in Newcastle died, compared with 6 out of 16 (37%) at Hammersmith and 9 out of 36 (25%) at Lewisham. Perhaps comparisons of later series will produce more equitable results, but meanwhile the combined English series compares favourably with results from series in the rest of the world—up to February 1967 291 patients receiving 507 intrauterine transfusions with 118 (41%) infants surviving.

Provided that it is recognized that this procedure is not the panacea to prevent all Rh-stillbirths and that there is still difficulty in selecting the most suitable cases, there seems little doubt that, in spite of its hazards, intrauterine transfusion has a select and important part to play in the management of some cases of Rh-haemolytic disease of the newborn

“diseases desperate grown
By desperate appliance are reliev'd,
Or not at all.”—*Hamlet*, IV, iii, 9.

Summary

The criteria for selection of patients for intrauterine transfusion are discussed and experience with the procedure in 1965 and 1966 in the Newcastle upon Tyne hospitals is presented. Thirty-five foetuses received a total of 77 intrauterine transfusions, and 19 were born alive; 16 survived. It is concluded that in spite of the hazards intrauterine transfusion has a select and important part to play in the management of some cases of Rh-haemolytic disease.

We would like to thank our obstetric colleagues in the area who kindly referred patients to us. We would also like to record our appreciation of the considerable part played in this work by medical and nursing staffs of the Princess Mary Maternity Hospital and the Newcastle General Hospital, the staffs of the radiological departments at Newcastle General Hospital and the Royal Victoria Infirmary, and the staffs of the Regional Blood Transfusion Service and the Attic Laboratory. Without the co-operation of this team of people the studies described could not have been undertaken.

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Skin Water Loss and Accidental Hypothermia in Psoriasis, Ichthyosis, and Erythroderma

KATHERINE A. GRICE,* M.B., B.S., D.C.H.; F. R. BETTLEY,* M.D., F.R.C.P.

Brit. med. J., 1967, 4, 195-198

Accidental hypothermia has been reported in patients with generalized eczema and other erythrodermas, the aetiology of the hypothermia being said to be obscure (Krook, 1960; Magnusson, 1960); rectal temperatures as low as 83-86° F. (28.3-30° C.) have been described. It has been suggested that hypothermia is related to the increased peripheral blood flow (Mali, 1952; Fox *et al.*, 1965). It has also been suggested that the heat loss in erythroderma is due to vaporization of water lost from affected skin, in these conditions the skin water loss being enormously increased (Zoon and Mali, 1957).

Hancock *et al.* (1929) pointed out that there are two kinds of water loss from the skin. The first is from sweating, the second from evaporation of water which has passed by diffusion through the epidermis, the corneous layer and its base behaving as a semipermeable membrane. The water loss by diffusion was designated by Rothman (1954) the transepidermal water loss.

The term "insensible perspiration" has been applied to the skin water loss, which is invisible to the naked eye, the sweat droplets evaporating as soon as they reach the skin surface (Jurgensen, 1924).

Few previous studies of the skin water loss have been done after inhibiting sweating, a satisfactory method for producing complete inhibition of sweating not hitherto being available.

In observations now reported the transepidermal water loss was measured in normal subjects and in patients with erythroderma, psoriasis, and ichthyosis.

Methods and Materials

The transepidermal water loss from normal skin was measured in 40 subjects after sweating had been inhibited with poldine. The apparatus and method have been described in detail previously (Bettley and Grice, 1965).

The apparatus, which estimates the total cutaneous loss from selected areas of the skin, consists of a collecting chamber placed on the abdomen, and dry air is passed over the skin. The amount of water is determined gravimetrically. Sweating is inhibited by the local application of poldine methosulphate (Nacton) (Grice and Bettley, 1966). The area of skin to be tested is marked out, painted with two or three coats of 2% poldine in alcohol, and covered with polyethylene, the edges being sealed. Next day the polyethylene is removed and the abdomen washed with soap and water; 4 to 24 hours later the transepidermal loss is measured.

The apparatus incorporates a thermistor for measuring skin temperature, and the presence of sweating is ascertained by the galvanic conductivity of the skin. The relative humidity in the collecting chamber was calculated from the measured skin water loss (mg./60 sq. cm./30 min.) contained in the total volume of air passing through the collecting chamber in 30 minutes (ml./30 min.) and the weight of water contained in saturated air at the air temperature in the collecting chamber. This was about 1-2° C. lower than the skin temperature.

* Institute of Clinical Research, Middlesex Hospital, London W.1.

The experiments were performed while the patients were at rest or sleeping, and the room temperature and humidity regulated so that sweating was minimal. The test lasted 30 minutes. During this period the presence of sweating on other parts of the trunk and limbs was ascertained by measuring the galvanic skin resistance and testing by the iodine-starch method (Wada and Takagaki, 1948; Wada, 1950).

Ichthyosis.—The transepidermal water loss was measured after inhibiting sweating with 2% poldine under occlusion in nine subjects. Seven had the sex-linked form of ichthyosis and two the autosomal dominant form (Wells, 1966).

Psoriasis and Erythroderma.—The transepidermal water loss was measured in areas of skin affected by localized psoriasis in eight patients and in six cases of erythroderma, five of the latter were psoriatics. In all these cases the skin was painted with 1% poldine and allowed to dry for 30 minutes. No further application was made to the skin. The next day the transepidermal water loss was estimated. In order to avoid irritating the skin polyethylene occlusion and adhesive plaster were not used. In four cases repeated measurements were made at various stages of activity of the disease. In two cases the water loss was measured in areas which had not been treated with poldine and compared with the treated areas. A total of 16 measurements of skin water loss were made in all. Owing to the enormous skin water loss that was found in these cases a slight variation was necessary. In normal subjects, after the transepidermal water loss was measured, no measurable condensation was found to take place in the apparatus. Appreciable condensation on the walls of the apparatus was found, however, to have occurred after measuring the skin water loss in cases of psoriasis and erythroderma. To allow for this the following method was used:

The apparatus was as usual washed out with dry air before starting. The collecting chamber was then placed on the abdomen and straight away the water given off by the skin was collected. A steady state as indicated by the humidity transducer was reached in one to two minutes. As soon as the 30-minute collecting period had come to an end, the collecting chamber was removed from the skin and the air flow turned off. An airtight base was fitted to the collecting chamber and the apparatus reconnected to another water tap. Dry air flow was then passed through the apparatus for 30 minutes, or until no further moisture could be obtained. (The monitoring of the humidity transducer was found to be a useful guide to the rate of drying of the apparatus.) The weight of water thus collected from the apparatus was added to that obtained during the 30-minute skin water loss estimation.

Normal Skin Areas in Eczema and Psoriasis.—After inhibiting sweating with poldine under occlusion the transepidermal water loss was measured in areas of normal skin in patients with eczema and psoriasis.

Results

Normal Transepidermal Water Loss

The water loss by diffusion through normal skin was remarkably small. This was in spite of a very low ambient humidity and free air movement.

The mean transepidermal water loss in 47 normal subjects was 0.35 (S.D. 0.09) mg./sq. cm./hr. (skin temperature 32–36° C., relative humidity 2–5%, air speed 23–25 mm./sec.).

No significant correlation was found with age (39 subjects). (Correlation coefficient, -0.22 ; 95% confidence limits for the population correlation coefficient are -0.5 to $+0.13$.)

The "maximal" possible whole-body daily transepidermal water loss may be estimated from the measured rate of transepidermal loss (mg./sq. cm./24 hr.) and the total surface area (Du Bois formula). The results in 29 patients are seen in Fig. 3. The ambient humidity in the collecting chamber was very dry (2–5% relative humidity); the results are therefore higher than would be expected under ordinary room conditions, since the rate of transepidermal water loss decreases with rising ambient humidity. The total actual daily loss will depend on the humidity of the air in direct contact with the skin, which depends on room humidity, the presence of sweating, and the effect of clothing.

The transepidermal water loss also increases with rising skin temperature. The temperatures during the measurements were those of "covered skin," the skin temperature under the collecting chamber being 1–2° C. higher than the adjacent uncovered areas. The transepidermal water loss from the calf and thigh was measured in a few cases, and, though significantly raised, was of the same order as that from the abdomen.

The transepidermal water loss from the calf in five subjects was 0.6 (S.D. 0.12) mg./sq. cm./hr. ($t=4.6$, $P<0.01$). The transepidermal water loss from the thigh in seven subjects was 0.46 (S.D. 0.14) mg./sq. cm./hr. ($t=2.3$, $0.05>P>0.01$).

The mean estimated daily transepidermal water loss in 19 normal subjects was 151 (S.D. 44.2) ml./day, range 63–280 ml./day.

The heat loss by evaporation of 1,000 ml. of water is 580 kilocalories. The daily heat loss from evaporation of the normal maximal transepidermal water loss is therefore 87 (S.D. 25) kcal.

Ichthyosis

The results are set out in Fig. 1. The mean transepidermal water loss was found to be 0.71 (S.D. 0.29) mg./sq. cm./hr.

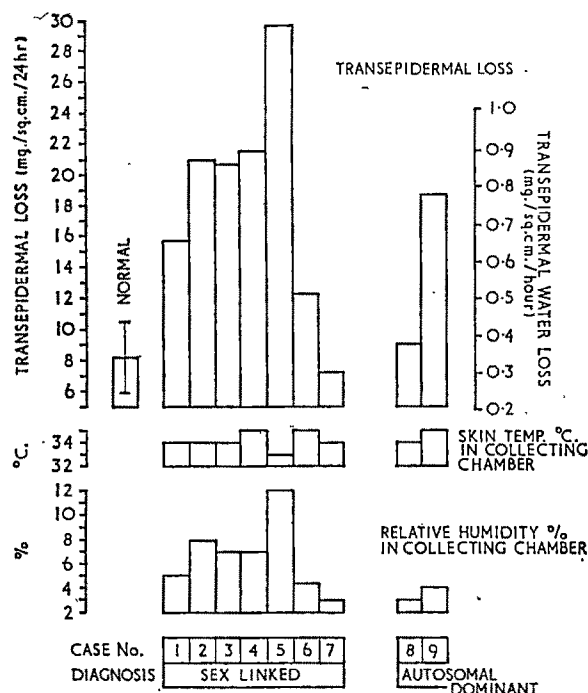


FIG. 1.—Ichthyosis. Transepidermal water loss compared with normal.

(skin temperature 32–35° C., relative humidity 2–12%). This was highly significantly greater than normal, though in three cases the transepidermal loss was normal ($t=3.9$, $P<0.01$).

On routine testing of sweating from the rest of the trunk and limbs the findings were of some interest. Sweating from the trunk and limbs was strikingly less than normal, while sweating from the areas of "constant emotive sweating" was normal in eight of the nine cases. These areas of emotional sweating are the axillae, face, palms, soles (Kuno, 1956), and over the distal dorsal phalanges and back of the interdigital webs (Grice and Bettley, 1966).

Only one patient had tylosis of the palms and soles (Case 9, Fig. 1), and she had normal palmar and plantar sweating. One patient (Case 6, aged 35) had remarkably little palmar and periungual sweating.

Sweating could not be detected on the trunk and limbs (apart from the emotive areas) in eight of the nine cases (Nos. 1–7 and 9). The room temperature and relative humidity were 20–23.5° C. and 52–66% respectively. The skin temperatures were 34–35° C.

To exclude the possibility that slight sweating was taking place in areas of skin in which sweating could not be detected by the iodine-starch or galvanic skin resistance test, six further measurements of skin water loss were made. Skin untreated with poldine was compared in the same patients with sweat-inhibited areas. The water loss was found to be the same in the two areas. On heating, sweating occurred from the trunk and limbs.

The maximal whole-body daily transepidermal water loss in six subjects was estimated (see Fig. 3). The mean was 348 (S.D. 124) ml./day (skin temperature 32–35° C., relative humidity 2–12%). The maximal daily whole-body transepidermal water loss was therefore about double that of normal subjects. Under ordinary environmental conditions the actual transepidermal water loss will probably be nearer the maximal than in the normal subjects. The reasons for this are, firstly, that in the cases with ichthyosis there was a higher ambient humidity (resulting from the increased skin water loss) in the collecting chamber, and, secondly, under normal conditions, as sweating is depressed in ichthyotics, the ambient humidity over the skin

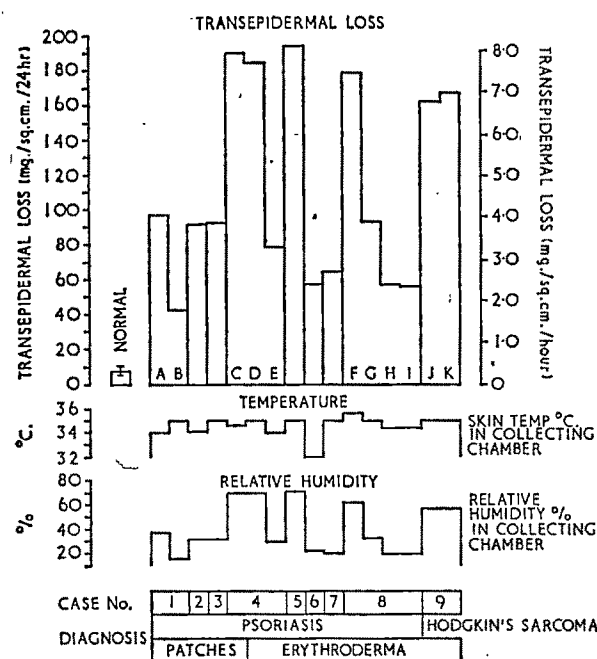


FIG. 2.—Psoriasis and erythroderma. Transepidermal water loss compared with normal. Case 1: B, 7 days after A. Case 4: D, 12 days after C; E, 22 days after C. Case 8: G, 10 days after F; H, 12 days after F; I, 12 days after F, different site from H. Case 9: K, same day, different site, no pretreatment with sweat-depressing agent.

is likely to be less than in a normal person. In normal subjects the relative humidity under a shirt has been shown (Mellanby, 1932) to vary widely between 20 and 70%.

Psoriasis and Erythroderma

The transepidermal water loss in psoriasis and erythroderma was greatly increased. This was in spite of high ambient humidities which resulted from the high skin water loss. The highest ambient humidities were produced in the cases with the greatest skin water loss (see Fig. 2).

The mean transepidermal water loss over patches of psoriasis in eight patients was 5.37 (S.D. 2.6) mg./sq. cm./hr. (skin temperature 34–35° C., relative humidity 10–70%).

When the psoriasis spread and became generalized in one patient with very active pustular lesions (Case 4, Fig. 2) the transepidermal water loss (D) was found to be little changed from the previous measurement over a patch (C). Three weeks later, when the eruption was still generalized but less active, the transepidermal water loss had decreased from 7.7 to 3.2 mg./sq. cm./hr. (Case 4, D and E).

Erythroderma

The mean transepidermal water loss of nine measurements in six cases was 4.96 (S.D. 2.5) mg./sq. cm./hr. (skin temperature 32–35.5° C., relative humidity 20–70%).

The water loss from skin untreated with poldine (Fig. 2, Case 8 I, Case 9 K) was compared in two patients with the transepidermal water loss after sweat inhibition. The water loss can be seen to be similar.

The mean daily whole-body transepidermal water loss in subjects with erythroderma, estimated from six measurements taken at different stages of the disease (see Fig. 3) was 2,158

The total daily loss of heat from evaporation of this transepidermal water is estimated to be 1,252 (S.D. 591) kcal./day.

Transepidermal Water Loss in Normal Skin Areas in Patients with Eczema and Psoriasis

In 17 cases of eczema the mean transepidermal water loss in unaffected skin areas which had never been affected was 0.55 (S.D. 0.15) mg./sq. cm./hr. (skin temperature 32–36° C., relative humidity 5–10%).

The transepidermal water loss is highly significantly greater in areas of normal skin in patients with eczema compared with normal subjects ($t=5.2$, $P<0.01$). The mean transepidermal water loss in unaffected skin areas in 16 cases of psoriasis was 0.41 (S.D. 0.16) mg./sq. cm./hr. (skin temperature 32.5–35° C., relative humidity 5–8%). This was not significantly different from normal ($t=1.8$, $P>0.05$).

Discussion

The present studies show that the loss of water by diffusion through normal skin is remarkably small, 0.35 (S.D. 0.09) mg./sq. cm./hr. This is well known, though in most previous studies of skin water loss sweating was not inhibited. Pinson (1942) found, under conditions similar to those in the present investigation, that the transepidermal water loss was 0.58–1.58 mg./sq. cm./hr. He, however, used the iontophoresis of formalin to inhibit sweating, and iontophoresis may increase the skin permeability (Rothman, 1954). Pinson's results then would be higher than expected. The rate of water diffusion through excised trunk skin is said to be 0.25–0.58 mg./sq. cm./hr. (Mali, 1956; Onken and Moyer, 1963).

In spite of a very low ambient humidity, free air flow, and skin temperature similar to that under clothes, the estimated whole-body daily transepidermal water loss was only 151 (S.D. 44.2) ml./day.

A study of skin affected by psoriasis and erythroderma has shown the transepidermal water loss to be enormously increased; this in spite of very high ambient humidities comparable with those of the clothed skin. This increase of skin water loss, which amounted to over 20 times normal in some cases, was in spite of sweating having been inhibited. A ten-fold increase in the skin water loss was reported in psoriasis and exfoliative dermatitis (Felsher and Rothman, 1945), and a sixteenfold increase in burns on the third day (Cohen, 1966). The apparatus used by Felsher and Rothman was a glass collecting chamber in which was suspended a bag filled with calcium chloride.

The daily whole-body transepidermal water loss in erythroderma was estimated to amount to 2,518 (S.D. 1,019) ml./day, being therefore 10 to 20 times normal. The daily insensible skin water loss in erythroderma, measured by weighing patients, was found by Zoon and Mali (1957) to be 1,183 to 2,370 ml./day. This included weight loss from sweating. Sweating is, however, known to be depressed in erythroderma, eczema (Cormia and Kuykendall, 1955), and psoriasis (Suskind, 1954). The total daily skin water loss in erythroderma may therefore well consist largely of the transepidermal water loss.

Complete sweat-duct blockage persisting after heating and methacholine stimulation has been described in erythroderma (Cormia and Kuykendall, 1955) and acute psoriasis (Mitchell and Forstner, 1962). In the present investigation in two of the cases of erythroderma (due to psoriasis and Hodgkin's sarcoma) the skin water loss was found to be the same whether or not sweating had been inhibited.

On the other hand, sweating had been observed in erythroderma during heating (Fox *et al.*, 1965), and in the present investigation palmar sweating was found to be present in

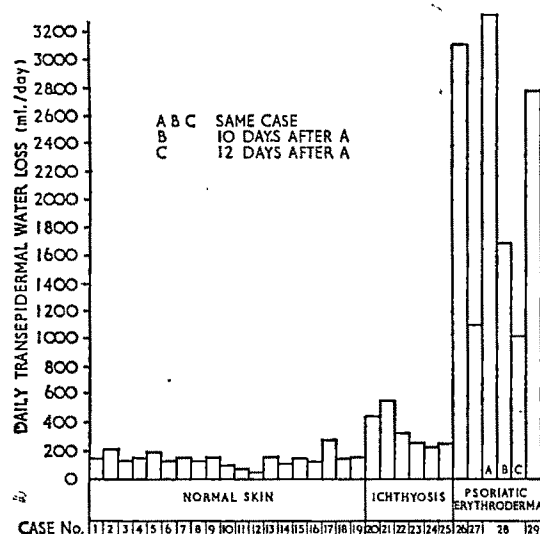


FIG. 3.—Daily transepidermal water loss in normal skin, ichthyosis, and psoriatic erythroderma.

(S.D. 1,019) ml./day (skin temperature 32–36° C., relative humidity 16–72%). The transepidermal water loss is therefore about 10 to 20 times normal.

The ambient humidity in the collecting chamber was very high, the highest water loss resulting in an ambient humidity of as much as 72% (see Fig. 2). Under normal conditions, therefore, the actual daily transepidermal water loss in erythroderma patients may well be nearly as high as that estimated.

The covering of skin with ointments which form an occlusive film will obviously decrease the skin water loss, and under normal conditions there will not be such a free air flow.

pustular psoriasis after the acute anhidrotic phase of the disease. In the cases where sweat-duct blockage is not complete there may be a partial functional depression of the sweat glands.

It has been suggested that the general state of hydration of the subject might influence the amount of sweat loss (Macpherson, 1960). The large transepidermal water loss with resultant heat loss might equally well influence the amount of sweating in erythroderma.

In normal subjects palmar sweating is constantly present while they are awake (Kuno, 1956); in three patients with erythroderma whose palmar skin was not affected, and had never been affected, palmar sweating we found was greatly depressed.

The increased heat loss, which may amount to 1,252 (S.D. 591) kcal./day from vaporization of the large transepidermal water loss through the skin in erythroderma may also explain the hypothermia which occurs in some of these patients. Mali (1952) showed that there is also increased heat loss from the raised skin temperatures which he found in 83% of the patients with erythroderma. The skin temperatures were about 1° C. higher than normal. In one patient of the present series (Case 4, Fig. 2) with acute pustular psoriasis that was becoming generalized, the skin temperature was 1° C. higher in the affected skin as compared with the adjacent unaffected skin. The heat loss by radiation from 1° C. rise of skin temperature over the whole skin surface is known to be 360 kcal./day (Keele and Neil, 1965).

The raised metabolic rates found in patients with erythroderma (basal metabolic rates +6% to +119%) could be explained by the increased heat loss in these conditions (Mali, 1952). The ¹³¹I excretion has been found to be normal (Magnusson, 1960; Fox *et al.*, 1965).

In the present investigation the transepidermal water loss in ichthyosis was found to be approximately double that of normal subjects. In two of these cases there was a history of atopic eczema (Cases 5 and 9), but both patients were free from eczema at the time of testing (for 23 and 40 years). Trunk and limb sweating was found to be depressed, as reported previously (Wells, 1966), but sweating from the palms, soles, and periungual regions was found to be normal in eight of the nine cases. Sweating from the trunk was present during heating, and in warm climates with increased sweating all the patients noticed an improvement of their skin. The comparative sparing of flexures found in ichthyosis vulgaris could perhaps be associated with the diminution of sweat or transepidermal water evaporation at these sites.

Summary

The transepidermal water loss from the skin, due to the passive diffusion of water through the epidermis, was found to be greatly increased in psoriasis and erythroderma, and slightly but highly significantly increased in ichthyosis.

Improvement of the skin condition showed a corresponding decrease in the water loss.

In 47 normal subjects the mean transepidermal water loss from the abdomen was extremely small: 0.35 (S.D. 0.09) mg./sq. cm./hr. (skin temperature 32–36° C., relative humidity

2–5%); the maximal loss from the whole body in a dry ambient humidity amounting to only 151 (S.D. 44.2) ml./day.

No significant correlation was found with age. A slight but significant regional variation was observed, the loss from the calf and thigh being greater than from the abdomen.

In patches of psoriasis the transepidermal water loss could be as much as 20 times that of normal, 5.37 (S.D. 2.6) mg./sq. cm./hr. (relative humidity 10–70%).

In ichthyosis the loss was about twice the normal, and sweating from the trunk and limbs was markedly reduced, though sweating from the constantly sweating emotional areas (palms, soles, axillae, dorsal distal phalanges, and face) was normal in eight of the nine cases.

In erythroderma the daily transepidermal water loss was about 14 times normal and could be as high as 2,158 (S.D. 1,019) ml./day.

It is suggested the loss of heat by vaporization of the increased transepidermal water loss could explain the hypothermia and increased basal metabolic rates which occur in some cases of erythroderma.

We thank Dr. R. S. Wells for kindly referring his patients; Dr. R. H. Meara for allowing us to study patients under his care; Mr. I. D. Hill, of the Medical Research Council Statistical Research Unit, for his help; the Medical Research Council for a grant to K. A. G.; and the Clinical Research Committee for granting facilities to undertake this work. We also thank the illustration department of the Middlesex Hospital. Poldine methosulphate (Nacton) was kindly provided by Beecham Research Laboratories Ltd.

This paper forms part of a thesis which has been submitted for the M.D. thesis by K. A. G.

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Intracardiac Pacing as Emergency Treatment in Adams-Stokes Syndrome

GUNNAR BAY,* M.D.; EGIL SIVERTSEN,* M.D.

Brit. med. J., 1967, 4, 199-200

In most cases of atrioventricular block with Adams-Stokes attacks the application of either an endocardial or an epicardial electrode for artificial pacing can be performed in the operating-theatre with all necessary equipment available. In some cases, however, the situation is more dramatic: electrical pacing may be necessary without any delay, and it may be impossible to transfer the patient to the operating-theatre or an x-ray laboratory with TV equipment. In such emergency cases we have used a technique which renders it possible to introduce an endocardial pacemaker electrode by means of very simple equipment, and the method which we have applied in 27 cases has proved to be safe and reliable. The principle is to use the pacemaker electrode for picking up the electrocardiogram from the heart cavities. As the electrocardiogram from the atrium

pacemaking is established. The electric defibrillator and the external pacemaker are held in readiness.

Materials

From September 1965 to April 1967 indications for intracardiac pacing were found in 62 patients. Twenty-seven of these were critically ill with repetitive Adams-Stokes attacks, and the emergency introduction of an endocardial pacemaker electrode by the described technique was therefore attempted (see Table). Fifteen of these had acute myocardial infarction. In 21 the electrode was successfully placed in the right ventricle, and effective stimulation of the heart was obtained in all of them. In one patient (Case 1) with sinoatrial block the tip

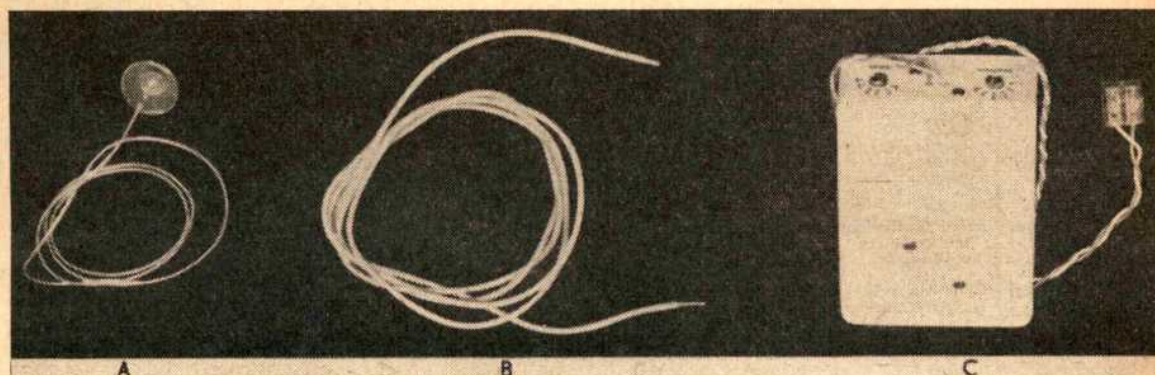


FIG. 1.—A, subcutaneous indifferent electrode. B, soft, flexible intracardiac electrode. C, external pacemaker (Elema-Schönander).

as well as from the ventricle is highly characteristic, the electrocardiographic pattern can easily be used as guide for a correct introduction into the right ventricle without the aid of fluoroscopy.

Method

Under sterile conditions and after cleansing and draping the area an incision is made over the antecubital or jugular vein. A soft flexible intracardiac electrode (Fig. 1) is introduced into the exposed vein and connected to the V terminal of an electrocardiograph by means of a clip. The electrode is then advanced to the right atrium under constant monitoring on oscilloscope or electrocardiograph. When characteristic atrial patterns are seen (Fig. 2), the patient is carefully rotated to the left lateral position to facilitate passage of the electrode through the tricuspid valve. The electrocardiographic patterns change suddenly when the electrode passes into the ventricular cavity. The atrial complexes become small, and the ventricular complexes large with the rS or QS appearance. The electrode is then advanced a further 5-6 cm. to place the tip in the apex region of the right ventricle. At this point typical contact patterns should be seen (Fig. 2). An indifferent electrode is thereafter placed subcutaneously in front of the sternum, and the two electrodes are connected to a battery-driven pacemaker. If the intracardiac electrode is in the correct position, effective stimulation of the heart is gained with an amplitude of 1-2 V.

Intravenous infusion of isoprenaline is started before beginning the procedure, and is continued until satisfactory

of the electrode did not pass into the ventricle, but effective stimulation was obtained from the right atrium. In one patient with atrioventricular block (Case 4) the typical endoventricular complexes were not registered, but, in spite of this, satisfactory stimulation was obtained. This patient died later in cardiac failure, and at necropsy the tip of the electrode was found in the coronary sinus. In four patients introduction of the electrode was unsuccessful: three (Cases 8, 24, and 25) died during the attempt, the fourth (Case 15) some hours later.

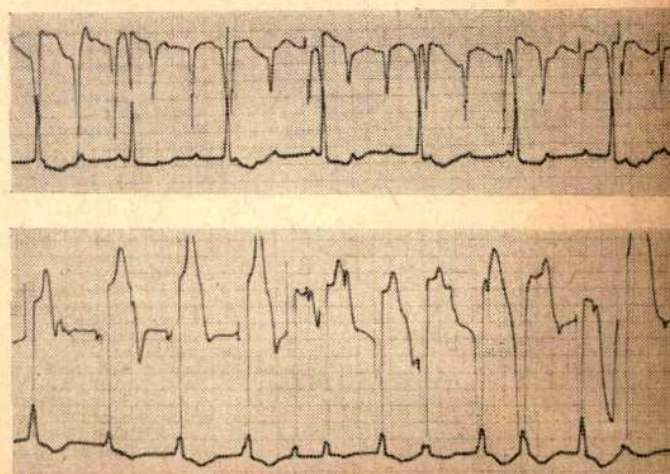


FIG. 2.—Intracavitary E.C.G.-registration during pacemaker electrode placement. Top: Registration from the right atrium and lead I. Bottom: Registration from the right ventricle with typical contact patterns.

* Ullevål Hospital, Department VIII, Oslo.

Nine of the 21 patients with effective pacing died during the hospital stay: four of them in ventricular fibrillation in spite of satisfactory pacing, and four in cardiac failure. Treatment with artificial pacemaker could be discontinued after 4 to 25 days in five patients in whom sinus rhythm returned. Indica-

tions for permanent pacemaker treatment were present in eight patients.

Discussion

Intracavitary electrocardiography has for many years been used in cardiac catheterization to determine the location of the catheter tip. The method has also been used in the daily clinical work as a supplementary method in the diagnosis of cardiac arrhythmias, utilizing a thin Teflon-coated stainless-steel wire with a platinum tip (Vogel *et al.*, 1964; Nutter and Kelser, 1965; Sivertssen, 1967). This electrode has been used for temporary pacing of the heart (Harris *et al.*, 1965; Kimball and Killip, 1965).

Introduction of the intracardiac pacemaker electrode should preferably be performed under fluoroscopy and TV monitoring. In urgent situations when such equipment is not available, the described method can be used as a bedside procedure. The technique is easy to perform, may be applied quickly, and does not require other special equipment than that usually available in most medical departments. The identification of the intracardiac electrocardiographic patterns is not too difficult in most cases, but extremely slow heart rates may cause a problem because so few ventricular patterns are seen. It is extremely important to make sure that the recorder and other instruments connected to the patient are properly earthed. Leaking of electric current through the intracavitary electrode may provoke ventricular fibrillation.

The electrode may be introduced in the vein percutaneously in patients with large antecubital or jugular veins. In most cases, however, a cut down on the vein is necessary. We have tried thin Teflon-coated steel-wire electrodes designed for intracavitary electrocardiographic diagnosis, but have not obtained effective stimulation. It is of great importance that the electrode is soft and flexible because of the danger of perforating the ventricular wall during the introduction.

In eight patients artificial pacemaking had to be continued as a permanent treatment. In these cases the external end of the electrode after thorough cleansing was taken out through an incision in the subclavian vein and then led subcutaneously to the right abdominal region, where it was attached to an implanted pacemaker. Infection or thromboembolic complications have not occurred. In most cases the electrode was introduced into an antecubital vein, usually the basilic vein of the right arm. When the electrode was firmly fixed in the elbow region, the patient was able to move the arm freely without displacement of the electrode. In one patient the electrode was pulled out accidentally during sleep. Usually the external jugular vein is used for introduction of pacemaker electrodes for permanent treatment. In urgent situations, however, it may be difficult to find a suitable vein in the neck.

The intracardiac electrode has been removed without difficulty even after 25 days, when further treatment with the artificial pacemaker was not indicated.

Summary

A simple and effective bedside method is presented for transvenous intracardiac pacing in urgent clinical situations when fluoroscopic equipment is not available. The method permits intracardiac electrode placement using the intracavitary electrocardiogram picked up by the pacemaker electrode as a guide.

Successful placement of the electrode was achieved by this method in 21 out of 27 critically ill patients with repetitive Adams-Stokes attacks.

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Case No.	Sex and Age	Diagnosis	Cardiac Arrhythmias	Course
1	F 48	Acute myocardial infarction	Sinoatrial block	Pacemaker electrode removed after 4 days. Patient discharged in sinus rhythm
2	F 51	Chronic polyarthritis treated with chloroquine	Complete A-V block (transient)	Pacemaker electrode removed after 2 days. Patient discharged in sinus rhythm
3	M 69	Acute myocardial infarction	Complete A-V block (transient)	Pacemaker electrode removed after 14 days. Patient discharged in sinus rhythm
4	M 66		Complete A-V block	Patient died in cardiac insufficiency in spite of effective pacemaker treatment
5	M 75	Coronary heart disease	Complete A-V block (permanent)	Patient discharged with permanent pacemaker
6	F 59	Acute myocardial infarction	Complete A-V block	Patient died in ventricular fibrillation in spite of effective pacemaker treatment
7	F 74	Rheumatic valvular disease	Atrial fibrillation and complete A-V block (permanent)	Patient discharged with permanent pacemaker
8	M 68	Acute myocardial infarction. Intracerebral bleeding	Complete A-V block	Patient died during attempt to institute pacemaker treatment
9	M 69	Coronary heart disease	Complete A-V block (permanent)	Patient discharged with permanent pacemaker
10	F 75	Acute myocardial infarction	Complete A-V block	Patient died in ventricular fibrillation during effective pacemaker treatment
11	F 67	Rheumatic valvular disease	Atrial fibrillation and complete A-V block	Pacemaker electrode removed after 9 days. Patient died 14 days later in cardiac failure
12	M 57	Acute myocardial infarction	Complete A-V block (transient)	Pacemaker electrode removed after 12 days. Patient discharged in sinus rhythm
13	F 67	Coronary heart disease	Complete A-V block (permanent)	Patient discharged with permanent pacemaker
14	F 85	" "	" "	Patient discharged with permanent pacemaker
15	M 68	Rheumatic valvular disease	Atrial fibrillation. Repeated attacks of ventricular fibrillation	Attempt to institute endocardial pacing failed. Patient died some hours later in ventricular fibrillation
16	F 72	Chronic polyarthritis treated with chloroquine	Complete A-V block (intermittent)	Patient discharged with permanent pacemaker
17	F 69	Acute myocardial infarction	Complete A-V block	Patient died in cardiac failure in spite of effective pacemaker treatment
18	F 61	Rheumatic valvular disease	Complete A-V block (permanent)	Patient discharged with permanent pacemaker
19	F 67	Chronic polyarthritis treated with chloroquine	Complete A-V block (intermittent)	Patient discharged with permanent pacemaker
20	M 71	Acute myocardial infarction	Complete A-V block	Patient died in cardiac failure in spite of effective pacemaker treatment
21	M 53		Complete A-V block (transient)	Pacemaker electrode removed after 25 days. Patient discharged in sinus rhythm
22	M 53			Patient died suddenly 7 days after pacemaker treatment had been discontinued
23	F 70		Complete A-V block	Patient died in ventricular fibrillation in spite of effective pacemaker treatment
24	M 48	Unknown aetiology. intoxication		Patient died during attempt to institute pacemaker treatment
25	M 55	Acute myocardial infarction	"	Patient died during attempt
26	F 67	"	Atrial fibrillation. Complete A-V block	Pacemaker electrode pulled out accidentally after 4 days, but heart rate and patient's condition was such that reintroduction was not thought necessary
27	F 56		Complete A-V block	Patient died in ventricular fibrillation in spite of effective pacemaker treatment

Oxygen Concentrations in Tents and Incubators in Paediatric Practice

HAMISH SIMPSON,* M.B., M.R.C.P.ED., D.C.H.; DOREEN J. RUSSELL,* S.R.C.N.

Brit. med. J., 1967, 4, 201-203

Oxygen therapy is a common requirement in paediatric practice and is generally administered in commercially available tents or incubators. Batson and Young (1958) stated that they were "unable to create and maintain therapeutic concentrations of oxygen in tents," and it is therefore surprising that alternative, more efficient, methods of administering oxygen (Burgess and Burgess, 1932; Morrison, 1955; Batson and Young, 1958; Godfrey, 1959) have not found wider acceptance.

Oxygen concentrations of at least 60% are claimed for many of their products by the manufacturers of tents and incubators, tested under laboratory conditions. As an inspired oxygen concentration of 40% does not invariably relieve hypoxia in infants with acute respiratory failure (Downes and Striker, 1966; Simpson and Flenley, 1967), it seems particularly relevant to report the oxygen concentrations attainable in present-day tents and incubators during clinical use.

Tents and Incubators

Six tents (Table I) and four models of incubator (Table II) were studied. Tents 1 (Air-Shields Type D Croupette), 2 (Air-

TABLE I.—Oxygen Concentrations in Tents Under Ideal Clinical Conditions

No.	Oxygen Tent Model	No. of Observations	Oxygen Flow Rate (l./min.)	Actual Concentration at Child's Mouth (%)		Possible Oxygen Concentration Claimed (%)	Notes
				Range	Mean		
1	Type D Croupette (Air-Shields, Inc.)	2	2 4 6 8 10	40-41 40-44 45-51 50-52 50-52	40 42 48 51 51	60	(a)
2	Universal Croupette (Air-Shields, Inc.)	4	10 20	28-31 28-35	30 30	65	(b)
3	Humidaire Tent (Oxygenaire Ltd.)	2	2 4 6 8 10 20	39-43 45-48 50-55 56-60 61-67 70-81	41 46 52 58 64 75	90	(c)
4	Universal Tent (CO ₂ washout off) (Oxygenaire Ltd.)	3	2 4 6 8 10 20	40-44 42-46 42-47 42-47 42-50 44-52	42 43 44 44 45 47	65	(d)
5	Mark V Tent (CO ₂ washout off) (Oxygenaire Ltd.)	2	2 4 6 8 10	40-41 41-44 45-51 50-52 50-52	40 42 48 51 51	70	(e)
6	Venturi Head Tent (Oxygenaire Ltd.)	3	2 4 6	23.5-24.5 26.5-27.5 32-34	24 27 33	24.5 28 32-34	

Notes: (a), (d), and (e) Flushing at 10 l./min. for 30 minutes; thereafter readings after 20 minutes at given flow rate. (b) Readings after flushing at 10 and 20 l./min. for 30 minutes. (c) Flushing at 20 l./min. for 20 minutes as recommended; thereafter readings after 20 minutes at given flow rate.

Shields Universal Croupette), and 3 (Oxygenaire Humidaire Tent) are used for infants and young children, whereas Tents 4 (Oxygenaire Universal Tent) and 5 (Oxygenaire Mark V Tent) are more suitable for older children who may find the others too confined. A high humidity is provided by each except Tent 4,

* Department of Child Life and Health, University of Edinburgh, and the Royal Hospital for Sick Children, Edinburgh.

but coolness for fevered children is obtainable in all. Tent 6 (Oxygenaire Venturi Head Tent) is designed to provide controlled oxygen therapy to adults with chronic respiratory insufficiency, during exacerbations of infection.

The incubators (Table II) are used in the neonatal period and provide high humidity and accurate temperature control in addition to oxygen. The Air-Shields Intensive-Care Isolette and the Oxygenaire New Incubator are fitted with a device to limit oxygen concentration to 40% or less, though higher concentrations are possible when necessary. The Oxygenaire Series III Incubator is included in this study as it is still widely used. The Oxygenaire Mark III Portable Incubator is generally used to transport newborn infants from home to hospital, thereby minimizing the risk of hypothermia and/or hypoxia during the journey.

TABLE II.—Oxygen Concentrations in Incubators Under Ideal Clinical Conditions

Incubator Model	No. of Observations	Oxygen Flow Rate (l./min.)	Actual Concentration at Child's Mouth (%)		Possible Oxygen Concentration Claimed (%)
			Range	Mean	
Intensive-Care Isolette (Air-Shields, Inc.)	3	1 (red handle horizontal)	26	26	
		2 " " "	30-31	30	
		3 " " "	34-35	34	28-30
		4 " " "	38-39	38	
		4½ (after 30 min. with red handle vertical)	40-44	43	32-35
New Incubator (Oxygenaire Ltd.)	2	1 (air intake open)	58-71	63	70+
		2 " " "		27	29
		3 " " "		34	34
		6 " " "		37	35
		6 (after 30 min. with red blanking disc in position)		35	35
Series III (Oxygenaire Ltd.)	5	1		63	80
		2	24-29	27	25
		3	29-40	36	35
Portable Incubator Mark III (Oxygenaire Ltd.)	1	2	35-45	41	45
		4		25	
		6		31	
		8		38	

Less than 30 unless special face-mask is used

Method

The tents and incubators were tested under normal working conditions. In Tents 1 to 4 the patients were infants or young children believed on clinical grounds to require oxygen therapy, whereas healthy children co-operated in testing Tents 5 and 6. The canopies of Tents 1 to 5 were carefully tucked in to avoid leakage, and all zips were tightly closed. Each tent was then flushed as recommended (usually 10 litres of oxygen per minute for 30 minutes) and the oxygen flow rate subsequently adjusted to 2, 4, 6, 8, 10, and 20 l./min. The oxygen flow meters used were supplied by the British Oxygen Company and are calibrated from 0 to 10 l./min. A dual outlet regulator was used to provide flow rates of 20 l./min. Samples of inspired gas were taken from within 1 in. (2.5 cm.) of the child's mouth after 20 minutes at each flow rate into 100-ml. lubricated glass syringes via stiff rubber tubing introduced through a small aperture in each tent. In this way samples were obtained under ideal clinical conditions. Tent 6 did not require flushing, and was sampled at oxygen flow rates of 2, 4, and 6 l./min.

Tents 1 to 4 were also sampled at random on numerous occasions. These tents were invariably flushed before initial usage, but routine refushing after feeding or other interference was often omitted.

The incubators were tested during use without previous flushing, every precaution being taken to avoid leakage. The oxygen concentration of gas samples was determined by a

Tent 4 (Fig. 4). The mean oxygen concentrations, ideal and random, in Tents 1 to 4 at oxygen flow rates of 10 l./min. are shown in Fig. 5. Oxygen concentrations greater than 50% are invariably attained in Tent 3.

Table II shows the oxygen concentrations measured in incubators and relates them to their manufacturers' recommendations.

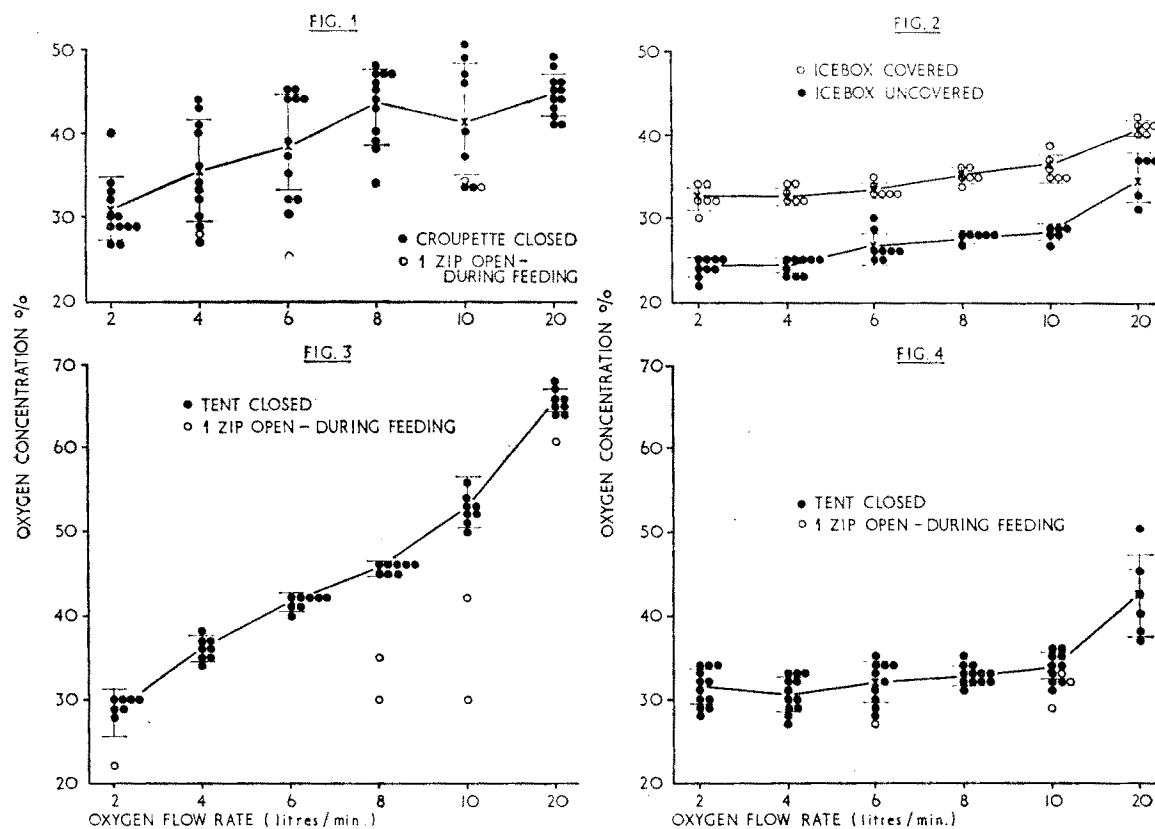


FIG. 1.—Concentration of oxygen (± 1 S.D.) achieved in Air-Shields Type D Croupette in relation to flow rate of oxygen (random measurements). FIG. 2.—Concentration of oxygen (± 1 S.D.) achieved in Air-Shields Universal Croupette in relation to flow rate of oxygen (random measurements). FIG. 3.—Concentration of oxygen (± 1 S.D.) achieved in Oxypaire Humidaire Tent in relation to flow rate of oxygen (random measurements). FIG. 4.—Concentration of oxygen (± 1 S.D.) achieved in Oxypaire Universal Tent in relation to flow rate of oxygen (random measurements).

D.C.L. 101 paramagnetic oxygen analyser calibrated with air and nitrogen (Nunn *et al.*, 1964).

Results

The oxygen concentrations attained in tents under ideal clinical conditions are shown in Table I. An oxygen concentration exceeding 50% was attained in Tents 1, 3, 4, and 5 at a flow rate of 10 l./min., whereas 31% was the highest concentration attained in Tent 2 at a similar flow rate. The oxygen concentrations in Tents 1, 3, and 6 are close to those claimed possible by their manufacturers, while the levels in Tent 5 are similar to those published by Freedman (1964).

The results of random sampling (Tents 1 to 4) are shown in Figs. 1-4. When Tent 1 is used as recommended with the pressure gauge in the "green area" (usually 6 l./min.), oxygen concentrations of 30 to 45% are achieved (Fig. 1). Higher concentrations (by 4-6%) are possible when the icebox is covered. Similarly, higher oxygen concentrations are attained in Tent 2 when the icebox is sealed over with polyethylene (Fig. 2). This improves contact between the outer and inner ice-tanks, where leaks may be associated with considerable air indrawing due to the Venturi circulation at that point. In Tent 3 an oxygen concentration of 40% is readily achieved at a flow rate of 6 l./min. (Fig. 3), whereas a flow rate of 10 l./min. is required to produce a similar concentration in

Comment

The oxygen requirements of hypoxic children may vary greatly, and depend on the cause and severity of the hypoxia. The principles underlying rational oxygen therapy have been reviewed (Brit. med. J., 1964), and Flenley (1967) has suggested that oxygen therapy should aim to provide a partial pressure of at least 10 mm. of mercury at the cellular mitochondria.

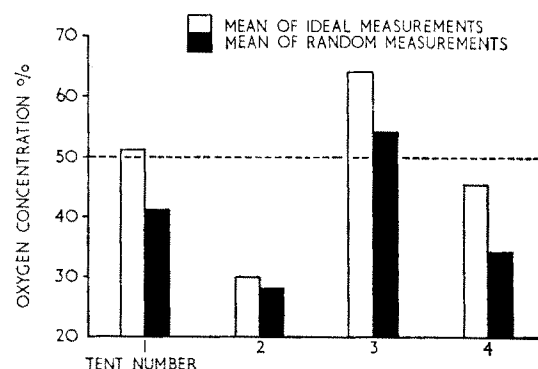


FIG. 5.—Oxygen concentrations in Tents 1 (Air-Shields Type D Croupette), 2 (Air-Shields Universal Croupette), 3 (Oxypaire Humidaire Tent), and 4 (Oxypaire Universal Tent) at an oxygen flow rate of 10 l./min. Comparison of means of ideal and random measurements.

It is probable that in many instances an oxygen concentration of 50 volumes %—that is, the standard recommended for tents by the Committee on Public Health Relations of the New York Academy of Medicine (1950)—fulfils this condition. While this concentration of oxygen may be dangerous to premature babies, such babies are generally nursed in incubators in which special provision is made to regulate the ambient oxygen concentration to under 40% (Table II), thus minimizing the risk of retrolental fibroplasia. Furthermore, the use of high oxygen concentrations in the treatment of chronic hypoxic children with hypoventilation may produce carbon dioxide narcosis (Bruck, 1957). There is, however, little risk of precipitating respiratory depression by this means in infants with acute lower respiratory tract infections (Reynolds, 1963; Simpson and Flenley, 1967). The main use of oxygen tents and croupettes is probably in the treatment of such cases, in which an inspired oxygen concentration of 40% or more may be necessary to ensure a normal arterial oxygen tension (PO_2) (Simpson and Flenley, 1967). This requirement is most likely to be met in Tent 3 (Figs. 3 and 5), in which an oxygen concentration of 50% is attainable at a flow-rate of 10 l./min.

In chronic respiratory insufficiency in infancy and childhood the place of oxygen therapy has yet to be defined precisely, though the risks of injudicious oxygen therapy to children with cystic fibrosis of the pancreas are recognized (Bruck, 1957). There may also be a place for controlled oxygen therapy in the treatment of asthma (Schiller *et al.*, 1951). In such instances Tent 6 may be of value, though a young child, apprehensive and fighting for breath, might find it too confined. The children who helped in testing this tent (aged 7–9 years) were fully at ease within a few minutes.

The indications for oxygen therapy in the newborn have been reviewed by Tizard (1964). Incubators are generally used in this period and are seldom appropriate for infants over 2–3 months of age. The recognition that retinal damage in premature babies is related more to a high arterial oxygen tension than the ambient oxygen concentration *per se* has resulted in improved incubator design. Newer models provide an ambient oxygen concentration of less than 40% at a flow rate of 3 l./min., but can be adjusted to supply 60–70% oxygen when necessary (Table II). This is of particular importance in the treatment of infants with venous-arterial shunts, as shunted blood does not perfuse the lung alveoli. Even so, the addition of oxygen to the blood which does undergo gas exchange in the lung may improve tissue oxygenation. The danger of pulmonary epithelial damage—the Lorrain-Smith (1899) effect—from the inhalation of high oxygen concentrations is probably of importance in humans (New Engl. J. Med., 1967), and should be borne in mind whenever high concentrations of oxygen are used therapeutically for a prolonged period.

Summary

The oxygen concentrations attained in the tents described during routine paediatric use are reported. A concentration of 50–60% is most readily attained in the Humidaire Tent—the most efficient of the tents described. Accurately controlled oxygen therapy in the range 40–60% is attainable in the Venturi Head Tent, which may be used in paediatric oxygen therapy. Incubators in use generally fulfil their manufacturers' specifications.

We wish to thank Professor J. O. Forfar, Dr. J. W. Ferguson, Dr. D. C. Flenley, and Dr. D. G. Barr for their advice and helpful criticism of this paper. We are also grateful to Air-Shields (U.K.) Ltd. and Oxygenaire Ltd. for their helpful co-operation throughout this study.

Requests for reprints should be addressed to Dr. H. Simpson, Department of Child Life and Health, 17 Hatton Place, Edinburgh 9.

ADDENDUM.—Since this paper has been prepared the canopy of Tent 2 (Air-Shields Universal Croupette) has been modified slightly. As a result there is now no distortion of the oxygen inlets to the tent. This allows closer apposition of the outer and inner tanks of the icebox than had previously been possible. On retesting this Croupette with the "new" canopy, an oxygen concentration of 45% was obtained after one hour at a flow rate of 10 l./min., under ideal clinical conditions. The provision of a spring-loaded clip between the outer and inner tanks of the icebox in future models of this Croupette may further minimize the possibility of leakage.

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Ulcerative Colitis in the Tropics

H. K. CHUTTANI,* M.D.; S. P. NIGAM,† M.D.; S. K. SAMA,‡ M.D.; P. C. DHANDA,§ F.R.C.P.
P. S. GUPTA,|| M.D.

Brit. med. J., 1967, 4, 204-207

Ulcerative colitis as a separate entity was first described by Wilks and Moxan (1875). Idiopathic ulcerative colitis has been defined as an acute and chronic inflammatory and ulcerative disease of the rectum and colon of unknown aetiology (Kirsner, 1959). Many reports on various aspects of the disease have appeared in the Western literature (Bargen, 1930; Felsen and Gorenberg, 1936; Palmer, 1948; Kirsner *et al.*, 1957; Kirsner and Goldgraber, 1960; Edwards and Truelove, 1963, 1964).

However, there has been very little documented evidence of this disease from tropical countries, and it is thought to be essentially a disease of temperate zones (Melrose, 1955). Almost 30 years ago Chopra and Ray (1939), from the School of Tropical Medicine, Calcutta, reported 120 cases of nonspecific ulcerative colitis. The clinical description and investigations leave little doubt that these were cases of this disease, as specific infections were effectively excluded. It is surprising that this report has gone unnoticed in the subsequent literature, and the impression has continued to persist that nonspecific ulcerative colitis is rare in the tropics. There were three important reasons why nonspecific ulcerative colitis was not often diagnosed: lack of facilities for precise diagnosis of dysenteric disorders; scarcity of antibacterial drugs by which a therapeutic test could be used to distinguish between recurrent specific infections and ulcerative colitis; and lack of the long-term observation of patients which is of such great help in making a diagnosis of this condition. This situation is gradually becoming corrected, and reports on nonspecific ulcerative colitis in the tropics have appeared in recent years (Pasricha *et al.*, 1958; Tandon *et al.*, 1965).

The present study had a threefold objective—namely, to assess the magnitude of the disease in this region, to compare the pattern with that reported in the West, and to emphasize the difficulties associated with the diagnosis of nonspecific ulcerative colitis due to the high prevalence of specific infections of the colon in the tropics.

Material and Methods

(1) A questionnaire was sent to the leading hospitals in different parts of the country for information regarding admission of cases of nonspecific ulcerative colitis during the period 1956-60. The inquiry covered the total number of admissions each year, the number of yearly medical admissions, and the number of ulcerative colitis cases admitted annually. The information received was analysed.

(2) Forty-six patients with ulcerative colitis were studied in detail. The diagnosis of ulcerative colitis was made on the basis of a clinical history of chronic dysentery not responding to adequate specific therapy, nonisolation of bacterial, protozoal, and helminthic pathogens on repeated smear and culture

examinations, and on sigmoidoscopic, radiological, and histological evidence of the disease.

(3) Three fresh stool specimens and a rectal swab taken during sigmoidoscopy were examined by means of saline and iodine preparations to exclude amoebic infection. Stool cultures for pathogenic bacteria were done on three consecutive days by a standard technique.

(4) The sigmoidoscopic findings were graded according to the classification of Matts (1961). Normal was taken as grade 1; mild granularity of the mucosa with mild contact bleeding as grade 2; marked granularity with oedema of mucosa, marked fragility with contact, and spontaneous bleeding as grade 3; and severe ulcerations of the mucosa with haemorrhage and/or pseudopolypoidosis as grade 4.

(5) The histological changes in the colonic biopsy were also graded (Matts, 1961): normal as grade 1; some infiltration of the mucosa, or lamina propria, with either round cells or polymorphs as grade 2; marked cellular infiltration of the lamina propria and submucosa as grade 3; the presence of crypt abscesses with marked infiltration of all the layers of the mucosa as grade 4; and ulceration, erosion, and necrosis of the mucosa with cellular infiltration of some or all of its layers as grade 5.

(6) Barium-enema examination was done in 38 patients. The extent of the disease was analysed and alterations in the radiological patterns of the colon were recorded.

Results

Admission Rate.—Information obtained from different hospitals in various cities of the country was analysed (Table I). It was observed that the admission rate in different hospitals varied from 3.6 to 26.1 cases per 10,000 hospital admissions. For medical cases alone the rate varied from 8.3 to 89.1 per 10,000 admissions. The overall admission rate came to 28.3 cases per 10,000 medical admissions and 9.4 cases per 10,000 total hospital admissions.

TABLE I.—Admission rate of Ulcerative Colitis in Various Hospitals

Name of City	Average No. of Cases per Year	Average Admissions per Year		Rate per 10,000 Admissions	
		Medical	Total	Medical Wards	Whole Hospital
(1) Calcutta ..	11.5	1,295	—	89.1	—
(2) Bombay ..	73	9,949	27,933	73.35	26.13
(3) New Delhi ..	48	17,079	57,810	41.5	10.41
(4) Amritsar ..	17	3,013	23,034	56.42	7.38
(5) Vellore ..	10.5	3,066	13,565	34.26	7.74
(6) Madras ..	16.5	18,744	37,118	8.8	4.44
(7) Gwalior ..	2.5	2,866	—	8.37	—
(8) Ahmedabad ..	8.55	10,241	23,358	8.3	3.65
Total ..	187.5	66,253	182,818	28.3	9.4

Clinical Profile.—About three-quarters of the cases were in the third and fourth decades, though the disease was seen in all age groups. The paediatric age group was not included in the study (Table II). The mean age at onset was 31.5 years for men and 25.3 years for women. The minimum age at onset was 9 years and the maximum age 56 years. Males were affected more often than females, the ratio being 2.3:1. The average duration of symptoms previous to the first examination was 3.2

* Additional Professor of Medicine, Maulana Azad Medical College, New Delhi.

† Assistant Research Officer, Indian Council of Medical Research, New Delhi.

‡ Lecturer in Medicine, G. B. Pant Hospital and Maulana Azad Medical College, New Delhi.

§ Senior Physician, Irwin Hospital, New Delhi.

|| Reader in Medicine, Maulana Azad Medical College, New Delhi.

years. The majority of patients came with symptoms of less than four years' standing. Most of the cases occurred in poor socio-economic groups. A family history of the disease was present in one case. Various factors incriminated by patients as precipitating an attack of the disease or aggravating the symptoms were milk in five cases, emotional disturbances in five, pregnancy in one, and respiratory infection in one. The symptoms and physical signs of these patients were carefully recorded and analysed (Table III). Loose motions with blood and mucus were the presenting symptoms in all cases. Abdominal pain and flatulence were present in most of the patients. General symptoms of the disease were less marked. On the basis of symptomatology (Truelove, 1956) 12 cases were graded as severe, 18 as moderate, and 16 as mild.

TABLE II.—Age and Sex Distribution

Age Group	Total Cases	Male	Female
12-20 years	6	2	4
21-30 "	8	8	—
31-40 "	24	16	8
41-50 "	5	4	1
51-60 "	2	1	1
61+ "	1	1	—
Total	46	32	14

TABLE III.—Clinical Features of Ulcerative Colitis

Symptoms	No. of Cases	Physical Signs	No. of Cases
Loose motions with blood and mucus	46	Abdominal tenderness ..	38
Frequency of stools ..	46	Pallor	26
Flatulence	36	Palpable liver	10
Pain abdomen (diffuse) ..	35	Hypovitaminosis B	10
Tenesmus	15	Oedema	7
Loss of weight	15	Clubbing	2
Fever	13	Palpable spleen	1
Anorexia	7		
Arthralgia	6		
Vomiting	3		
Rectal itching	3		

Complications.—Local complications were common. Pseudopolypoid (Fig. 1) was observed in seven, severe haemorrhage in two, perforation in one, pararectal abscess in one, fissure-in-ano in one, and haemorrhoids in four cases. Systemic complications were encountered in only two patients, who suffered from thrombophlebitis and arthritis respectively. The arthritis involved metatarsophalangeal, hip, knee, and ankle joints. The Rose-Waaler test was negative and the serum uric acid level was normal in this case. Four patients died during the period of

study, one from perforation, one from uncontrolled haemorrhage, one during the postoperative period after resection of the colon and ileostomy, and the fourth from fulminating disease not responding to treatment.

Sigmoidoscopic Findings.—On sigmoidoscopic examination all cases had varying degrees of abnormality. Ten patients had severe or grade 4 changes, 20 moderate or grade 3, and 16 mild or grade 2 (Matts, 1961). Pseudopolypoid was seen in three cases with severe changes.

Histological Findings.—Colonic mucosal biopsy was done in 32 cases. Severe changes (grades 4 and 5) were observed in 13 cases, moderate changes (grade 3) in 11, and mild (grade 2) changes in eight. No patient had normal (grade 1) biopsy. Cryptitis and crypt abscesses were seen in 13 cases (Fig. 2).

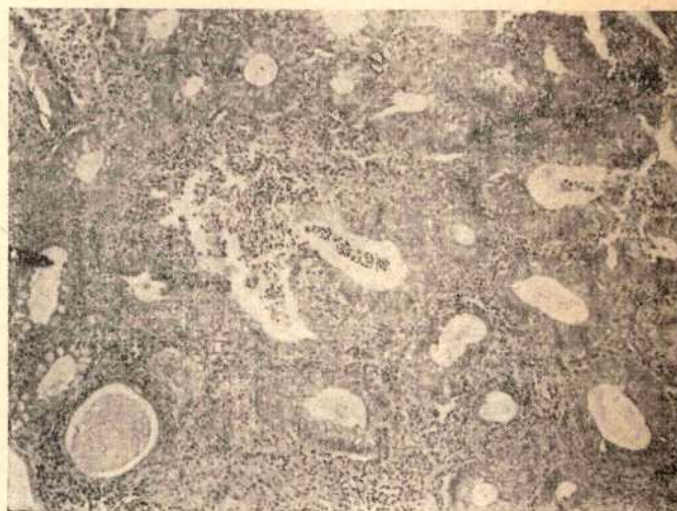


FIG. 2.—Rectal mucosa showing glandular hyperplasia with heavy mononuclear infiltration in the lamina propria and crypt abscess.

Radiological Findings.—Barium enema was done in 38 patients (Fig. 3). Irritability of the colon, oedema, and loss of haustration were the early and most important radiological findings in the majority of the cases. Radiological evidence of gross ulceration was seen in 11, narrowing of the lumen in 10, lead-pipe deformity in six, pseudopolypoid in six, and dilatation of the lumen of the bowel in four. The extent of the disease as seen by barium enema was analysed (Table IV). In

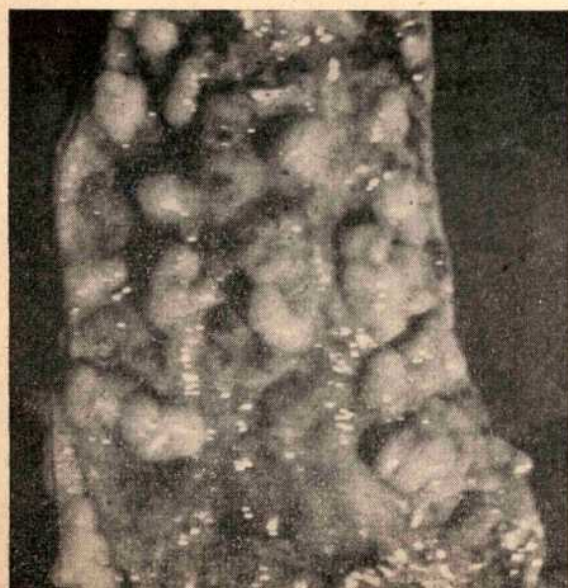


FIG. 1.—Gross appearance of colonic mucosa showing extensive ulceration and a number of pseudopolypi (resected specimen).



FIG. 3.—Representative radiological finding in a patient with extensive ulcerative colitis showing ragged serrations, pseudopolypoid, and narrowing of the lumen of the descending colon.

about half the cases the disease extended from the rectum to the splenic flexure. Six patients had normal radiological appearances. The disease in these cases was limited to the rectum and rectosigmoid regions only.

TABLE IV.—Extent of Disease on Barium Enema Examination in 38 Cases

Normal colon	..	..	..	..	6
Rectum to sigmoid	..	..	..	..	4
.. .. splenic flexure	..	..	..	..	21
.. .. mid-transverse colon	..	..	..	..	3
.. .. hepatic flexure	..	..	..	..	2
Entire colon	..	..	..	..	2

Discussion

The information obtained from the leading hospitals in different parts of the country revealed marked variations in the admission rate of cases of ulcerative colitis. From these figures (Table I) it would be wrong to assume that there is such an extreme variation in the prevalence of this disease. These differences are likely to be due to variations in the type of patient visiting the hospital, in the degree of interest that the attending physicians have in the disease, in the facilities available for diagnosis, and in the criteria employed for the diagnosis of ulcerative colitis. As these were not uniform it is not possible to draw any firm conclusion about the relative frequency of the disease and the factors responsible for regional differences. For this, one would need a planned prospective study.

Similar observations made in Britain (Melrose, 1955) revealed a frequency varying from 2 to 20 per 10,000 hospital admissions in different regions. Hospitals in Scotland had lower figures than those in England. The overall admission rate for ulcerative colitis from our data is 9.4 cases per 10,000 hospital admissions. This is not very different from the reported admission rate of 10 cases per 10,000 hospital admissions in the United Kingdom. Comparable figures for U.S.A. are 50–100, for Switzerland six, for New Zealand 0.55, and for Norway 5 per 10,000 admissions (Bebchuk *et al.*, 1961). One can safely conclude that ulcerative colitis is not a rare disease in tropical regions of India. Therefore early differentiation of cases of ulcerative colitis from specific dysenteries in the tropics is of importance in view of its high mortality and morbidity compared with what occurs in the specific dysenteries (Craig, 1947).

There was no significant difference in the age distribution and duration of symptoms when compared with Western reports (Bacon, 1958; Sloan *et al.*, 1950; Edwards and Truelove, 1963, 1964). Males were affected more often than females, while in Western series they are either equal or the females predominate (Sloan *et al.*, 1950; Edwards and Truelove, 1963, 1964). The smaller number of females in this series may be partly due to the fact that the number of women admitted to hospital is much lower than that of men.

Complications of ulcerative colitis may either be local in and around the large bowel or be systemic, affecting distant parts of the body. In all, complications were encountered in 12 cases (26%). This figure is on the low side compared with the Western reports of 31 to 40% (Rankin *et al.*, 1932; Ricketts and Palmer, 1946; Dennis and Karlson, 1952). Except for one case of arthritis and one case of thrombophlebitis, systemic complications were conspicuously absent. Sloan *et al.* (1950) and Edwards and Truelove (1964) recorded arthritis in 7.7 and 5.6% cases respectively in their series. In the present series there was no case of erythema nodosum, pyoderma gangrenosum and other skin rashes, eye lesions, ankylosing spondylitis, oral moniliasis, hepatitis, pulmonary embolism, or renal complications. Local complications such as pseudopolypoidosis, massive haemorrhage, perforation, pararectal abscess, and anal fissure were also found less frequently in this study than in Western surveys (Sloan *et al.*, 1950; Edwards and Truelove, 1964). Acute dilatation of the colon, fibrous strictures, fistulae, and carcinoma of the colon were not encountered. Sloan *et al.* (1950) observed fibrous strictures in 11.1% of cases, perianal and

perirectal infections and fistulae in 6%, and carcinoma of the colon in 5.4%. Edwards and Truelove (1964) reported figures of 6.3%, 7.7%, 3.5%, and 1.6% for fibrous strictures, fistulae, carcinoma, and acute dilatation of the colon, respectively.

Severe abnormalities on sigmoidoscopy were found in 10 out of 46 cases. In the remaining 36 the changes were mild to moderate. Matts (1961) observed severe or grade 4 changes in 46 (36.5%) of his series of 126 patients of ulcerative colitis. Rectal biopsy showed histological abnormalities of varying grades in all cases. Severe changes (grade 5 and 4) were seen in 13 cases (40.6%). Matts (1961) reported severe changes in 50% of rectal biopsies in cases of ulcerative colitis.

On radiological examination the disease was less extensive and more often confined to the rectum, sigmoid, and descending colon. The entire colon was involved in only two cases. There was no case of backwash ileitis. Ricketts *et al.* (1948) reported extensive disease involving the whole of the colon, with or without backwash ileitis, in 30% of cases.

Thus ulcerative colitis as seen in this region appears to be a milder disease with fewer complications and less severe sigmoidoscopic and histological changes. Why the disease is milder with limited involvement of colon than that seen in the West is not apparent. Is it that the repeated infections made the colon less prone to nonspecific ulcerative colitis or is it that this is a disease of the sophisticated and our population has not reached a comparable degree of sophistication with resulting psychological stresses? Psychological stresses are thought to have a bearing on the causation of the disease (Finch and Hess, 1962; Fullerton *et al.*, 1962; Daniels *et al.*, 1962).

The diagnosis of ulcerative colitis in the tropics is more difficult than in Western countries because of the high prevalence of amoebic and bacillary dysenteries. In addition, diffuse colonic tuberculosis and lymphogranuloma venereum also create difficulty in diagnosis, because the clinical picture of chronic nonspecific ulcerative colitis is sometimes virtually indistinguishable from those conditions. Fortunately, diffuse colonic tuberculosis is rare (Glenn and Read, 1946; McColl, 1956; Virmani, 1963) and lymphogranuloma is present in only isolated areas.

Sigmoidoscopic and radiological appearances similar to those seen in ulcerative colitis have been observed in cases of proved bacillary and amoebic infections (Manson-Bahr, 1943). Cryptitis and crypt abscesses on rectal biopsy have also been seen in cases of specific dysenteries, though much less frequently. Microbiological and parasitological study may not reveal the pathogens in many cases of specific infections, especially when patients have received some antimicrobial agents before investigation. Powell and Wilmont (1966) have raised the interesting problem of ulcerative post-dysenteric colitis resulting from amoebiasis. Whether this condition is a separate entity or whether amoebic infection is associated with nonspecific ulcerative colitis is not apparent. Further study and follow-up are required to clarify this situation. There is thus distinct difficulty in the differential diagnosis of ulcerative colitis and specific infections of the colon in the tropics, and often one has to depend on therapeutic tests to exclude the latter. It has therefore been a routine in some centres, even when repeated examinations have failed to demonstrate pathogens in the stools, to give adequate antibacterial and anti-amoebic therapy in every case of the chronic dysenteric syndrome before diagnosing the case as idiopathic nonspecific ulcerative colitis.

Summary

A survey of the medical records of leading hospitals in different parts of India for the period 1955–60 revealed that ulcerative colitis is not rare in this part of the world. The admission rate in different hospitals varied from 8.3 to 89.1 cases per 10,000 hospital admissions.

Forty-six cases of ulcerative colitis were studied in detail. By comparison with Western series, ulcerative colitis as seen in this region is a milder disease with fewer complications and with less severe changes on sigmoidoscopy and rectal biopsy. The disease remains limited to the rectum, sigmoid colon, and descending colon in the majority of cases.

Owing to the high prevalence of specific infections of the colon there are difficulties associated with the diagnosis of ulcerative colitis, and these are discussed.

We are thankful to the Director-Principal of Maulana Azad Medical College and associated hospitals for permission to publish this work. We are indebted to Professor D. N. Gupta and Professor O. P. Bhardwaj for histological and radiological studies of the relevant material. We are grateful to Dr. J. B. Chatterjee, Dr. R. Subramaniam, Dr. P. Raghavan, Colonel R. D. Ayyar, Dr. R. P. Malhotra, Dr. P. Koshy, Dr. P. N. Laha, and Dr. O. P. Gupta for assisting in the collection of information regarding the admission rate of ulcerative colitis. Thanks are also due to Dr. M. C. Watsa, Medical Department, Glaxo Laboratories Private Limited, for a liberal grant to carry out this study.

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Electroencephalogram and Retinal Vessels in Congenital Cyanotic Heart Disease Before and After Surgery

EVA M. KOHNER,* M.B., B.SC., M.R.C.P.; E. M. ALLEN,† M.B., B.CHIR., M.R.C.P.
 K. B. SAUNDERS,* M.D., M.R.C.P.; V. M. EMERY‡; C. PALLIS,§ D.M., F.R.C.P.

Brit. med. J., 1967, 4, 207-210

The electroencephalogram (E.E.G.) is often abnormal in patients with congenital cyanotic heart disease (Shev and Robinson, 1958; Lesny *et al.*, 1960; Fowler *et al.*, 1962; Allen *et al.*, 1967). The reason for this is unknown. The disturbance of cerebral function might be due to structural brain disease, which is commonly present (Cohen, 1960), to chronic arterial desaturation, or to decreased cerebral blood flow resulting from a high packed cell volume (P.C.V.). Many of these patients also have abnormal fundi for which the polycythaemia has been incriminated (Taussig, 1960).

We have recently had the opportunity to study the retinal and E.E.G. changes in 12 patients with congenital cyanotic heart disease both before and at various intervals after operative treatment of their cardiac defects. The data obtained may throw some light on the cause of the abnormal E.E.G.s seen in these cases.

Angiographic study of the cerebral circulation in these patients is dangerous because of their known liability to cerebral thrombosis. The retinal vessels, however, are readily accessible for repeated examination, and their response to cardiac surgery may give some indication of what is happening at the level of the cerebral vasculature.

* Medical Registrar.

† Clinical Neurophysiologist.

‡ Senior Recordist.

§ Consultant Neurologist.

Department of Medicine, Royal Postgraduate Medical School, London W.12.

Patients and Methods

Clinical and operative details concerning the 12 patients are given in Table I.

E.E.G. Studies.—All 12 patients had preoperative records. All except two (Cases 8 and 9) were again studied two weeks

TABLE I.—Clinical Details of 12 Patients with Cyanotic Congenital Heart Disease

Case No.	Diagnosis	Age*	Sex	Previous Surgery	Present Surgery
1	Transposition. PS, VSD, PDA	23	F	—	Brock's procedure (C)
2	Fallot's tetralogy	6	M	—	—
3	PS and ASD	9	F	Brock's procedure aged 8 (C)	Closure of ASD (O)
4	PS and ASD	44	F	—	Brock's procedure (C)
5	Fallot's tetralogy	12	F	Blalock anastomosis aged 5 (C)	Total correction (O)
6	—	8	F	—	—
7	Transposition. PS, VSD	11	M	Blalock anastomosis aged 3 (C)	Blalock-Hanlon (C)
8	Fallot's tetralogy	17	F	Blalock anastomosis aged 13 (C)	Brock's procedure (C)
9	—	7	M	—	Total correction (O)
10	Transposition. Pulmonary atresia, VSD	12	F	—	Blalock anastomosis (C)
11	Fallot's tetralogy	5	M	—	Brock's procedure (C)
12	—	14	M	Blalock anastomosis aged 2 (C)	Total correction (O)

* At time of surgery.

PS = Pulmonary stenosis. VSD = Ventricular septal defect. PDA = Patent ductus arteriosus. ASD = Atrial septal defect. C = Closed surgical procedure. O = Open procedure involving total body perfusion.

postoperatively. Cases 1 to 9 (inclusive) were further investigated three months after the operation. In Cases 3, 12, and 9 further records were obtained at six months, 12 months, and three years respectively. Routine bipolar recordings were taken with a Kaiser 8-channel portable machine (T.R. 60), the international system of electrode placement being used.

Retinal Studies.—Retinal photographs were taken within 24 to 48 hours of the E.E.G. in all patients with the exception of one (Case 6), who was not studied, and of two (Cases 4 and 9) who had no pictures taken at three months. Case 8 was studied two weeks postoperatively as well. The pupils were dilated with 0.5% cyclopentolate and 10% phenylephrine. Retinal photographs were taken with a Zeiss fundus camera and Kodachrome II film. The disc, superior temporal, and macular areas were studied routinely. The prints were identified by code and allocated by three observers into one of four groups: normal or mildly, moderately, or severely abnormal. For purposes of grading, the following features were taken into account: degree of cyanosis of fundus, vascularity of disc, and calibre and tortuosity of retinal vessels.

Results

Retinal Changes

Preoperative.—In all the patients cyanosis gave the fundus a much darker hue than normal. The discs appeared more vascular than normal in Cases 1-4 and in Case 9. In Case 2 there was frank papilloedema (Fig. 1). In all patients both arterioles and venules were markedly dilated and tortuous. In addition there was a general increase in vascularity of the entire fundus, with many prominent small vessels. The excessive vascularization appeared to be due to normal, though dilated, arterioles and venules. These changes were most pronounced in the patients with severe or moderately severe cardiac disability. These were the patients with the highest P.C.V. (Table II).

Postoperative.—The greatest changes occurred during the first two weeks (the general condition of the patients precluded an earlier photographic assessment), and there was further improvement at three months. The fundi became much pinker (less cyanosed). Of interest was the development of "atrophic"

("albinotic") fundi in three of the patients studied (Cases 3, 7, and 9). This may have been masked preoperatively by the engorgement of the retina and choroid.

The abnormal vascularity of the disc returned to normal in most instances. In the patient with papilloedema (Case 2) there was remarkable improvement, though the disc was still not quite normal at three months (Fig. 2).

The tortuosity and dilatation of the vessels decreased at two weeks and improved further at three months. The number of small vessels appeared to be reduced.

The greatest change in the fundal appearance (Case 2) occurred in the patient who also exhibited the greatest postoperative fall in the P.C.V. (from 80 to 44%). The only patient whose fundal appearances remained unchanged at two weeks (Case 10) was found at operation to have a defect not amenable to correction. Her P.C.V. was not significantly affected by the operation.

E.E.G. Changes

(a) **Preoperative.**—Only two patients had normal records (Cases 7 and 9). In eight patients (Cases 1, 3-5, 8, and 10-12) the E.E.G. was unequivocally abnormal, showing various combinations of abnormally slow dominant rhythm, excess theta and delta activity, focal delta and sharp waves, and runs of spike and wave. The records of Cases 2 and 6 were doubtfully abnormal.

(b) **Early Postoperative.**—One record (Case 5) showed improvement: a reduction in spike and wave. This patient had been given anticonvulsant cover during the operation and was still receiving phenobarbitone. In one patient (Case 1) the record was unchanged. In the other eight patients the records had deteriorated. The deterioration usually consisted of a slower and more irregular dominant rhythm and/or increased theta and delta activity, usually bilateral.

(c) **Late Postoperative.**—Nine patients had records taken about three months after operation. Comparison with the preoperative records showed improvement in only three patients (Cases 1, 2, and 4). In these the alpha rhythm was more regular and there was a reduction of slower components. In two other patients (Cases 5 and 7) the E.E.G.s had reverted to their pre-

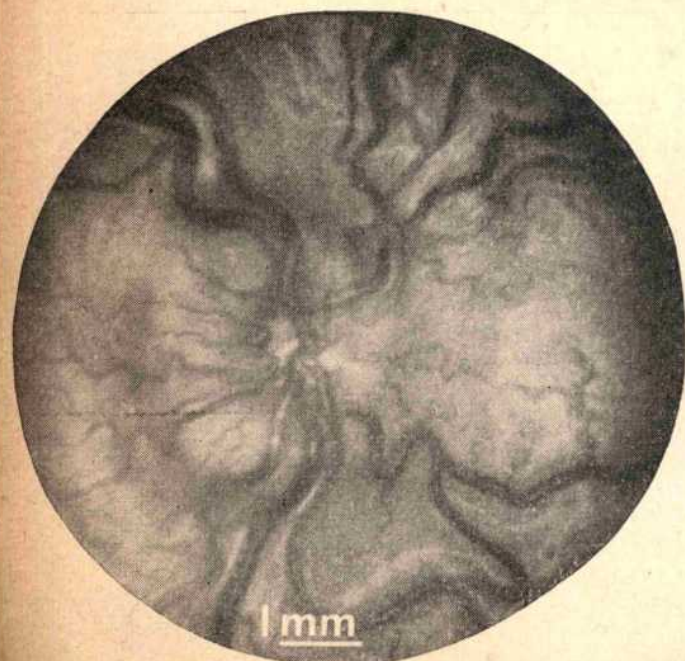


FIG. 1.—From a colour slide of Case 2, showing the disc area preoperatively. Note papilloedema, dilatation, and tortuosity of both arterioles and venules.

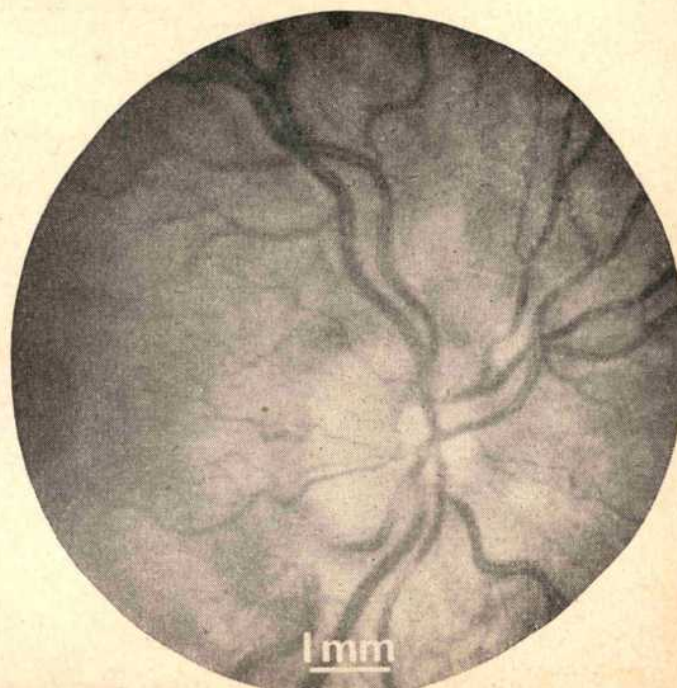


FIG. 2.—Same as Fig. 1, three months after operation. Disc margins almost normal. Dilatation and tortuosity of vessels much less.

operative pattern. In four patients (Cases 3, 6, 8, and 9) the records were worse (slower and less rhythmic alpha activity and increased theta and delta activity). Fig. 3 illustrates the changes in a typical case.

Three years after operation the E.E.G. in Case 9 showed a return to the preoperative state.

Details concerning retinal appearances, E.E.G.s, and P.C.V.s are summarized in Table II.

Discussion

All patients had abnormal retinal vessels and a cyanosed fundus before operation. The abnormalities were most severe in the patients with the highest P.C.V., but it is probable that these patients also had the most severe arterial desaturation. The postoperative improvement in the appearance of the retinal vessels was associated with a fall in the P.C.V., but the arterial saturation had also reverted towards normal. The relative importance of a low PO_2 and a high P.C.V. with increased blood viscosity in the causation of the retinal vascular changes were not ascertained in this study. Investigations of patients with hypoxia (and hypercapnoea) due to respiratory failure, a high haematocrit due to polycythaemia rubra vera, and a high plasma viscosity due to macroglobulinaemia are now in progress and may clarify this aspect of the problem.

The high incidence of abnormal E.E.G.s in congenital cyanotic heart disease has been confirmed. It is of interest that only two patients had clinical neurological abnormalities.

Case 1 had a history of past cerebral abscesses and still suffered from epilepsy. Case 2 had bilateral synergic movements ("mirror-movements") of the upper limbs and both clinical and radiological evidence of a craniovertebral anomaly.

No relation was established between the level of the P.C.V. and the degree of abnormality of the E.E.G.

The deterioration in six of the 10 E.E.G.s recorded two to three weeks postoperatively was unequivocal. One patient (Case 4) was thought to have suffered a postoperative cerebral embolus, but the other patients had been free from overt neurological complications. These early deteriorations in the E.E.G. occurred whether or not the patient had been perfused during the operation, and were often observed despite the fact that the patients had clinically improved.

Similar deterioration of the E.E.G. recorded some two weeks after surgery for congenital heart disease was reported in 16 out of 24 cases by Torres *et al.* (1959) and in 13 out of 36 cases by Fowler *et al.* (1962). Their data, however, are not strictly comparable to ours in that they refer to mixed groups, including both cyanotic and non-cyanotic cases. Torres *et al.* (1959) found no relation between the occurrence of abnormal postoperative E.E.G.s and the constancy or intermittency of the cyanosis, blood pressure readings during surgery, oxygen saturation measured during the surgical procedure, or the duration of extracorporeal circulation. Similar early and reversible deterioration in the E.E.G. was found in two "controls" who had uncomplicated cardiac operations without perfusion (resection of coarctation of the aorta and exploratory thoracotomy only). In a series of 24 children

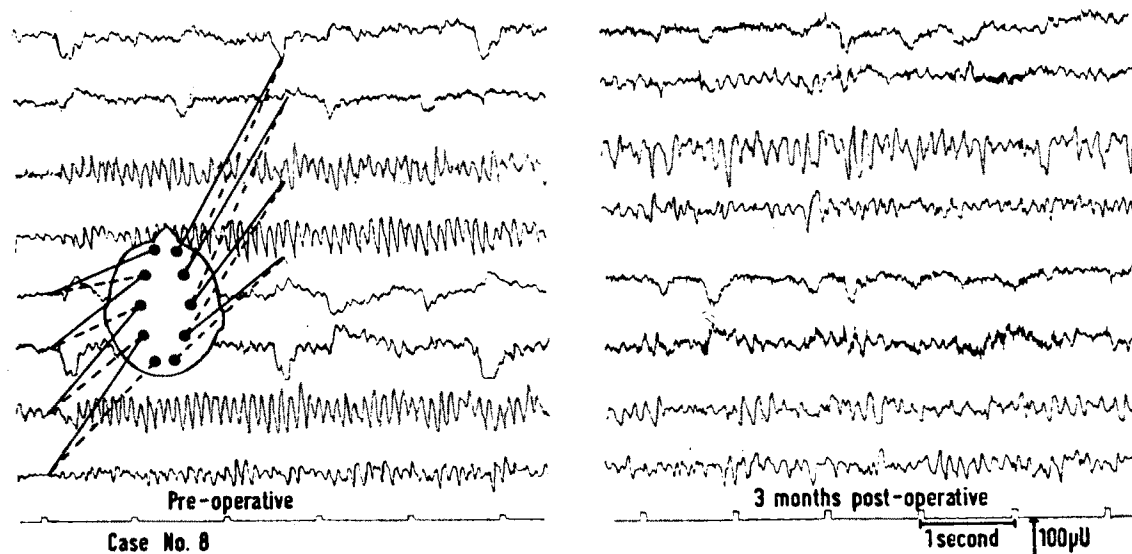


FIG. 3.—Case 8. E.E.G. records (preoperative and three months postoperative). Patient alert with eyes closed. Note postoperative slowing of alpha rhythm and increase of theta and delta activity, post-centrally.

TABLE II

Case No.	Retinal Photographs				E.E.G.				P.C.V. (%)		
	Preoperative	Postoperative			Preoperative	Postoperative (Compared with Preop. Record)			(a)	(b)	(c)
		(b)	(c)	(d)		(b)	(c)	(d)			
1	Severely abnormal	Improved	Much improved		Abnormal	Unchanged	Slightly improved		75	61	65
2	"	Much improved	Improved		Doubtful	Slightly worse	Improved		80	44	44
3	Moderately abnormal	Improved	"		Abnormal	Worse	Worse	Worse (6/12)	70	41	48
4	"	"	—		"	"	Improved		73	53	54
5	Mildly abnormal	"	Improved		"	Improved	Unchanged		63	49	—
6	"	—	—		Doubtful	Worse	Worse		45	41	—
7	Mildly abnormal	Improved	Improved		Normal	"	Unchanged		60	44	51
8	"	Slightly improved	"		Abnormal	—	Worse		50	43	—
9	Severely abnormal	—	—	Much improved (3 years)	Normal	—	"	Unchanged (3 years)	76	43	48
10	Mildly abnormal	Unchanged	—		Abnormal	Slightly worse			66	62	—
11	"	Improved	—		"	Worse			64	57	—
12	"	Slightly improved	—		"	"		Worse (1 year)	55	38	—

(a) Preoperative. (b) Two weeks postoperative. (c) Three months postoperative. (d) More than 3 months postoperative.

submitted to various unspecified cardiothoracic operations Pampiglione (1965) found similar changes in the early post-operative E.E.G.s. These subsided within a week and were attributed to a metabolic response to trauma. In our patients the early deterioration lasted somewhat longer but was also usually reversible. In five of our eight patients with such early deterioration, records taken three months postoperatively had returned towards their preoperative state.

The deteriorated E.E.G.s at three months were more difficult to explain. In only two of our four patients where this occurred was any kind of explanation in fact forthcoming. One (Case 9) had a severe chest infection at the time of the record, and the other (Case 3) developed signs of congestive cardiac failure some time after the E.E.G. Though one patient (Case 6) developed unexplained ascites immediately after the operation, this had cleared by the time of the third E.E.G. We are also unable to explain why the record in Case 8 became worse. This patient had had "closed" heart surgery and had remained free from all complications four months postoperatively. A similar deterioration in the records of 9 out of 33 patients examined one to two years after surgery was found by Fowler *et al.* (1962). Long-term follow-up is obviously necessary to determine the significance of these findings.

In only three of our 10 patients having late postoperative E.E.G.s was surgical treatment of the cardiac lesion eventually followed by an improvement in the E.E.G., despite the fall in packed cell volume and the increase in oxygen saturation that resulted from the operation. In 20 out of 33 patients with abnormal preoperative E.E.G.s examined by Fowler *et al.* (1962) the record was *unchanged* one to two years after cardiac surgery. That initially abnormal records should remain abnormal for months or even years after operation is perhaps not surprising when one recalls the high incidence of microscopic abnormalities of the brain in patients with congenital heart disease (Cohen, 1960), even if not submitted to surgery. The effects of chronic hypoxia may outlast the hypoxia itself. It is not inconceivable that long-acting hypoxia may permanently impair the normal maturation of cerebral rhythms, the net result being that adults with congenital cyanotic heart disease, even if operated on, may still show E.E.G. patterns of juvenile type.

From these studies it would appear that either postoperative changes in the retinal vasculature are not paralleled by similar

changes in the cerebral blood vessels, or that if changes in the cerebral vasculature do occur they are not followed by an improvement in the E.E.G., persistent abnormalities of which reflect other irreversible disturbances.

Summary

Retinal vascular changes are present in all cases of congenital cyanotic heart disease. The severity of these changes is most marked in patients with the highest P.C.V.s.

The E.E.G. is frequently abnormal in congenital cyanotic heart disease even in the absence of overt neurological symptoms and signs. The degree of E.E.G. abnormality bears no relation to the P.C.V.

The dramatic reversion towards normality shown in the retinal vessels after correction of the cardiac lesion is not paralleled by improvements in the E.E.G. In only a minority of cases is an improvement in the E.E.G. detectable three months after operative correction of the cardiac defect.

The E.E.G. defect in congenital cyanotic heart disease is not a simple functional disturbance directly related to arterial desaturation or to a diminution of cerebral blood flow from polycythaemia.

We would like to thank Professor J. F. Goodwin, Professor H. H. Bentall, and Dr. C. Oakley for allowing us to study patients under their care, and Dr. C. Dollery for helpful criticism.

E. M. K. was supported by the Tobacco Research Council and the photographic material was supplied by the Medical Research Council.

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Catabolism of Serum γ G-globulins in a Cancer Patient and a Normal Volunteer

D. E. H. TEE,* M.B., B.S., M.C.PATH.; J. WATKINS,* B.SC., PH.D.

Brit. med. J., 1967, 4, 210-212

It has been shown that the half-life of serum γ G-globulins is apparently characteristic of the species of origin (Spiegelberg and Weigle, 1965). However, it is also well established that the half-life value may be influenced by several factors, in particular by its dependence on the concentration of γ G-globulin in the serum (Fahey and Robinson, 1963; Fahey and Sell, 1965).

Several workers have studied the catabolism of electrophoretically and antigenically distinct components of the γ G-globulin of mice (Fahey and Sell, 1965; Tee, Watkins, and Wang, 1965). Each of these components was found to have a different half-life in the normal mouse. In view of the heterogeneity in biological functions of the antibodies associated with these components and the possible implications for immuno-

logical tumour enhancement (reviewed by Bloch, 1965), it is surprising that little significance appears to have been attached to the findings of those workers (Mills, Calkins, and Cohen, 1961) whose experiments indicate a similar catabolic heterogeneity of γ G-globulins in man.

This paper reports some preliminary results of studies being made in this laboratory of the catabolic heterogeneity of human γ G-globulins.

Volunteers and Methods

Two male volunteers were used in this study. The control subject was one of us (J.W.) aged 31. The other volunteer was a patient aged 43, who over the previous seven years had undergone surgery for the removal of six distinct primary carcinomas. In 1960 he had a laryngectomy for carcinoma of

*Department of Pathology, King's College Hospital Medical School, London S.E.5.

the larynx; in 1962 a total colectomy for four distinct primary carcinomas of the caecum, transverse colon, descending colon, and rectosigmoid junction respectively; and in 1965 a pancreaticoduodenectomy for an adenocarcinoma of the duodenum. In addition, since 1960 he has had excised a number of hamartomata arising from sebaceous glands of the face. More complete details of this patient have been presented as a case report (Muir, Yates-Bell, and Barlow, 1967). There is no clinical or histological evidence of any of these primary neoplasms metastasizing to lymph nodes or distant organs. Indeed, it might be suggested that he possesses some immunological mechanism that prevents the development of metastases.

Two sources of serum γ G-globulins were used in this experiment. The first was pooled normal plasma obtained from a blood bank. The second was serum obtained from the patient. γ G-globulins were isolated from these plasma and serum samples by chromatography on diethylaminoethanol cellulose columns.

Starch-gel electrophoresis of these protein preparations showed the characteristic broad zone associated with γ G-globulins and the complete absence of other serum proteins. Under sedimentation velocity conditions in the analytical ultracentrifuge the preparations gave a single symmetrical schlieren peak, sedimenting with the velocity of 7S proteins. There was no evidence of the presence of dimer. These γ G-globulin preparations reacted with anti-human γ G-globulin antiserum and not with either anti-human γ A-globulin or γ M-globulin antiserum.

The normal γ G-globulin from the plasma pool was labelled (McFarlane, 1958) with iodine-131 and the γ G-globulin from the patient was labelled with iodine-125. The labelled proteins had a specific radioactivity of about 20 μ Ci/mg. protein. The two radioactive preparations were mixed and diluted with pooled plasma to produce a solution containing approximately 25 μ Ci of iodine-131 and 25 μ Ci of iodine-125 per ml. Each iodine isotope in the mixture has a characteristic radiation energy and can be measured quantitatively in the presence of the other.

Aliquots (2 ml.) of this solution were injected into the ante-cubital vein of each volunteer. The volunteers received sodium iodide (40 mg./day) for a week before injection of the radioactive dose and subsequently throughout the period of the experiment.

Residual radioactivity in each of the volunteers was measured over a period of nine weeks by means of scintillation counting of serum samples and by whole-body radiation counts.

The radiation counts so obtained were corrected for isotope decay. Biological half-life values were calculated in the usual manner from plots of the logarithm of the corrected count against time.

Observations

The relation between residual activity and time could not be satisfactorily represented as linear in either of the volunteers. The lines joining the experimental points took the form of shallow curves showing increasing positive divergence from linearity with time. For practical purposes the curves could be thought to be made up of two intersecting straight lines, fitting very closely the experimental points measured over the periods 7 to 28 days and 28 to 63 days respectively. The half-life values obtained from serum counting are summarized in Fig. 1.

Geiger-Müller probes were used for whole-body radiation counting. Since the emission energies of iodine-125 are too low to be detected by this method, it was only possible to measure iodine-131-labelled protein. However, the half-life values obtained for "normal" γ G-globulin by means of whole-body counting were in excellent agreement with those obtained from serum counting.

The γ G-globulins were broken down at different rates in the two volunteers. γ G-globulins in the patient were broken down at a faster rate than those in the control subject. The original source of the labelled proteins appears to have no effect on the observed breakdown rate.

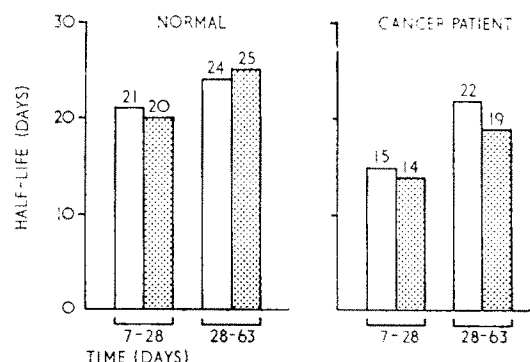


Fig. 1.—Half-life values of γ G-globulins. □ γ G-globulins from normal plasma. ■ γ G-globulin isolated from serum of patient with cancer.

The breakdown rates showed some degree of time dependence, since half-life values measured over the period 28 to 63 days are higher than those measured over 7 to 28 days. A more satisfactory demonstration of the time dependence of the half-life was provided by quantitative starch-gel electrophoresis of γ G-globulins in serum samples taken at various times (Tee *et al.*, 1965).

Under the starch-gel electrophoresis conditions we employ in this laboratory (discontinuous borate-glycine buffer system pH 8.6; 4 hour; 8–10 v. cm.⁻¹) the γ G-globulin preparations from normal serum contain approximately equal amounts of proteins migrating towards the anode (γ_1 fraction) and towards the cathode (γ_2 fraction), as measured by the radioactive label.

The radioactivity ratio γ_2/γ_1 was calculated for each serum sample and the logarithm of this ratio plotted against time (Fig. 2). It can be seen that the ratio is not constant, as would be the case if both γ_2 and γ_1 fractions were broken down at identical rates. Instead the γ_2 fraction is being broken down at a considerably faster rate than the γ_1 fraction.

Discussion

Though most workers (reviewed by Schultze and Heremans, 1966) have thought pure γ G-globulin to be degraded at a homogeneous catabolic rate, most of these workers have measured the half-life over a period of only a few weeks. It would be practically impossible to demonstrate heterogeneity of catabolism over short periods of time in terms of changes in rate of disappearance of radioactive protein.

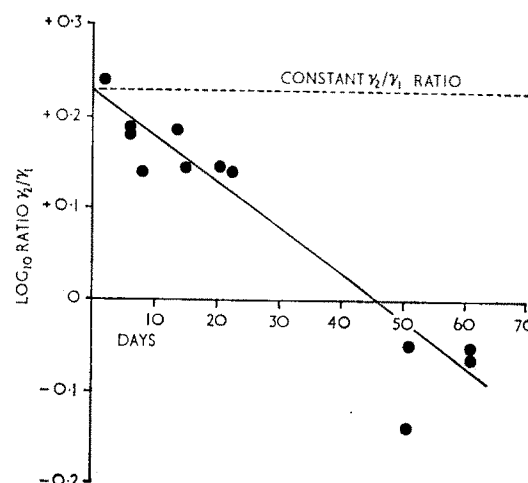


Fig. 2.—Relative survival of the serum γ_1 and γ_2 fractions in man.

The experiments reported in this paper, conducted over a period of nine weeks, indicate that different electrophoretic fractions of γ G-globulin possess different breakdown rates; the observed half-life of the entire γ G-globulin preparation being a mean of the individual values. The overall breakdown rate is non-linear and the half-life values increase with time. However, mean half-life values measured over the nine-week period were 25 days (J. W.) and 18 days (patient) respectively. These half-life values are in good agreement with those of Cohen and Freeman (1960), who reported half-life values of 21–26 days for γ G-globulins in the normal individual.

The half-life values obtained from the present experiment appeared to be characteristic of the catabolism of the individual and to be independent of the source of the labelled γ G-globulin.

The difference in the half-life values found for γ G-globulins in J. W. and the patient cannot be attributed to concentration dependence of γ G-globulin catabolism, since it was found that their serum γ G-globulin levels were 838 and 940 mg./100 ml. respectively. However, starch-gel electrophoresis experiments showed that in the patient the serum γ_2/γ_1 ratio was approximately 2:1, as compared with 1:1 in J. W. The 2:1 γ -globulin ratio would be expected to predispose the overall γ G-globulin catabolic rate in the cancer patient to be faster than that in the control subject with a 1:1 ratio, since it has been shown (Fig. 2) that the γ_2 fraction is broken down faster than the γ_1 fraction.

The possibility that the catabolic rates are affected by allo-zytic differences between the donor γ G-globulins and those of the recipient cannot be overlooked. The patient had had several transfusions during the course of operations for removal of his neoplasms. However, J. W. carried out a similar experiment to that reported in this paper on himself a year previously using homologous γ G-globulin from a normal individual. Two γ G-globulin preparations were used for this particular experiment. One was obtained from the normal donor directly and labelled with ^{125}I , the other was obtained from this donor after a "booster" injection of tetanus toxoid and labelled with ^{131}I . Both labelled γ G-globulin preparations showed the same heterogeneous breakdown pattern over a period of 15 weeks. The apparent biological half-life values were identical to those reported for J. W. in this paper. The results of this experiment

(Watkins and Tee, 1966), together with the present observations, indicate that the observed catabolic phenomena are not artifacts produced by immune response to the injected homologous γ G-globulin.

This work is now being extended to study the catabolism of γ G-globulins in other subjects, including both normal volunteers and patients with various pathological conditions.

Summary

The survival of radioiodine-labelled serum γ G-globulins was determined in a normal volunteer and in a cancer patient over a period of nine weeks.

It was found that different electrophoretic fractions of the γ G-globulin broke down at different rates. This catabolic heterogeneity of the γ G-globulins gave rise to an apparent time dependence of the observed half-life value. Mean half-life values, as measured over the entire nine-week period, were 25 days for γ G-globulins in the normal volunteer and 18 days for the same γ G-globulin preparation in the cancer patient. The breakdown rates in both individuals appeared to be independent of the source of the labelled γ G-globulins.

We thank Mr. E. G. Muir, Dr. S. B. Osborn, and Mr. M. B. Clark, of King's College Hospital, for their help and interest; and Mr. B. Godfrey, of the Radiological Protection Service, for some of the measurements of total body radiation. This work was carried out with the aid of a grant from the British Empire Cancer Campaign for Research.

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Preliminary Communications

Demonstration of an Enzyme Variant in a Case of Congenital Methaemoglobinaemia

Brit. med. J., 1967, **4**, 212–214

In normal individuals methaemoglobin in the red cell is maintained at a very low level (<1%). Raised levels may be due to: (a) intake of certain drugs which overcome the normal mechanism for maintaining a high reduction potential in the cell—removal of the toxic influence results in disappearance of methaemoglobin; (b) presence of an abnormal haemoglobin which is more susceptible to oxidation as well as being more resistant to reduction in the cell; and (c) deficiency of reduced nicotinamide adenine dinucleotide coupled methaemoglobin reductase.

Numerous cases of congenital methaemoglobinaemia due to deficiency of the reduced nicotinamide adenine dinucleotide coupled "diaphorase" have been described, the affected individual showing very low enzyme activity in both haemolysates and red cells, while the parents show intermediate levels of

activity (for review, see Jaffé and Heller, 1964). However, it has not been clear whether the defect was one of enzyme synthesis or of enzyme structure.

In the case of congenital methaemoglobinaemia here reported, it is shown by starch-gel electrophoresis of a partially purified red cell extract that the propositus possesses an electrophoretically distinct enzyme, indicating that the defect lies in the synthesis of a structurally altered enzyme protein. Normal individuals appear to possess at least two isoenzymes.

CASE REPORT

The patient, a boy aged 9, had a history of frequent upper respiratory infections and of becoming blue since birth. His milestones of development were slightly delayed, and he was not progressing well at school.

On clinical examination his lips were slightly greyish blue and his complexion was rather dusky; this finding suggested the possibility of methaemoglobinaemia as a diagnosis. There were no other abnormal physical signs. Investigations confirmed the presence of methaemoglobin in his blood, and this was again found on

numerous occasions. Chest x-ray films, routine urine analysis, and urinary chromatography for amino-acids were all normal. The tuberculin test and the Wassermann reaction were negative.

An educational psychologist, using the Wechsler Intelligence Scale, assessed the patient's full-scale I.Q. as 105 (verbal I.Q. 101, performance I.Q. 108), and noted that his "functioning fluctuates between near subnormal and very superior." Since that time, though slow and lacking in concentration, he has made reasonable progress with the aid of a remedial teacher.

Treatment with large doses of oral ascorbic acid had no obvious effect on the slight cyanosis, though his mother stated that he was better for it.

Family History.—Mother and two siblings are alive and well. There is a history of diabetes on the maternal side, and a cousin has suffered from acute haemolytic anaemia associated with glandular fever.

Investigations.—Haemoglobin 13.6 g./100 ml.; P.C.V. 40%; red cell count 4,700,000/cu. mm.; reticulocytes <1%; M.C.H.C. 34 g./100 ml.; M.C.H. 28 μ g.; M.C.V. 85 cu. μ . The red cells appeared normal on the stained blood film. Serum iron 97 μ g./100 ml. Haptoglobins (type 2-2) present in plasma. The methaemoglobin present amounted to 4.4% of the total haemoglobin. Starch-gel electrophoresis of haemoglobin showed no abnormal haemoglobin; Hb-A₂ was within normal limits. The methaemoglobin A present migrated in the normal position for methaemoglobin A. Spectroscopic examination showed that the α -absorption band was between 630 and 635 m μ . The starch-gel electrophoretic and spectroscopic properties of the methaemoglobin indicated that it was normal haemoglobin and not a type of haemoglobin M.

PREPARATION OF ENZYME EXTRACT FROM PATIENT'S RED CELLS

The separation of haemoglobin from other red cell proteins was carried out with diethylaminoethyl (D.E.A.E.) cellulose by means of a batch technique adapted from the methods of Hennessey *et al.* (1962) and Stansell and Deutsch (1965). Heparinized venous blood was centrifuged, plasma and buffy coat were removed, and the packed cells were washed three times with 0.9 g. of sodium chloride per 100 ml. Five millilitres of packed red cells were haemolysed in four volumes of ice-cold 0.005M tris (tris-(hydroxymethyl)-aminomethane) brought to pH 7 with phosphoric acid and centrifuged for 30 minutes at 35,000 g at 0° C. to remove stroma.

The decanted supernatant was passed through a Sephadex G-25 column (3 by 18 cm.), pre-equilibrated with the 0.005M tris-phosphate buffer, pH 7. The equilibrated haemolysate was collected direct into approximately 60 g. of D.E.A.E. cellulose (Whatman DE-52) equilibrated with the same buffer.

The haemolysate-cellulose suspension was stirred gently in the cold for three hours, then filtered under vacuum and washed with 0.005M trisphosphate, pH 7, until the washings were clear. This removed most of the haemoglobin and left the enzyme protein on the cellulose. The cellulose was then resuspended in the same buffer and packed under gravity into a column, 1.5 by 60 cm. The enzyme fraction was eluted from the column with 1M sodium chloride brought to pH 5.6 with phosphoric acid. This process concentrated the non-haemoglobin proteins to about 30 ml., and these were further concentrated to about 0.5 ml. by vacuum dialysis against the tris-borate-E.D.T.A. buffer, pH 8.6, used for electrophoresis. This concentrated extract had about 10 times the enzyme activity of packed red cells and was used for electrophoresis. The extract also contained a number of other red cell enzymes and proteins as well as a small amount of haemoglobin.

ELECTROPHORESIS AND STAINING OF THE GEL

Electrophoresis was carried out on starch gels with tris-borate-E.D.T.A. buffer, pH 8.6 (see Huehns and Shooter, 1965). A current of 30 mA was passed for four hours.

The enzyme has about 9,000 times the activity with the dye 2:6-dichlorophenolindophenol as substrate than it has with methaemoglobin (Scott and McGraw, 1962). The property of reducing this dye in the presence of reduced nicotinamide adenine dinucleotide was therefore used in locating the different bands of enzyme activity on the gel. Chromatography paper (Whatman 3 MM) was dipped into a concentrated filtered solution of 2:6-dichlorophenolindophenol containing about 50 mg. of reduced

nicotinamide adenine dinucleotide per 100 ml. of 1M tris buffer, pH 7.5, with 0.3 mM E.D.T.A. The saturated paper was placed on the cut surface of the gel and the whole covered with a fine polyethylene sheet to exclude air. When sufficient dye had diffused into the gel to give a uniformly blue background the paper was removed and the polyethylene replaced. The diaphorase activity could be seen on the gel as decolorized bands after approximately 15 minutes at room temperature. Photographs were taken with transmitted light on microfilm (Kodak type 5453) with a deep yellow filter.

ASSAYS OF METHAEMOGLOBIN REDUCTASE

In whole cells the method of Jaffé (1959) was used, with adenosine as "nutrient" substrate. Methaemoglobin was estimated, utilizing the difference in spectral absorption of the met- and carbonmonoxy-derivatives of haemoglobin at 632 m μ . This method is capable of measuring as little as 0.5% of the oxidized pigment. For haemolysates the enzyme was estimated as described by Scott (1960).

RESULTS

Whole Cells.—The results are shown in Fig. 1. The patient's cells show a very low rate of reduction of methaemoglobin compared with those of the mother and normal controls, which had almost completely re-formed oxyhaemoglobin after 17 hours. The mother falls within the range for normal individuals. In the absence of nutrient substrate there was a rise in the methaemoglobin level in the first three hours of incubation of about 10%, after which time the levels remained constant.

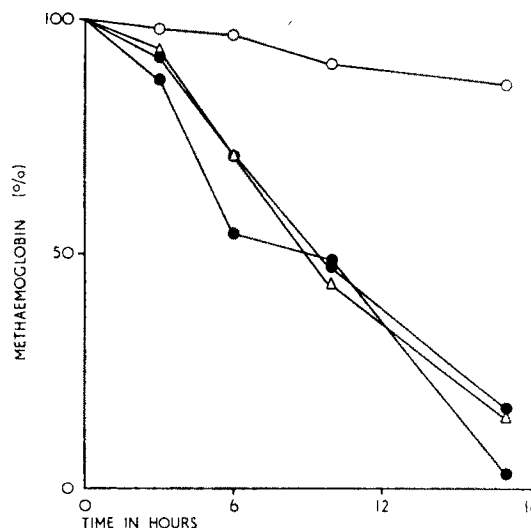


Fig. 1.—Reduction of methaemoglobin to haemoglobin during incubation of nitrite-treated red cells. The reduction of methaemoglobin is expressed as a percentage of the methaemoglobin content of the nitrited washed cells at the start of the incubation. ○—○ Patient with methaemoglobin reductase deficiency. △—△ Mother of patient. ●—● Normal controls.

Haemolysates.—The results are shown in the Table. The propositus again shows very low activity while the mother falls within the normal range.

Methaemoglobin Reductase Activity in Haemolysates

	Change in optical density at 600 m μ /1 ml. packed red cells per minute
Patient	0.15
Mother	0.95
Normal controls (25)	1.37 $\pm$ 0.40 (S.D.)

Starch-Gel Electrophoresis.—In normal individuals at pH 8.6 two light bands appear migrating more slowly than Hb A towards the anode (Fig. 2). The patient has only one band of intermediate mobility and much lower activity as judged by the rate and intensity of decolorization of the dye. The patient's mother shows the two normal bands, as well as a weak band in the same position as

that of her son. This is not shown in the photograph, as the relative intensities of the bands made this technically difficult. No such band has been seen in 35 unrelated normal individuals studied in this way, and dilution of the normal concentrate did not alter the electrophoretic pattern.

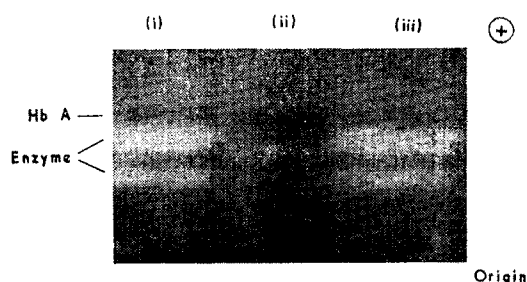


FIG. 2.—Starch-gel electrophoresis of enzyme extract prepared from red cells stained for reduced nicotinamide adenine dinucleotide-methaemoglobin reductase. (i) normal red cells, (ii) methaemoglobinaemic red cells, (iii) normal red cells.

DISCUSSION

The deficiency of "coenzyme factor I" (diaphorase, reduced nicotinamide adenine dinucleotide linked methaemoglobin oxidoreductase) described by Gibson (1948) has been confirmed in many patients with congenital methaemoglobinaemia.

The deficiency could be the result of two possible situations: (a) reduced rate of synthesis of a normal enzyme; and (b) normal rate of synthesis of an abnormal enzyme which is either stable, with a low specific activity, or unstable, resulting in non-uniform distribution of activity in old and young cells.

Scott (1962) and Scott *et al.* (1965) have partially purified reduced nicotinamide adenine dinucleotide methaemoglobin reductase from methaemoglobinaemic red cells. This enzyme shows altered properties with respect to pH and temperature stability compared with enzyme from normal individuals. Keitt *et al.* (1966) found that old red cells separated by ultracentrifugation from patients with this enzyme deficiency contained more methaemoglobin than young cells. These results suggest that in these patients the enzyme activity in the red cells is due to the presence of an abnormal unstable enzyme. The present finding of an electrophoretically abnormal enzyme is consistent with this idea. However, the defect present in this family may be different from that found by other investigators, because the amount of methaemoglobin in the patient was only 4.4% of total haemoglobin, whereas in other reported cases values range between 8 and 45% (Jaffé and Heller, 1964; Fialkow *et al.*, 1965; Jaffé *et al.*, 1966). Furthermore, the mother of our patient has an enzyme activity which falls within the normal range, whereas the heterozygotes reported by Scott (1960) have approximately half the normal enzyme levels. The finding of normal enzyme levels in the mother of our patient is consistent with the presence of both normal and abnormal enzymes. The presence of the abnormal enzyme protein in the mother allows the definite identification of the heterozygous state, which previously has only been presumptive, being based on the level of enzyme activity present. The father of our patient has so far not been studied.

The association of the synthesis of abnormal proteins or enzymes with disease has been well documented in, for example, the haemoglobinopathies (see Huehns and Shooter, 1965) and

in glucose-6-phosphate dehydrogenase deficiency (Marks, 1964). The present investigation suggests that congenital methaemoglobinaemia due to reduced nicotinamide adenine dinucleotide methaemoglobin reductase deficiency is also of this type, and study of other patients with this disease may show that it can also be caused by a number of electrophoretically distinct enzymes.

SUMMARY

A partially purified protein extract was prepared from the red cells of a patient with congenital methaemoglobinaemia and from normal individuals. Electrophoresis of these extracts at pH 8.6 and staining with a 2:6-dichlorophenolindophenol/reduced nicotinamide adenine dinucleotide system showed two decolorized bands of diaphorase activity in normal individuals and a single band of intermediate mobility in the patient. The mother of the patient showed both normal and abnormal enzymes. It is suggested that the enzyme deficiency in this patient is the result of the synthesis of an abnormal form of reduced nicotinamide adenine dinucleotide linked methaemoglobin reductase.

We wish to thank Dr. G. A. Matthews, consultant pathologist, West Herts Hospital, for his co-operation in undertaking many of the laboratory investigations, and Dr. H. M. Brunt for having kindly referred this patient.

C. A. WEST, B.A.,
Biochemist.

B. D. GOMPERTS, PH.D.,
Biochemist.

E. R. HUEHNS, M.D., PH.D.,
Senior Lecturer in Haematology.

Medical Research Council Group in Haemolytic Anaemias,
University College Hospital Medical School,
London W.C.1.

I. KESSEL, M.B., M.R.C.P., M.R.C.P.E.D., D.C.H.,
Consultant Paediatrician.

J. R. ASHBY,* M.B., B.S., D.C.H.,
Formerly Senior House Officer.

Department of Paediatrics,
West Herts Hospital,
Hemel Hempstead.

* Present address: P. & O. Lines, Medical Department, London E.1.

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Medical Memoranda

Severe Anaphylactic Reaction after a Soap Enema

Brit. med. J., 1967, 4, 215

While local reactions and skin eruptions have been described following the use of soap enemas (Barker, 1945; Bendit, 1945; Turrell, 1959) there appears to be no record of an anaphylactic reaction of the type and severity shown in the following case.

CASE REPORT

The patient, a 33-year-old para-1, was booked for domiciliary confinement. Her past obstetric career had been uncomplicated and her previous health good. In particular, she had no history of asthma, skin rashes, or other allergic phenomena, and there was no such family history. Three days before her expected date of delivery she experienced vague abdominal pains, but labour failed to become established. The district midwife administered an enema, using a solution of "two handfuls" of a proprietary brand of soap-flakes in approximately 2 pints (1,140 ml.) of warm water and instilled by means of a tube and funnel. Immediately this solution was run in the patient noted that her mouth was becoming swollen, and that she had "pins-and-needles" in her limbs and tightness in her chest. She was unable to swallow and felt as if she was choking. On attempting to rise she collapsed and became unconscious, and when medical aid arrived shortly afterwards the pulse and blood pressure could not be recorded and the foetal heart was 40 beats a minute. Oxygen therapy was begun and she was brought to the near-by hospital without delay.

On admission she was pale and acutely shocked, but was conscious and able to answer simple questions. The blood pressure was 70/40 mm. Hg. The radial pulse was barely palpable and the apical heart rate 88 a minute. There was a spreading urticaria on the thighs, upper arms, trunk, and face which became more pronounced during examination. On auscultation of the chest there was generalized bronchospasm. The foetal heart rate was 160. Treatment was instituted promptly with 0.5 ml. of 1:1,000 adrenaline in 5 ml. of sterile saline subcutaneously and 100 mg. of hydrocortisone and 10 mg. of Piriton (chlorpheniramine maleate) intravenously. Oxygen therapy was continued. Within two hours her blood pressure had risen to 110/90, the rash was beginning to fade, and regular labour contractions had begun. Labour progressed rapidly and after a further two hours, when the cervix was almost fully dilated, the membranes ruptured and there was thick meconium staining of the liquor. The foetal heart rate dropped to 80. Mid-cavity forceps delivery was effected without difficulty.

The baby, a male weighing 5 lb. 8 oz. (2.5 kg.), had inspired meconium and had an Apgar score of only 4, but after clearing of the airways, endotracheal intubation, and oxygen administration his condition improved and spontaneous respiration was established after 15 minutes. The third stage of labour was completed normally within 10 minutes. The puerperium was normal. Bowel function returned on the second day and continued normally. The infant progressed well and his condition was satisfactory on dismissal.

COMMENT

Many substances have been employed in clearing enemas—olive oil, paraffin, glycerin, turpentine, and soap, to name but a few. The commonest of these is undoubtedly soap, which varies widely in chemical composition and may contain such irritating substances as strong alkali, phenol, and potash. Turrell (1959) described the irritating effects of hypertonic phosphate on the colonic mucosa. Lewis (1965) condemned the use of strong sodium biphosphate solution for enemas and

quoted instances where different kinds of hospital soap were collected together in a jar and diluted quite arbitrarily with 200–2,000 ml. of water. One of his cases (settled out of court) had received an enema with scouring powder. As reported by Lewis (1965), Shambotte and Degrotte in 1960 recorded a fatal case of renal anuria where an 8-day-old baby received an enema containing a phenol soap.

Local reactions have varied from simple irritation to frank necrosis. According to Gabriel (1937) these are more common than is generally supposed, and Hicks (1944) found that one-third of his series had suffered irritative effects. Bendit (1945) described a case of rectal gangrene in a patient who received two successive soap enemas, and a case of severe haemorrhage is reported from Minneapolis (Lewis, 1965) following the use of undiluted soap. Turrell (1959) stated that where there is local reaction, proper evaluation of the colonic mucosa at sigmoidoscopy may be interfered with, and not only may a barium enema be much more uncomfortable, but x-ray appearances may be misleading owing to loss of haustrations.

In most of the cases quoted recovery occurred, but abnormal bowel function persisted for three months or more (Lewis, 1965), and Pinnock (1937), Murray (1937), and Gabriel (1937) quote six deaths from soapsuds enemas. While specific series are lacking, standard works of dermatology quote erythematous, papular, or scarlatiniform rashes as "occasional complications" of enemas and mention the danger of stirring up an anal eczema, which may become more generalized and may follow the use of water alone.

Enemas are sometimes used in hospital and domiciliary practice and occasionally by patients themselves without a valid indication. They are usually effective, but often oral preparations or suppositories might have been equally so. Many of the substances used may be harmful. Phenol-containing soaps are absolutely contraindicated and proprietary soap powders or flakes may be highly dangerous. It appears that insufficient attention has been paid to the chemical composition of the soap and the strength of the solution. The recommended dose of soft soap is one teaspoonful diluted in a quart (1,140 ml.) of warm water. Where serious reactions occurred preparations other than soft soap were used and the solution was often very much more concentrated. Repeated soap enemas may cause mucosal damage, particularly if a portion of the first enema is retained. Introduction of the enema fluid under high pressure is hazardous as the haemorrhoidal venous plexus may be entered, bypassing the portal circulation and liver detoxification. There is also the risk of bowel perforation where local infection pre-exists. Finally, it is suggested that enemas may be contraindicated where there is a history of allergic phenomena or sensitivity reactions, particularly to soap derivatives.

I wish to record my thanks for helpful advice and literature to Mr. M. R. Neely, consultant obstetrician, Ulster Hospital, Dundonald, Belfast, under whose supervision this patient was treated.

DONALD SMITH, M.B., CH.B., M.R.C.O.G.,
Senior Registrar, Royal Maternity Hospital, Belfast.

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Fatal Lactic Acidosis after an Overdose of Phenformin

Brit. med. J., 1967, 4, 216

A number of papers have been published concerning the dangers encountered in the use of the diguanide phenformin as an oral hypoglycaemic agent (Walker *et al.*, 1960; Ewy *et al.*, 1963; Tranquada *et al.*, 1963). The purpose of this report is to record the fatal outcome in a patient who had ingested 50 mg. of phenformin in excess of the prescribed dose.

CASE REPORT

The patient, a 64-year-old housewife, had been known to suffer from maturity-onset diabetes for four years. She was treated with chlorpropamide for 18 months, and then with a 1,000-calorie diet (130 g. of carbohydrate) alone for three months. She remained more than a stone (6.4 kg.) above the standard weight for her height and was therefore started on phenformin in May 1964 in order to treat her mild hyperglycaemia and to facilitate weight reduction. The dose of phenformin was gradually increased and for five months before admission to hospital, on 10 June 1965, she was taking 25 mg. q.i.d. She had been in good health until 24 hours before admission, when the sudden onset of generalized abdominal pain was closely followed by vomiting of watery material. Her bowels were regular and a normal motion was passed in the interval between the onset of symptoms and admission. She denied any dyspeptic history or symptoms referable to the renal tract or cardiovascular system. The pain remained generalized and did not radiate from the abdomen. Twelve hours before the onset of her symptoms (36 hours before admission) she had mistakenly ingested two 25-mg. phenformin tablets in excess of her normal dose—that is, a total of 50 mg. in divided dosage in 12 hours.

On examination the patient, who lived in comfortable circumstances, was ill, pale, and obese and had acidotic respirations, but acetone could not be detected in the breath. She was moderately dehydrated. The rectal temperature was 88.2° F. (31.2° C.), she was orientated and examination of the peripheral nervous system showed no abnormality, though the plantar responses could not be elicited. Neither pupil reacted to light or to accommodation, and the left was larger than the right. The left fundus was normal and the right was obscured by cataract. Her chest was clinically and radiologically normal, and examination of the abdomen (including rectal investigation) showed no abnormality. The pulse was of poor volume, though regular at 100 per minute. No signs of cardiac failure were observed and the heart sounds were normal. Blood pressure was recordable at 96/60 mm. Hg only after 7 mg. of metaraminol (Aramine) had been given intravenously.

The laboratory findings on admission were as follows: Hb 16.6 g./100 ml.; W.B.C. 20,600/cu. mm., differential normal; E.S.R. 11 mm. in the first hour. Urinalysis showed moderate proteinuria, no glycosuria, and only a trace of ketones to Acetest and negative ferric chloride reaction. There were no cells or casts in the urinary deposit. E.C.G. showed left ventricular hypertrophy and ischaemia; J waves were not present. Serum and electrolyte values (sodium, potassium, and chloride) were normal. Blood urea was 140 mg./100 ml., falling to 84 mg./100 ml. after dehydration. No salicylates were detected in the serum, and the values of serum transaminases (S.G.O.T., S.G.P.T.) and of serum amylase were normal. The plasma CO₂ combining power was 1.8 mEq/l. Blood sugar was 140 mg./100 ml. and the serum lactic acid level was 240 mg./100 ml. (26.7 mM./l.) five hours after admission.

Therapy was started with intravenous dextrose 5% and isotonic saline with added metaraminol and sodium bicarbonate. After 12 hours of such treatment her condition remained desperate. Despite giving 400 mEq of sodium bicarbonate and 120 mg. of metaraminol a total of 2,700 ml. of intravenous fluid she remained oliguric and grossly acidotic. At this point, 12 hours after starting treatment, the CO₂ combining power was 4.9 mEq/l. and the arterial pCO₂ 6.92 (Pco₂ less than 30 mm. and standard bicarbonates less

than 6 mEq/l.). The rectal temperature had risen to 94° F. (34.5° C.).

The patient's condition and blood pressure improved slightly after the infusion of 540 ml. of 10% dextrose in two hours, and 600 ml. of urine was passed in the second 12 hours, the blood pressure being 90 to 110/50 to 60 mm. Hg. Twenty-eight hours after admission she had a cardiac arrest. Immediate resuscitation was unsuccessful. Post-mortem examination failed to reveal any significant disease apart from thrombosed splenic vein.

Comment.—The only recognized factor which could contribute to the metabolic acidosis was the history of taking 50 mg. in excess of her usual 100 mg. daily of phenformin. She had no significant uraemia, salicylism, infection, or external cause for her acidosis and there was no preceding period of severe carbohydrate deprivation.

DISCUSSION

Walker *et al.* (1960) discussed the action and side-effects of phenformin. It was suggested that associated acidosis was more likely to occur in juvenile diabetics on phenformin than in older diabetics. The degree of lactic acidosis found in our patient is an example of a rare occurrence in such an elderly mild diabetic. Dobson (1965) reported a case of attempted suicide by means of phenformin. A dose of 850 mg. was ingested but no acidosis was present. It was suggested that the gastrointestinal irritation may protect against the absorption of an overdose of this drug. This was not the position with our patient.

Huckabee (1961) described an ill-defined group of patients, not necessarily diabetic and not having any drug in common, who died in severe metabolic acidosis caused mainly by raised serum lactic acid. He believed the common factor in such cases was widespread tissue hypoxia of indeterminate cause. Such a vague description could of course fit our patient, irrespective of any drugs, but the distinct possibility exists that the trigger mechanism for the development of lactic acidosis was the modest overdose of phenformin. It is known that blood lactic acid levels may be expected to rise under the influence of phenformin in doses similar to those taken by our patient, but normally the rise is modest—for example, 4 to 31 mg./100 ml. (Craig *et al.*, 1960). The finding of 240 mg./100 ml. in our patient is clearly of a different order of magnitude and difficult to explain. There was no clinical or post-mortem evidence of any process to cause hypoxia, which is a well-recognized cause of hyperlactacidaemia (Shepardson *et al.*, 1962).

We gratefully thank Mr. T. Clark (City Analyst) and Professor S. C. Frazer and their staffs for the biochemical estimations so willingly carried out.

D. W. PROCTOR, M.B., CH.B., D.OBST.R.C.O.G.
J. M. STOWERS, M.A., M.D., F.R.C.P., F.R.C.P.ED.

City Hospital,
Aberdeen.

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New X Wave in Electrocardiographic Complex

Brit. med. J., 1967, 4, 217

Changes in the electric potentials during a cardiac cycle producing positive or negative deflections in an electrocardiographic tracing have been designated by the well-known PQRSTU (including R' or r' and S' or s'). All these waves can be individually recognized in most of the leads. An additional upright deflection after U is described below which so far as we are aware has not been reported in English literature. This was encountered during routine electrocardiographic recordings of cases of cerebrovascular accidents.

CASE REPORT

The patient, a 55-year-old Hindu man, was admitted to hospital on 16 February 1966 with a history of sudden loss of consciousness lasting about half an hour and inability to use the right upper and lower limbs two hours before admission.

On examination he was found to be of average build. He was conscious, but had expressive aphasia. Pulse was 56 per minute,

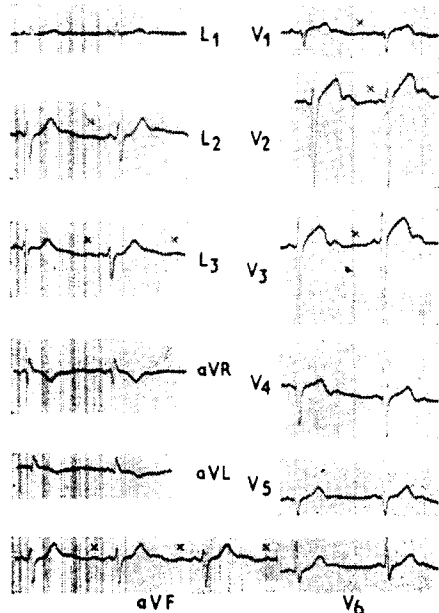


FIG. 1.—Electrocardiographic record taken on 18 February 1966, showing an additional upright wave marked X in L2, L3, aVF, V1, V2, and V3.

B.P. 160/98 mm. Hg. There was right hemiplegia with exaggeration of deep tendon reflexes. Right plantar response was extensor. Fundus showed arteriosclerotic changes. Cerebrospinal fluid and routine blood and urine examinations were normal. Venereal disease research laboratory test was negative in blood. He remained more or less in the same state until 28 February, when he suddenly lost consciousness and died an hour and a half later. Necropsy was refused.

Electrocardiograms were taken on 16, 18, 20, 26, and 28 February. The first immediately on admission and the last a few minutes before death.

Electrocardiographic Findings.—Analysis of the record of 18 February (Fig. 1), two days after admission, shows a heart rate of 50 per minute, P-R interval 0.12 sec., and Q-Tc 0.46 sec. Configurations of PQRST can be recognized in all the leads. The U wave is distinctly identifiable in nearly all the leads. An extra upright deflection (termed X) following U and just preceding P of the second cycle is seen in L2, L3, aVF, V1, V2, and V3. It is most prominent in lead aVF (Fig. 2), where it measures a little more than 0.5 mm. in height and 0.2 sec. in duration.



FIG. 2.—Prominent X in lead aVF.

This additional wave was not seen in any of the electrocardiograms (Fig. 3) recorded on four other occasions during his stay in hospital.

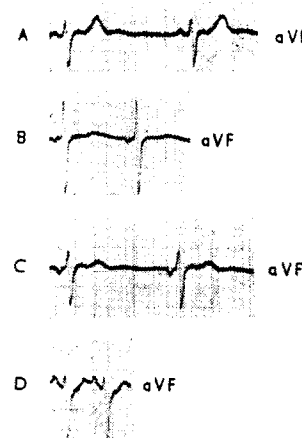


FIG. 3.—Normal tracings without any extra deflection. Only leads aVF shown. A, 16 February. B, 20 February. C, 26 February. D, 28 February.

COMMENT

Our first impression was to reject this extra deflection as an artifact due to stylus or other mechanical defect. But the isoelectric line was steady and unwavering and all the neighbouring waves—T, U, and P—were prominent and unmistakably clear. This extra deflection could also be made out in a number of leads at the same time sequence. On this basis identity of this extra upright deflection as a separate wave could not be doubted.

We venture to suggest that, like the U wave, the X wave may also indicate a very delayed completion of the process of repolarization. Readjustment of potassium and sodium ions through the cell membrane may not have been stabilized by the end of the U wave.

B. L. AGARWAL, M.D., M.R.C.P.,
Professor and Head of Department of Medicine,
M.L.N. Medical College, Allahabad.

C. B. GUPTA, M.B., B.S.,
Registrar, Department of Medicine,
M.L.N. Medical College Allahabad.

Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Hiatus Hernia

MICHAEL ATKINSON,* M.D., F.R.C.P.

Gastro-oesophageal reflux is one of the commonest causes of dyspepsia in this country and is usually due to hiatus hernia. Yet many clinicians still in the prime of their careers were trained before the syndrome of gastro-oesophageal reflux or the significance of hiatus hernia was generally appreciated, and 20 years ago these received little attention in the medical curriculum. It is hardly surprising that today hiatus hernia is often overlooked, and it is worth restating the ways in which it may present.

Types of Hernia

On anatomical grounds hiatus hernia is commonly divided into three types.

The *sliding type* is most frequently encountered, and here the oesophago-gastric junction moves up through the hiatus into the chest producing a bell- or funnel-shaped configuration. These hernias present with symptoms of gastro-oesophageal reflux, and though they are often quite small and reducible the severity of symptoms bears no relation to their size or mobility. Only when oesophagitis has caused much fibrosis is the oesophagus shortened, and hence "short oesophagus" is virtually always the consequence and not the cause of the hernia.

The *para-oesophageal* variety is characterized by herniation of the fundus of the stomach and gastro-colic omentum through the hiatus alongside the cardia, which retains its normal position. This is the least common variety and often produces few symptoms. It may be impossible to distinguish from herniation through a diaphragmatic defect separate from but close to the oesophageal hiatus—which is not of course a true hiatus hernia yet is believed by many to be the usual origin of this type of hernia.

The *mixed* variety is far commoner than a true para-oesophageal hiatus hernia, with which it is often confused because of difficulty in determining the positions of the cardia relative to the hiatus. Here the symptoms are usually those of gastro-oesophageal reflux, though many remain silent. Symptoms of obstruction may occur, since the cardia lies above the diaphragmatic hiatus—the herniated portion of the stomach may become distended with food if the hiatus is small.

Causation of Hiatus Hernia

Hiatus hernia is usually an acquired condition, the causes of which are still incompletely understood. Unlike other abdominal hernias it is seldom clearly related to trauma or to sudden muscular straining increasing intra-abdominal pressure. Very occasionally a patient does feel a sharp tearing retrosternal pain on straining shortly before symptoms of gastro-oesophageal reflux commence, but it seems probable that this is a separate entity from the common type of hiatus hernia, and it usually occurs in younger subjects.

*Consultant Physician, Worcester Royal Infirmary.

At one time congenital laxity of the diaphragmatic hiatus was believed to be the basic abnormality causing hiatus hernia. However, hernia is not common after diaphragmatic paralysis, when the hiatus might be expected to be lax, which casts doubt upon this view. Perhaps of greater causative importance is impairment of the normal anchoring mechanism of the stomach. The role of the phreno-oesophageal ligament has been stressed by surgeons. It is normally a diaphanous structure which may atrophy with advancing age, permitting herniation to occur. Loss of muscle tone in the stomach may facilitate the upward passage of the cardia through the hiatus; this would explain the increased incidence of hiatus hernia in progressive systemic sclerosis, in which the musculature of the alimentary tract becomes atonic. After partial gastrectomy the mobility of the remaining portion of the stomach is increased, and this might well account for the frequency of small hiatus hernias and symptoms of reflux after this procedure.

Hiatus hernia may appear during pregnancy but disappear again after delivery, suggesting that it is not a congenital abnormality but one acquired as a consequence of the upward displacement of the stomach and possibly of hormonally induced gastric muscle hypotonicity occurring during pregnancy.

Clinical Presentation

Hiatus hernia may exist without producing symptoms, and it has been estimated that in only 25% of cases are these severe enough to cause the patient to seek medical advice. This accords well with the frequent finding of asymptomatic hiatus hernia on barium meal examination done for some other disorder. Furthermore, symptoms may abate spontaneously for long periods or even permanently, which of course makes assessment of the results of therapy difficult. Fluctuations in body weight and emotional state may determine their presence or absence or the disability they may cause.

Symptoms when present are usually caused by gastro-oesophageal reflux and its consequences, but with larger hernias obstructive symptoms may be encountered at the level of the diaphragm.

Gastro-oesophageal Reflux

These symptoms usually dominate the clinical picture in patients with sliding hiatus hernia. Most of the population has had occasional heartburn, belching, or acid-tasting fluid rising into the mouth at one time or another, and it is difficult on occasions to distinguish the point at which these become pathological.

Heartburn and Chest Pain.—Heartburn is a word commonly used by patients to describe a burning discomfort in the front of the chest sometimes radiating up into the neck or into the interscapular region. Many will deny that the discomfort

amounts to pain, but others experience severe pain, which may be difficult to distinguish from cardiac pain. The postural relationships of the pain are useful diagnostic pointers. Oesophageal pain often wakes the patient at night, and many have learned by experience that this can be corrected by sleeping propped up on pillows. Stooping or bending forward—when weeding the garden, sitting behind the wheel of a car, or in front of a television set—are characteristic aggravating factors. Swallowing hot or irritating fluids may aggravate the pain.

The differentiation of oesophageal from cardiac pain is not always easy, and the consequences of error are serious. No single feature of the pain provides a completely reliable guide, and the clinician must consider many factors in the history in coming to a diagnosis. The character of the pain is of some value, since oesophageal pain is commonly burning, while cardiac pain is often constricting in character.

Oesophageal pain may radiate to the arms, but pain down both arms is most frequently cardiac in origin. Pain brought on by emotional stress is as likely to be oesophageal as cardiac, and pain occurring after a heavy meal might well be anginal. Relief by antacids points strongly towards an oesophageal source for pain, but amyl nitrite seldom relieves oesophageal pain. If in doubt it is wise to assume that the pain is cardiac, at least for the first few days, bearing in mind however that recumbency and anticoagulant therapy may aggravate reflux oesophagitis and on occasion precipitate bleeding from the inflamed oesophageal mucosa.

Acid regurgitation into the mouth is a less common manifestation of gastro-oesophageal reflux, because the presence of gastric juice in the gullet frequently evokes a secondary peristaltic wave which sweeps it back into the stomach. Like heartburn, acid reflux has a postural relationship, occurring in recumbency or on stooping, and in its mildest form causes only a sour taste in the throat on waking. When more severe, large quantities of acid-tasting fluid rise into the throat without the physical effort of retching or straining. If regurgitation is copious choking attacks may wake the patient at night and aspiration pneumonia can occur.

Belching often complicates gastro-oesophageal reflux in hiatus hernia and usually results from air-swallowing to relieve heartburn. It may at times cause abdominal discomfort from distension and excessive flatus.

Anaemia and Bleeding

Inflamed oesophageal mucosa is friable—as every endoscopist knows. When the mucosa is inflamed the passage of food through the gullet may induce bleeding of sufficient degree eventually to cause anaemia. Furthermore, tablets of aspirin or phenylbutazone may remain in contact with the inflamed mucosa for a long enough period to induce bleeding and may precipitate haematemesis or melaena in patients with hiatus hernia.

One of the difficulties which may impede clinical diagnosis is the frequent paucity of dyspeptic symptoms in patients with reflux oesophagitis severe enough to cause bleeding. The bleeding may be intermittent, and therefore occult blood tests on the stools are not always positive. Hence reflux oesophagitis is often overlooked in elderly patients with iron deficiency anaemia and the diagnosis can only be verified directly by oesophagoscopy—which of course is not free from risk in the patients in this age group.

A further cause of acute bleeding in patients with hiatus hernia is a mucosal tear at the cardia (Mallory-Weiss syndrome). The presence of a small sliding hernia appears to predispose to the occurrence of such tears, presumably because this part of the stomach is then exposed to the considerable abdomino-thoracic pressure gradient which occurs during retching and vomiting.

Dysphagia

Dysphagia in hiatus hernia may be caused by stricture formation or less frequently by muscle spasm. Stricture is easily the most serious complication of reflux oesophagitis and is characterized by constant dysphagia in contrast to the much more variable difficulty encountered in patients with oesophageal spasm. The development of a tight stricture usually results in cessation of heartburn or acid reflux into the mouth, since the upward passage of gastric juice is impeded by the narrowing. Dilatation of the stricture may relieve dysphagia only for this to be replaced by heartburn and acid regurgitation. Radiological diagnosis of hiatus hernia may be difficult when stricture is present, because little barium passes down into the stomach, and the extent of the narrowing is then also difficult to define.

Dysphagia caused by oesophageal spasm is seldom severe enough to cause nutritional impairment. Heartburn is usually prominent and the differentiation from fibrous stricture by radiological or endoscopic means is not difficult. While the typical radiological appearances of corkscrew oesophagus caused by muscle spasm are readily recognized, the crenated, sawtooth outline of the gullet seen when the spasm is less marked must be distinguished from the filling defects of oesophageal varices.

Spasm commonly occurs in the middle and lower portions of the oesophagus, but a localized muscle contraction or thickening at the oesophago-gastric mucosal junction has been described in patients with hiatus hernia and has been called the lower oesophageal ring. This causes intermittent dysphagia and is visible as an annular narrowing just above the level of the diaphragm on x-ray films of the barium-filled oesophagus. At endoscopy such rings are often missed, but a shelflike fold of mucosa may be visible at the cardia. It is important that the rings should not be confused with fibrous strictures, since the disability they cause is seldom sufficient to warrant surgical intervention and the outlook with conservative treatment is good.

Obstructive Symptoms

These are confined to patients with larger hernias of the para-oesophageal or mixed type, which have often been known to be present for many years. Acute symptoms result from mechanical obstruction at diaphragmatic level with incarceration or strangulation. When the diaphragmatic hiatus remains tight food may impact at this level causing distension of the herniated portion of the stomach. Torsion of the stomach may occur with forward and upward rotation of the body through the diaphragm pulling the pylorus upwards. The greater curvature becomes the most cephalad portion of the stomach, the fundus falls back into the abdominal cavity, and the body of the stomach is left above the diaphragm. Acute angulation occurs at the junction of the body with the antrum where the stomach passes through the hiatus, and gangrene of the herniated stomach often rapidly supervenes from obstruction to the blood supply.

The onset of severe pain in the lower chest and upper abdomen, often associated with shock, frequently leads to confusion with cardiac infarction and fatal delay in instituting surgical treatment. Absolute dysphagia occurs but can be masked by constant retching. The herniated portion of the stomach is often enormously distended, and the presence of a fluid level behind the heart shadow is a useful radiological pointer to the diagnosis. The heart may be displaced by the distended stomach, and this positional change may give rise to electrocardiographic abnormalities, notably T wave inversion in leads III and AVF, which in conjunction with the clinical picture may lead to a mistaken diagnosis of posterior cardiac infarction.

Associated Disease

Oesophageal spasm has already been mentioned as a result of reflux oesophagitis. When it is severe and persistent it may cause pronounced hypertrophy and muscular wall of the oesophagus.

Gastric Ulcer.—Chronic gastric ulcer of the level of the diaphragmatic hiatus occasionally complicates the larger hiatus hernias due to trauma from food passing through the narrowing in this situation. After reduction of the hernia the ulcer usually heals rapidly.

Carcinoma of the Oesophagus.—Carcinoma of the gastric cardia has been reported in patients with hiatus hernia, but it seems doubtful whether this can be recognized as a true complication of reflux oesophagitis. These tumours are usually adenocarcinomas and not the squamous growths which might be expected if chronic irritation is an aetiological factor—as for example in oesophageal carcinoma after ingestion of corrosive poisons. Moreover, oesophagitis is frequently the consequence of a neoplasm in this situation interfering with the competence of the cardia. Bleeding from chronic reflux oesophagitis complicating hiatus hernia often causes iron deficiency and may so favour the occurrence of postcricoid carcinoma.

Management of Hiatus Hernia

The real difficulty which the management of hiatus hernia presents stems from the extreme variability of the disability it causes. On the one hand in many patients it is symptomless, but on the other hand it can lead to oesophageal stricture, which in the elderly carries a considerable mortality. It is not surprising that widely divergent views have been expressed about the relative merits of the numerous surgical procedures which have been used. Information is needed about the natural history of untreated hiatus hernia and the influence which the presence and severity of changes of oesophagitis seen at endoscopy have upon the outlook.

Before embarking on treatment adequate radiological studies are required to determine whether symptoms of reflux have been precipitated by delay in gastric emptying caused by duodenal or pyloric ulcer or by gastric carcinoma either near the pylorus or at the cardia.

Medical Measures

Two features of hiatus hernia which commend medical measures, at least at the onset, are its predilection for the middle aged and elderly and the mildness and tendency to spontaneous remission of the symptoms in many cases. The aims of medical treatment are fourfold:

- (1) To minimize reflux of gastric juice into the gullet.
- (2) To neutralize the acid of the gastric juice.
- (3) To protect the oesophageal mucosa by the use of demulcents.
- (4) To deal with any superadded emotional tension.

Since heartburn is precipitated by lying flat and by stooping and bending forwards, and since oesophageal acidity measurements reveal these movements to be accompanied by acid reflux, it seems logical to ask the patient to avoid such positions as far as possible. Sleeping propped up on pillows affords relief early in the night, but sooner or later the patient slips down and reflux occurs. For this reason and also to avoid the slight abdominal compression which occurs in the lying posture it is preferable to tilt the whole bed using 4–8 in. (10–20 cm.) blocks (one or two builder's bricks) under the head of the bed. Should the patient slide down the bed the patient is unaltered. In severe cases a cardiac bed may be required, but these are rare. The avoidance of constricting clothing around the abdomen is usually recommended but often

ignored by the obese. Many patients with hiatus hernia develop symptoms of reflux after gaining weight, and in these weight reduction gives striking symptomatic relief. Indeed, the major importance of diet in hiatus hernia is in the control of obesity, and a strict gastric diet has little value and may cause harm by increasing obesity. Very hot drinks and hard foods such as toast may cause pain when swallowed, while other patients find foods such as onions and cucumber—which may remain in the stomach for long periods exciting acid secretion—cause heartburn and are best avoided.

Antacids usually give relief from pain in reflux oesophagitis, and treatment should aim at neutralizing the gastric as well as the oesophageal contents for as long as possible. Aluminium hydroxide gel remains one of the most effective remedies, as it also has a demulcent action. Anticholinergic drugs have no place in the treatment of reflux oesophagitis, since they not only relax the oesophago-gastric sphincter and thus favour reflux but abolish oesophageal peristalsis and so allow any gastric juice to remain in the gullet for long periods during the night.

In patients with severe symptoms milk with added aluminium hydroxide dripped continuously into the mid-oesophagus for 7–10 days is often strikingly effective in relieving symptoms and improving oesophagitis. The patient should be propped up to reduce the risk of aspiration into the lung.

Polymethyl siloxane is a silicone preparation which reduces surface tension, thus preventing foaming by allowing coalescence to form a single large gastric air bubble which is more easily expelled and in the process less likely to carry gastric juice up into the gullet. Furthermore, it has some coating action and may protect the inflamed oesophageal mucosa. To be of benefit it must be given regularly in doses of 250 mg. and is combined with antacids in the preparation Asilone.

Oxethazine is a surface anaesthetic, which is usually combined with an antacid in preparations such as Mucaine. When pain from oesophagitis is refractory to other measures it is frequently effective, particularly during pregnancy. Caution is necessary, since relief of pain does not imply improvement in oesophagitis, which may actually progress. Use of the drug is therefore best confined to patients who have pain with minimal changes at oesophagoscopy, and it is inadvisable to give it for long periods, since a stricture may quietly develop.

Finally the patient's emotional state may determine his reaction to his oesophageal symptoms. Anxious patients have a particular fear of chest pain, and reassurance together with tranquillizing drugs may help to restore to its true perspective discomfort due to mild reflux.

Retrospective surveys of patients with hiatus hernia managed conservatively suggest that ten years later 60% remain symptom-free or much improved, but this figure falls to 40% if endoscopic evidence of oesophagitis is present. Medical measures are ineffective in giving adequate relief in a minority of patients and surgical treatment has to be considered.

Surgical Treatment

If a tight stricture and fibrotic shortening of the gullet are absent the simplest surgical procedure is reduction of the hernia and tightening of the hiatus by suturing posteriorly and repairing the phreno-oesophageal ligament to restore the abdominal segment of oesophagus. The results of this type of operation vary considerably in different surgical hands; the recurrence rate of herniation is usually 10–30% and an even greater proportion have radiologically demonstrable reflux. This has led other surgeons to devise ways of reconstituting the oesophago-gastric angle and some combine repair with vagotomy-pyloroplasty. Symptomatic relief does not correlate closely with radiological findings after repair, and fortunately benefit persists in many in whom herniation and reflux are still present

—suggests that at least symptomatic improvement might be achieved without operation. While none would dispute that surgery often succeeds where medical measures have failed, it is also true that surgical series often contain patients in whom these measures have never been given a fair trial.

The selection of patients with hiatus hernia for surgical treatment depends on the degree of disability and the physical condition of the patient. The younger and fitter the patient the more readily should surgery be considered.

The following are indications for surgical treatment of hiatus hernia:

(1) Dissatisfaction of the patient with symptomatic relief after six months' conservative treatment or unwillingness to continue such treatment. Certain patients have severe pain with only minimal evidence of oesophagitis, and surgery should not be withheld simply because of the absence of gross pathological changes.

(2) The persistence of oesophagitis after six months' medical treatment and the development of peptic ulcer in the oesophagus or in the stomach at the level of the hiatus.

(3) Signs of a stricture developing. If mild this may respond satisfactorily to a simple reparative operation, but if it is tight and causing nutritional impairment resection with interposition of a jejunal loop or taking the stomach into the chest is mandatory.

(4) Recurrent bleeding in a younger person is best treated surgically, but the elderly often do well with conservative measures in such a situation.

(5) The occurrence of aspiration pneumonia.

(6) Incarceration or strangulation is an urgent indication for operation.

Unfortunately hiatus hernia is common in the older age group, where other disease, notably cardiac ischaemia, often coexists. Here the risk of operation, intrathoracic or intra-abdominal, might be judged too great even in the presence of the above indications and no choice is left but to continue medical measures.

B.M.J. Publications

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Collapse after Triple Antigen

Q.—It was stated in an answer to a question¹ that collapse occurring one to four hours after immunization with triple antigen is not an anaphylactic reaction. What is the evidence for that statement?

A.—The statement that collapse after triple antigen is not an anaphylactic reaction was made on the following grounds:

(1) None of the physicians concerned with the treatment of reported cases of "collapse" have associated the condition with anaphylaxis.²⁻⁴ Similarly, Sir Graham Wilson,⁵ who examined the literature and perused Ministry of Health files on complaints, does not suggest that any of the reactions were anaphylactic in origin.

(2) Respiratory embarrassment, swelling of lips and eyelids, and restlessness and cyanosis are common features in a severe anaphylactic reaction. They do not occur in "collapse." A collapsed infant is extremely pale, limp, listless, and lifeless.

(3) The interval between injection of antigen and onset of anaphylactic reaction is a matter of seconds or of only a few minutes, but there is usually an interval of three to four hours and never less than one hour between pertussis vaccination and the onset of collapse.

(4) Collapse occurs as frequently after the first as after the second or third injection of pertussis vaccine. Though children who have collapsed after receiving pertussis vaccine are prone to do so after a repeat injection, a high proportion are unaffected by the second dose. Collapse is not therefore the result of sensitization.

(5) The incidence of collapse may be substantially reduced by merely halving the dose of pertussis vaccine given.⁶ It may be, therefore, that the dose of vaccine given in relation to body weight is an important factor. Anaphylactic reactions are not greatly affected by these considerations.

I do not know of any detailed studies carried out on infants with a history of "collapse" after triple antigen.

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- ⁴ Haire, M., Danc, D. S., and Dick, G., *Med. Offr.*, 1967, 117, 55.
- ⁵ Wilson, Sir Graham, *The Hazards of Immunization*, 1967, London.
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Muscular Spasms in Paraplegia

Q.—Can anything be done in a patient aged 86, suffering from paraparesis of the lower limbs, to reduce muscular spasm in one thigh which has increased considerably since the femur was fractured and operated on eight months ago?

A.—Flexor spasms may be initiated in patients with paraplegia by a painful lesion or an irritative focus such as a pressure sore. These spasms, however, are usually bilateral. It would seem most likely in this case that the spasm is associated with the lesion in the hip.

On the whole, treatment is unsatisfactory. A physiotherapist should try gentle stretching to overcome the spasm, and heat and massage may help. If the patient is develop-

ing a flexion contracture of the hip on the affected side an effort should be made to nurse him in the prone position. Much perseverance is needed, but sometimes the results are good. If the flexor spasms are occurring at the knee joint the use of light-weight plastic splints, as described by Brennan,¹ can be helpful in overcoming spasm and preventing permanent contractures developing.

REFERENCE

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Oral Diuretics and Hyperuricaemia

Q.—Some elderly patients develop high blood uric-acid levels and gout-like pains while taking chlorothiazide or frusemide. Is there an effective oral diuretic which does not have these effects, or, alternatively, should a uricosuric agent be given with the diuretics?

A.—It is recognized that most oral diuretics—all the thiazides, chlorthalidone, quinethazone, ethacrynic acid, and frusemide—may cause hyperuricaemia and precipitate attacks of clinical gout in susceptible subjects. Triamterene, which has a different mode of action, does not have this effect and can be used in these circumstances. Triamterene is, however, a relatively weak diuretic on its own and often requires the addition of one of the other diuretics to obtain a satisfactory response.

It is also possible to prevent diuretic-induced hyperuricaemia and to relieve the symptoms of gout by giving a uricosuric agent such as probenecid or sulfinpyrazone along with the oral diuretic.¹⁻³

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Gastroenterological Conference

A Case of Crohn's Disease in a Patient with Treated Adult Coeliac Disease

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL

Clinical History

Professor C. BOOTH: This patient (Case No. 204058; P.M. No. 11730) was an Irish housewife aged 34 at the time of death in 1966. In 1957 she had had an attack of acute glomerulonephritis one week after full term normal delivery of her second baby. She had completely recovered from this illness.

On 7 September 1964 she was admitted to Hammersmith Hospital under the care of Dr. Cope complaining of diarrhoea, swelling of the ankles, loss of weight, and amenorrhoea. The stools were loose, pale, and greasy, and she had had as many as 10 motions a day during the previous 18 weeks. Swelling of the ankles had been present for nine weeks. She had also recently noticed pins and needles and stiffness in her fingers.

On examination she was thin and markedly wasted, weight 103 lb. (44 kg.). There was marked oedema extending from the ankles up to the thighs and on to the abdominal wall. There was clubbing of the fingers. The blood pressure was 9/70 mm. Hg, the pulse rate regular, and the heart normal. The chest and abdomen were normal. The central nervous system was normal except that both the Chvostek and the Trousseau signs were positive.

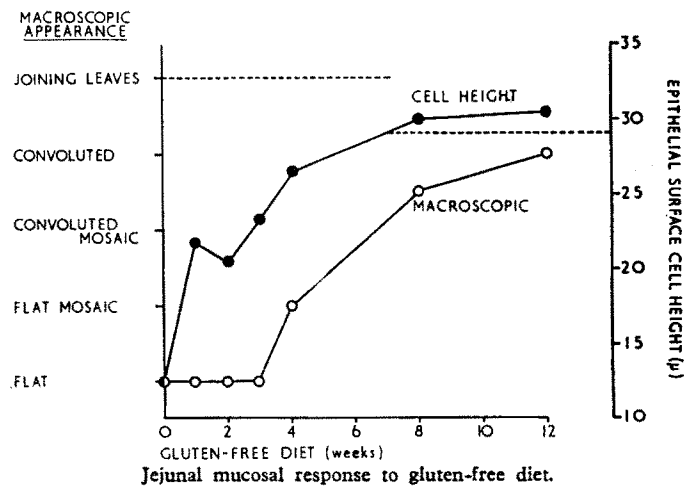
Investigation at this stage showed the haemoglobin to be 9 g./100 ml., P.C.V. 35%; stained blood films showed evidence of macrocytosis and the bone marrow was megaloblastic. The serum folate was 1 $\mu\text{g.}/\text{ml.}$ (normal $>6 \mu\text{g.}/\text{ml.}$) and the serum B_{12} 200 $\mu\text{g.}/\text{ml.}$ (normal range $>140 \mu\text{g.}/\text{ml.}$). The blood urea was 14 mg./100 ml., the bicarbonate 29, sodium 142, potassium 2.7, and chloride 103 mN. The calcium was 2.7, magnesium 1.7, and phosphate 1.3 mN. The alkaline phosphatase was 32 King-Armstrong units; the serum albumin was 1.0 and globulin 2.3 g./100 ml. A barium meal showed marked dilatation of the small bowel loops.

A jejunal biopsy showed a completely flat mucosa under the dissecting-microscope, and on histological examination there was subtotal villous atrophy. Absorption tests were then carried out. The faecal fat excretion was 72 g./day, and the fat excretion in the urine was 1.1 g. following a 25 g. dose. A glucose tolerance test was done; the blood glucose levels at 15-minute intervals after an oral dose of 50 g. glucose were 63, 70, 75, 70, and 55 mg./100 ml. The Schilling test showed 1.3% of the oral test dose excreted (normal range 10%; test dose was 1 $\mu\text{g.}$ of radioactive vitamin B_{12} given with intrinsic factor).

Response to Treatment

In view of this evidence of intestinal malabsorption and the finding of subtotal villous atrophy in the jejunal biopsy, a diagnosis of adult coeliac disease was made. On 12 September treatment was started with a gluten-free diet. She made an excellent response to the gluten-free diet clinically, biochemically and histologically. Within a month there had been a marked improvement in the appearance of the jejunal biopsy,

the mucosa had reverted to a convoluted appearance, and the surface cells had become normal in height (Chart). She was discharged home on 3 October taking a gluten-free diet, folic acid 5 mg. daily by mouth, Calcium-Sandoz two tablets three times daily, and calciferol 100,000 units once monthly. By June 1965 she was feeling very well. Her weight had increased by 3 stones (18 kg.), her haemoglobin was now 12.2 g./100 ml., the calcium 5.2 mN., the phosphate 1.9 mN., and the alkaline



phosphatase had fallen to 10 King-Armstrong units. The steatorrhoea was markedly improved, the faecal fat excretion having fallen to 6.9 g./day. In November 1965 her periods returned after 18 months' amenorrhoea.

Six months later, however, she was readmitted to Hammersmith Hospital with vaginal bleeding, fever, abdominal pain, diarrhoea, and vomiting. She had clearly lost weight. She was wasted and oedematous, with a dry mouth and tongue. The Chvostek and Trousseau signs were again positive. There was tenderness in the lower abdomen.

Investigations revealed a haemoglobin of 11.1 g./100 ml., but the sternal marrow was now normoblastic. The white cell count was elevated at 14,000/cu. mm. Her blood urea had risen to 155 mg./100 ml.; electrolytes were as follows: sodium 132, potassium 3.1, chloride 99, and bicarbonate 27 mN.; calcium was 3.8, magnesium 1.2, and phosphate 1.7 mN. The alkaline phosphatase was 14 King-Armstrong units. The serum albumin had again fallen to 1.3 g./100 ml. She was treated with intravenous fluids and on 23 March aborted an 18-week twin pregnancy. Following abortion, however, the fever, diarrhoea, and vomiting persisted, and by 3 April 1966 she had developed a skin rash. In view of her severe deterioration she was started on treatment with prednisone 20 mg. daily on 7 April, and on 14 April a barium meal was carried out. This showed multiple areas of constriction of the mid and distal small intestinal loops and it was concluded that she might be suffering from lymphoma of the intestine.

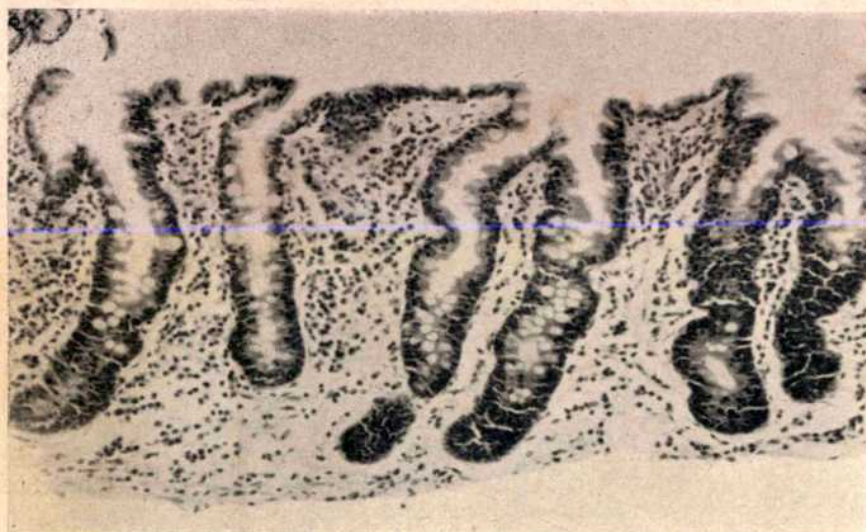


FIG. 1A.—Jejunal biopsy before treatment. Subtotal villous atrophy is seen with thin covering epithelium. (Average cell height 13 microns.) (H. and E. $\times 160$.)

FIG. 1B.—Jejunal biopsy three months after treatment. Severe partial villous atrophy is still present, but covering epithelium is almost normal. (Average cell height 32 microns.) (H. and E. $\times 160$.)

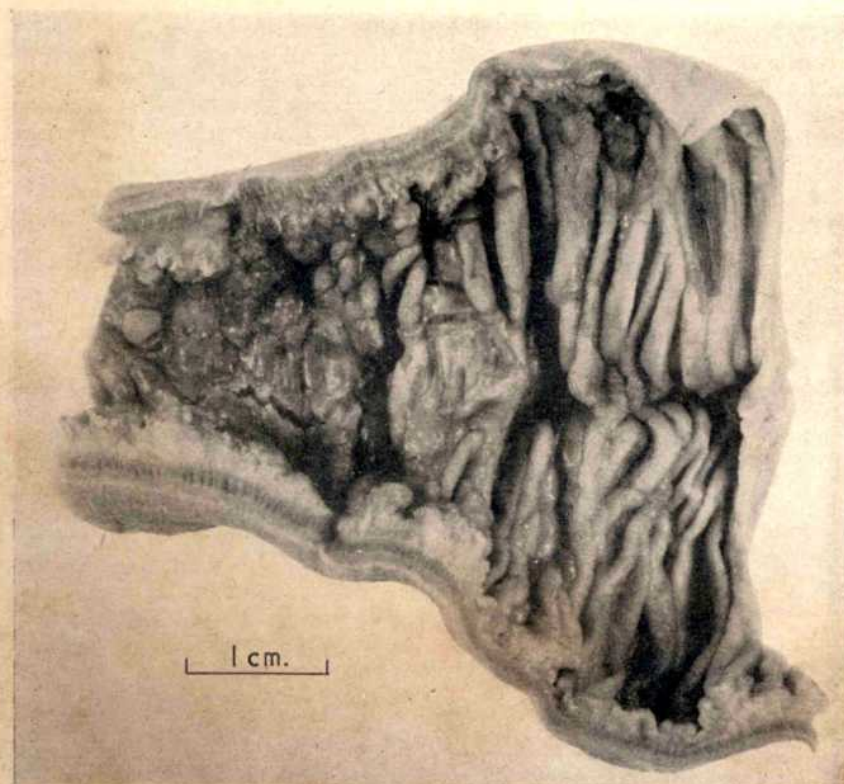
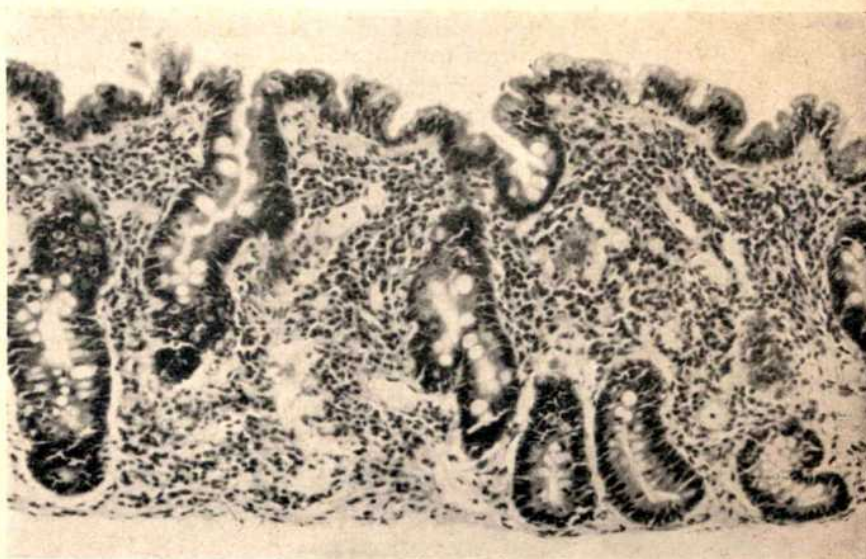


FIG. 2.—Macroscopic appearance of jejunum of the junction of stricture and relatively normal bowel. The stricture (left) shows severe submucosal thickening and has a "cobblestone" appearance.



FIG. 3.—Jejunum showing ulceration of the mucosa and gross thickening of the submucosa. A chronic inflammatory infiltrate—occasionally arranged focally—is seen as well as lymphangiectasia. Covering mucosa with an intact muscularis mucosa can be seen on the left. (H. and E. $\times 45$.)



FIG. 4.—Fissure lined by granulation tissue extending deeply into the submucosa. (H. and E. $\times 45$.)

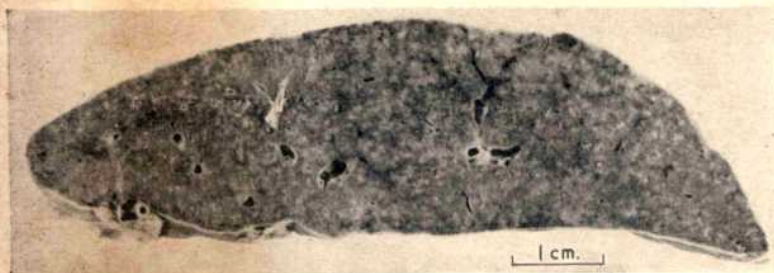
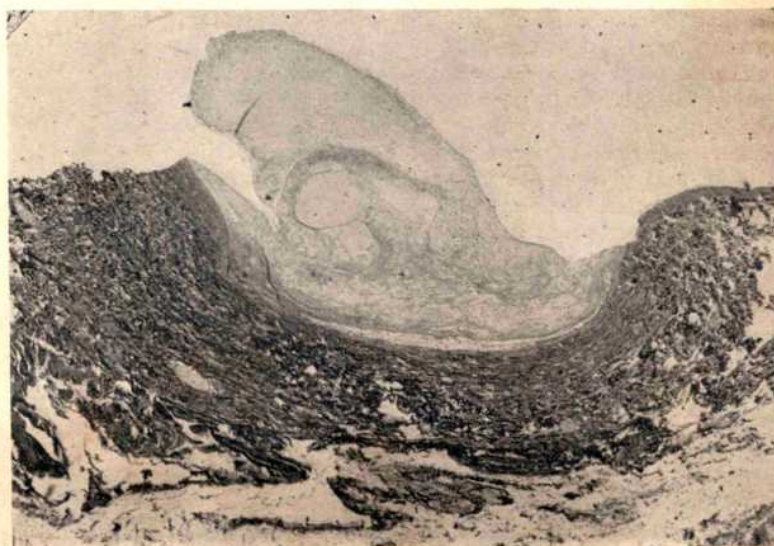


FIG. 5.—Spleen showing atrophy. Hardly any red pulp is seen.

FIG. 6.—Part of right hepatic vein showing organizing thrombus near the vessel wall and recent thrombus towards the lumen. (Elastic van Gieson. $\times 65$.)



Exploration

On 19 May 1966 an exploratory laparotomy was carried out. This revealed many areas of thickened and reddened bowel extending from approximately 2½ ft. (75 cm.) distal to the duodeno-jejunal flexure to the terminal ileum. There were similar lesions in the transverse colon. The macroscopic appearances suggested Crohn's disease. No operative procedure was carried out and no biopsy was taken. Treatment was continued with intramuscular methyl prednisolone 60 mg. daily, but there was no response. Her haemoglobin fell and she required blood transfusions on four occasions. She was given albumin infusions in an attempt to correct her hypoproteinaemia, but the serum albumin never rose higher than 1.5 g./100 ml. On 28 June 1966 she developed signs of consolidation and cavitation in the right upper lobe. Sputum cultures at this stage yielded *Pseudomonas pyocyanea*. Despite treatment with gentamicin and polymyxin her condition steadily deteriorated until she died on 4 July 1966.

Clinical Diagnosis

- (1) Adult coeliac disease treated with gluten-free diet.
- (2) Crohn's disease.
- (3) Lung abscess.

Biopsy Findings

Dr. J. S. STEWART: When we first examined this patient's untreated proximal intestinal mucosa under the dissecting-microscope it was about as flat as any we have seen. Histologically (Fig. 1A), the most striking feature was the severe abnormality of the epithelial surface cells, which showed many signs of damage. The simplest way to quantitate this is to measure the reduced surface cell height, in this instance 13 µ, the normal range in our series being from 29–36 µ. The other salient features are the increased mucosal thickness and the dense chronic inflammatory cell infiltration.

One week after she had started taking a gluten-free diet a repeat jejunal biopsy showed a dramatic increase in the surface cell height from 13 to 22 µ. Macroscopically it was still almost completely flat. Repeat biopsy at two months showed a partially convoluted appearance. At three months (Fig. 1B) the mucosa showed only convolutions.

This patient kindly allowed us to do weekly biopsies for four weeks and then again at two and three months. While the surface cell height rose rapidly within the first few weeks and reached normal levels at two months, the macroscopic appearance showed no significant change until four weeks after the start of gluten withdrawal. At three months it was not yet quite normal.

At that time we were engaged in a collaborative study with Professor Pearce's department of histochemistry to assess the significance of the enzyme changes known to occur in the intestinal mucosa of patients with idiopathic steatorrhoea. Dr. Ernst Riecken, working with Professor Pearce, did the histochemistry and drew attention to certain changes in the distribution of acid phosphatase in the epithelial surface cells. In this patient, before the start of her gluten-free diet, the two dominant features were the diffuse distribution and the reduction in the intensity of the staining. This diffusion appeared to be due to rupture of the lysosomes, the intracellular organelles containing lytic, destructive enzymes. It is probable that the rupture of the lysosomal membranes accounts for much of the damage in the epithelial surface cells. We think that this rupture is in turn brought about by the direct action of gluten on the cells.

To summarize these findings, serial biopsies provided evidence of gluten sensitivity in this patient by demonstrating rapid return of the proximal intestinal mucosa towards normal after withdrawal of gluten.

Post-mortem Findings

Dr. E. OLSEN: Permission for a limited necropsy only was granted. The body was that of a wasted female. Bilateral ankle oedema and mild finger-clubbing were present. The laparotomy scar had healed.

The mid and distal parts of the *jejunum* and the proximal part of the *ileum* showed multiple tubular strictures (Fig. 2) of varying lengths (longest about 30 cm.). In these the wall was thick. The mucosa had a "cobblestone" appearance and was for the most part devoid of epithelium. Adjacent to the "cobblestone" appearance flat mucosa was seen under the dissecting-microscope. The gut between the strictures was predominantly normal, but patches of flat epithelium were also found. The remainder of the gastrointestinal tract was normal.

On histology the mucosa was largely ulcerated (Fig. 3), but flat epithelium was seen in patches. Pyloric gland metaplasia was also seen. The submucosa showed gross thickening consisting mostly of fibrous tissue, but areas of oedema with lymph-angiectasia were found. There was a severe chronic inflammatory infiltrate as well as focal collections of lymphoid tissue. Fissures (Fig. 4) lined by granulation tissue extended into the submucosa. The muscle coats showed inflammatory cells and the serosa was thick and fibrous. Adjacent lymph nodes were normal. Despite the absence of giant cell granulomas a diagnosis of Crohn's disease was made.

The right *lung* weighed 800 g. (normal upper limit 400 g.) and the left *lung* 650 g. (320 g.). The bronchi contained greenish pus. The lungs showed infarct-like areas and were oedematous and patchily consolidated. An abscess measuring 4 cm. was found in the right upper lobe. A recent thrombo-embolus was found in a segmental pulmonary artery. Histology showed widespread bronchopneumonia. *Pneumocystis carinii* was identified. Small vessels occluded by thrombi were found near the abscess.

The *spleen* was atrophic and weighed 60 g. (normal 100–150 g.). Histology showed no red pulp (Fig. 5). Reticulo-endothelial cells in the trabeculae were stuffed with iron.

The *liver* weighed 1,300 g. The right hepatic vein showed a thrombus (Fig. 6) which did not occlude the lumen. Two areas of intense congestion were seen in the right lobe of the liver. Histology of these areas showed sinusoids distended with blood. Elsewhere the liver showed severe fatty change. Iron was found in abundance in Kupffer and liver cells. Some smaller intrahepatic veins were occluded by organized thrombi. The thrombus in the right hepatic vein showed varying degrees of organization and was capped by very recent thrombus.

The right *kidney* weighed 140 g., the left 122 g., and showed tiny abscesses.

The *parathyroid glands* showed predominantly chief-cell hyperplasia. The *adrenal glands* weighed 4 g. each (normal 6–7 g. each) and showed lipid depletion.

The *uterus* still showed evidence of pregnancy three months after abortion.

Pathologist's Diagnosis

- (1) Idiopathic steatorrhoea (consistent with adult coeliac disease).
- (2) Crohn's disease.
- (3) Renal and lung abscesses.
Bronchopneumonia.
Pulmonary thrombo-embolism.
Pneumocystis carinii.
- (4) Hepatic vein thrombosis.
- (5) Splenic atrophy.
- (6) Secondary parathyroid hyperplasia.

Discussion

Professor BOOTH: This is an extremely interesting problem. I should stress that we haven't previously seen a patient like this who presented originally as an adult coeliac and who then developed Crohn's disease.

It has been suggested that coeliac disease may be due to a congenital peptidase defect in the intestinal mucosa. Gluten is normally digested in the lumen of the gut, probably not entirely to amino-acids, but also to some extent only as far as peptides. In coeliac disease a toxic peptide may then diffuse into the cell, where there is a deficiency of an intracellular peptidase which normally digests it. The toxic peptide may then rupture the lysosomal membrane, allowing the diffusion of autolytic enzymes throughout the cell with subsequent destruction of the intestinal cell. It has been suggested that the condition may be inherited as an incomplete dominant. There are, however, facts which conflict with this simple theory. Firstly, a discordant pair of identical twins, one with the disease and one without, has been described. Secondly, there is the failure of response to a gluten-free diet in some patients. Thirdly, there appears to be some association of adult coeliac disease with malignancy. The practical point is that the simple genetic theory of coeliac disease in the adult as a peptidase defect doesn't fit all the patients we see, and certainly not the patient we've seen this morning, for the necropsy findings suggest Crohn's disease.

The splenic atrophy found in this patient occurs very frequently in this condition and produces a characteristic haematological picture with Howell-Jolly bodies in some patients. We missed the pneumocystis—an interesting finding, sometimes seen in patients with lymphoma as well as in patients who have been treated with corticosteroids. The liver changes are also extremely interesting. The parathyroid hyperplasia is presumably secondary to the chronic steatorrhoea.

Intestinal Lesion

Dr. B. MORSON: The pathological diagnosis of the gut lesion in this patient is probably Crohn's disease. I haven't much to add to Dr. Olsen's excellent description of the gross pathology and the microscopic appearances, except to emphasize the value of fissuring in the diagnosis. What I mean by fissuring is the presence of intercommunicating cracks or crevices in the cobblestone mucosa, which was confirmed histologically. I regard this morphological feature as supporting the diagnosis of Crohn's disease here. The other macroscopic appearances in general are certainly consistent with this diagnosis. The first thing that struck me in the microphotographs was the notable widening of the sub-mucosa, which was filled with inflammatory infiltrate accompanied by oedema and lymphectasia. Pyloric gland metaplasia is very commonly present in surgical specimens and necropsy material of Crohn's disease. Was there any neuromatous hyperplasia in the gut wall? That, I think, would be helpful in the diagnosis.

Dr. OLSEN: No, none was found. What we did find, however, was hyperplasia of the actual ganglion cells.

Dr. MORSON: This is quite common in Crohn's disease—it is a Schwann cell proliferation, and the nerves appear like large knotted structures, but I doubt that this is pathognomonic.

Professor BOOTH: I don't think it is either, because Dr. Williams will remember a patient some years ago with chronic ileal obstruction due to a simple stricture of the ileum which was associated with the same neuromatous picture. Does anybody disagree with Dr. Morson that this is Crohn's disease?

Professor D. MOLLIN: Did anyone look for acid-fast bacilli?

Dr. OLSEN: Yes, we did in one section only, but in the absence of granulomata this investigation was not pursued further.

Professor BOOTH: Could it be tuberculosis?

Dr. MORSON: I don't think so.

Professor BOOTH: Why?

Dr. MORSON: There are none of the morphological signs of tuberculosis in the form of collections of epithelioid cells and giant cells. It's true that the diagnosis of tuberculosis can be made in the absence of these, but there are usually areas of necrosis in which you may find tubercle bacilli. The other point is that the lymph nodes were normal, and this is unlike tuberculosis.

Dr. OLSEN: Professor Booth, you mentioned earlier that the gut lesions look to you like inflammatory lumps, but I considered these to be Crohn's disease. Did you in fact refer to the four cases which have been described by Goulston *et al.*? These showed non-specific jejunitis associated with coeliac disease. Two of these patients responded to a gluten-free diet, but this was non-specific proximal jejunitis, quite different from our patient today, who showed the more specific pathological changes of Crohn's disease.

Professor BOOTH: One might add that in our family studies of coeliac disease I have seen one patient with coeliac disease whose brother had Crohn's disease. Professor Mollin, would you like to make any further comments?

Professor MOLLIN: There are only two points. One concerns the Figlu tests, and I think Dr. Hoffbrand ought to talk about that. The other point is about the amount of iron in her tissues. She doesn't seem to have suffered from iron deficiency anaemia at any stage, although she suffered from idiopathic steatorrhoea and had been pregnant. At necropsy there was iron everywhere—you could see it quite readily in the liver parenchyma, which is definitely abnormal.

Professor BOOTH: How many pints of blood did she have?

Dr. G. HEPNER: Between March and her death in June she had 22 pints.

Dr. OLSEN: I think transfusion could partly explain the excess iron, but in addition to this there was hepatic vein thrombosis. In the slide I showed it did not obstruct the lumen of the main vein on the right side, but there was also widespread and long-standing intrahepatic venous occlusion within the right lobe of the liver. Although both lobes of the liver were strongly positive for iron, the right lobe (with widespread venous occlusion) showed slightly more iron. So there are probably two components at least which could explain the iron in the liver.

Professor BOOTH: Shall we take the other point about the Figlu test?

Histidine Metabolism

Dr. V. HOFFBRAND: This patient was most unusual for a patient with idiopathic steatorrhoea in her handling of the amino-acid histidine. Just to remind you of the metabolic pathway, histidine is broken down in the body to the amino-acid glutamic acid, but in the presence of folate deficiency the pathway is blocked at the level of formiminoglutamic acid (Figlu) and this compound appears in the urine. Patients with untreated idiopathic steatorrhoea almost invariably excrete raised amounts of Figlu after an oral dose of histidine because of folate deficiency. On her admission in 1964 this patient excreted Figlu but also excreted urocanic acid, the precursor of Figlu in the histidine breakdown pathway. Urocanic acid excretion is not directly related to folate deficiency, but is due to deficiency of the hepatic enzyme urocanase, and this occurs in protein deficiency and in liver disease. Urocanic acid excretion was reported in 1961 by Whitehead and Arnstein² in children with kwashiorkor. Studies here with Dr. Neale on postgastrectomy patients with hypoproteinaemia have shown that they also excrete large amounts of urocanic acid. In 1964 this patient was, as Professor Booth has said, hypoproteinaemic,

and this is the probable explanation of why she excreted urocanic acid as well as Figlu. When she was treated with a gluten-free diet and folic acid, both compounds disappeared from the urine—Figlu because folate deficiency was corrected, and urocanic acid because her protein deficiency improved. When she was subsequently admitted in 1966, she was found to be excreting vast amounts of urocanic acid. The normal range is up to approximately 6 mg. in eight hours after a 15 g. oral loading dose of histidine, and she was excreting more than 2,000 mg. in eight hours. She was already receiving folic acid in large doses, her marrow was normoblastic and Figlu excretion was normal, so this was certainly nothing to do with folate deficiency. However, she was severely hypoproteinaemic, and when she was given albumin infusions urocanic acid excretion fell to 200 mg. in eight hours, but it was never completely corrected, and just before she died she was still hypoproteinaemic and excreting over 1,000 mg. of urocanic acid in eight hours. I wonder if protein deficiency could explain the fatty changes found in the liver at necropsy.

Professor MOLLIN: Could I ask Dr. Hoffbrand one question? Would you think that if a patient with idiopathic steatorrhoea excretes urocanic acid this is a sinister sign?

Dr. HOFFBRAND: We have found raised urocanic acid excretion in only three patients among over 60 with idiopathic steatorrhoea examined. Two of these three, including the present patient, suffered from severe hypoproteinaemia, and both died. The third probably had liver involvement by an associated virus infection and he is now well and does not excrete urocanic acid.

Malignant Disease and Steatorrhoea

Dr. J. HOBBS: Between 12 and 16 April 1966 (before laparotomy on 19 May) the serum alkaline phosphatase rose from 12 to 21 King-Armstrong units, the 5-nucleotidase from 12 to 39 i.u./l., the isocitrate dehydrogenase to 12 i.u./l. and the bromsulphalein retention to 47%. In retrospect this is probably when the hepatic venous thrombosis occurred.

Turning to the lysosomal hypothesis Allison³ has reviewed the evidence that lysosomal D.N.A.-ase can damage D.N.A. and might thereby result in neoplastic mutation. It is therefore very interesting that there is a 15% incidence of malignant disease associated with idiopathic steatorrhoea.

Professor BOOTH: The association with malignant disease is also interesting in relation to the lymphoreticular atrophy and the small spleen. The Bristol workers have claimed that the lymph nodes are small in adult coeliac disease. Did we have immune globulin studies in this lady?

Dr. HOBBS: Three months before death the serum levels were γ G 540, γ A 150, and γ M 85 mg./100 ml. She did not show the low γ M found in 18 out of 60 of your patients with coeliac disease.

Dr. G. NEALE: Dr. Hobbs suggested that rupture of the lysosomes might lead to neoplastic mutation. In coeliac disease the epithelial cells of the small intestine suffer direct damage by gluten, but the associated malignancy is not usually an adenocarcinoma of the small intestine. It is, in fact, malignant lymphoma.

Professor BOOTH: The commonest malignancy is a reticulosis, but the next commonest appears to be carcinoma of the oesophagus.

Dr. STEWART: Complementary to Professor Mollin's point about urocanic excretion in idiopathic steatorrhoea, this is perhaps a bad prognostic sign. Certainly, hypoalbuminaemia appears to be. From a clinical point of view, the only other patient who presented predominantly with oedema was a lady who died of idiopathic steatorrhoea without, apparently, any other complicating disease.

Professor BOOTH: They tend to do badly, don't they. This is quite true.

Dr. M. BERRY: Has anyone digested gluten with pepsin, trypsin and then administered the digest to patients with idiopathic steatorrhoea?

Professor BOOTH: Yes, this has been done with peptic and tryptic digests and this material retains its toxic quality. However, that material is digested further with hog intestinal mucosa, then the toxic quality is lost.

Bone Changes

Dr. A. DOUGLAS: I wonder if I might ask two questions—firstly, it's very interesting that she was given 60 mg. of prednisone per day, and she in fact did not become Cushingoid. Is that the usual sort of thing in patients with Crohn's disease? Secondly, she had a low serum calcium, very high alkaline phosphatase, a Chvostek and Trousseau sign, and parathyroid hyperplasia, yet apparently no radiological changes.

Dr. G. JOPLIN: I would agree that attention should be drawn to the disproportion here between the alkaline phosphatase and serum calcium on the one hand and the bone changes on the other hand. This is by no means rare. In a series of about 80 patients that Dr. Gilbert Thompson and I did some combined studies on, we found that there were quite a number of patients who did show this disproportion, and I think it is important to recognize that bone changes need not be radiologically obvious before the diagnosis of osteomalacia can be made. In fact in this particular patient we measured the 24-hour strontium space, and the result was very high indeed. This tallies with the high alkaline phosphatase and the low serum calcium, and this really prompts the question to the pathologists—what about the bones at necropsy?

Professor BOOTH: Well, what about the bones?

Dr. OLSEN: They appeared normal, macroscopically and microscopically.

Dr. JOPLIN: That's very difficult to accept, unless there had been some effective treatment. How long had the patient been on vitamin D?

Dr. HEPNER: She'd been put on vitamin D in October 1964 and she'd been taking oral calciferol intermittently until she was admitted in March 1966, and she'd also been on calcium sulphate.

Professor BOOTH: That explains the normality of the bones.

Dr. MORSON: Could I just ask one more question? Was there any alteration in the Paneth cell population in the small intestinal biopsy?

Dr. OLSEN: There was no alteration at all.

Dr. J. W. LAWS: The radiological changes were interesting. In the second barium follow-through examination, multiple stenosing lesions with an abnormal mucosal pattern were shown. Knowing the patient had idiopathic steatorrhoea and knowing that lymphoma is commonly associated with it, we thought the changes might be due to lymphoma. In fact, the appearances fit in perfectly well with Crohn's disease—which would have been our diagnosis if we had not been put off by knowing that the patient had proved idiopathic steatorrhoea.

Steatorrhoea tends to make the barium flocculate, when it is difficult to show the anatomical abnormality very clearly. Flocculation isn't a very useful sign, as it occurs in steatorrhoea of any cause.

Dr. OLSEN: One very often sees finger clubbing with steatorrhoea and coeliac disease. May I ask the mechanism of this finger clubbing? It has at one time been said it is associated with vitamin deficiency. But what is the actual mechanism?

Professor J. GOODWIN: This is a question which needs a very long answer. In patients with cyanotic congenital heart diseases there is an overgrowth of the terminal phalanx and an excess of capillaries. This sort of thing tends to happen elsewhere in the body as well, in the renal glomeruli, for example.

and reflects perhaps a generalized capillary abnormality or excessive local capillary development as a result of reduced arterial saturation. It differs from the clubbing that develops in chest disease due to excessive reduced apoferritin. The clubbing that I cannot understand at all is the clubbing in bacterial endocarditis, left atrial myxoma, and coeliac disease.

Professor BOOTH: Thank you very much. We must conclude this was a patient with adult coeliac disease who developed Crohn's disease, whatever that may be.

We are grateful to Professor J. P. Shillingford and Dr. E. D. Williams for assistance in preparing this report, and to Mr. W. Brackenbury for the photomicrographs.

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NEW APPLIANCES

Repeated Haemodialysis with a Straight Silicone Rubber Cannula

Dr. J. B. HAWKINS, registrar, and Dr. B. H. B. ROBINSON, consultant physician, Renal Unit, East Birmingham Hospital, write: The Quinton-Scribner Silastic/Teflon cannula (Quinton, Dillard, and Scribner, 1960; Quinton, Dillard, Cole, and Scribner, 1962) has made possible the widespread use of repeated haemodialysis for the treatment of chronic renal failure. This system is also valuable in the management of those patients with acute renal failure for whom repeated or frequent haemodialysis is necessary (Clark

Renal Unit for nine months. It is easy to clear of thrombus, relatively simple to insert, and cheap.

The cannula (Fig. 1) is made from medical-grade silicone rubber tubing (Esco Rubber Ltd.) similar in size to that used for conventional cannulae. To this is attached a silicone rubber wing 2.5 cm. wide by means of an appropriate adhesive (Dow Corning silicone type A). The edges of the wing slope away from the vessel tip at an angle of approximately $22\frac{1}{2}^\circ$. Small holes may be

Thus a Teflon tip can be inserted higher up the same vessel with a minimum of tissue disturbance. After cannulation of artery and vein a single Teflon connector is used to produce an arteriovenous shunt (Fig. 2).

CLINICAL EXPERIENCE

Specially moulded cannulae available commercially are expensive. This cannula was originally designed as a cheap device for managing hypercatabolic acute renal failure by repeated haemodialysis, and has proved entirely satisfactory. It is relatively simple to insert compared with the conventional cannula, and is easy to clear of clot. There is a possible danger, however, that the over-vigorous passage of a declotting catheter might dislodge the vessel tip or damage the vessel wall. So far we have not had this experience. Once inserted, the cannula will withstand a direct pull in excess of 2.5 kg., sustained or intermittent, without dislodgement of the vessel tip.

Encouraged by the success of this cannula for acute cases, we have made use of it in several patients undergoing long-term intermittent haemodialysis. Initial results are good. Although specially prepared silicone rubber is not used for these cannulae, clotting episodes are no more frequent than with Quinton-Scribner shunts. Blood flow rates through Kiil dialysers are, on average, higher than with curved cannulae, though direct comparison is clearly not possible.

This shunt has the disadvantage that it cannot be placed as far distally in the limb as the Quinton-Scribner shunt, but an exit hole 4 cm. above the proximal wrist crease has been found satisfactory, and we believe that with either type of shunt it is better to cannulate the vessel well above this in order to minimize movement due to flexion and extension at the wrist. We have not found that a 60° step at the exit site is necessary, and its absence facilitates placing of the cannula.

The original pair of cannulae inserted for intermittent dialysis are still in use for home dialysis seven months after insertion, while three other pairs are in use after approximately five months. Only one pair of cannulae has required reimplantation (as a result of infection).

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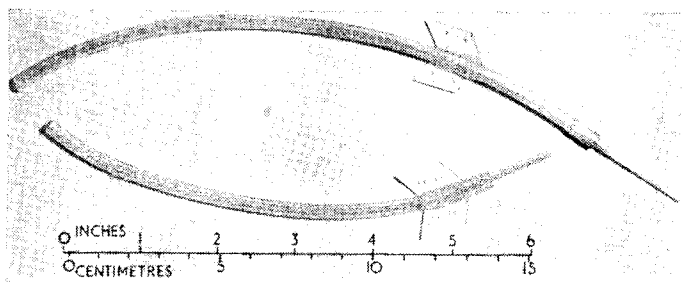


FIG. 1

and Parsons, 1966). The system suffers from the disadvantage that it is often difficult to clear clotted cannulae because of the 180° bend as well as the 60° step, which interfere with the passage of a declotting catheter. The insertion of these cannulae requires careful judgement if the loop and the step are to lie in the appropriate position for alignment of the Teflon vessel tip in the cannulated vessel. Ramirez, Swartz, Onesti, Mailloux, and Brest (1966) described a "winged in-line" cannula which overcame the difficulty in declotting. We have developed a modification of this cannula, which has been in use in the East Birmingham

made in each wing, and the proximal portion of the cannula projects 5 cm. ahead of the wing.

METHOD OF INSERTION

The vessel is exposed for cannulation. A space distal to this site just large enough for the wing is made between two tissue layers (usually beneath the deep fascia, or between muscles), while the distal part of the cannula is passed along the same tissue plane and out through an oblique stab incision at a suitable site. Care is taken to ensure that the cannula lies in line with the vessel to be cannulated. The holes in the wing can be used for suturing the wing to the deep fascia if desired; this may be useful in confused and violent patients, but is probably undesirable if it is intended that cannulae should remain in situ for more than a few weeks.

The proximal portion of the cannula is normally trimmed to within 0.5 to 1 cm. of the wing. A Teflon vessel tip of appropriate size is then inserted, a fine silk suture is passed through the vessel wall to anchor the intima, and the vessel is cannulated in the usual way, one proximal and two distal ligatures round vessel and cannula normally being used. If recannulation of the same vessel is required on a later occasion, a similar cannula is used, but is trimmed to leave a longer portion ahead of the wing; it is then possible to use the same track as before.

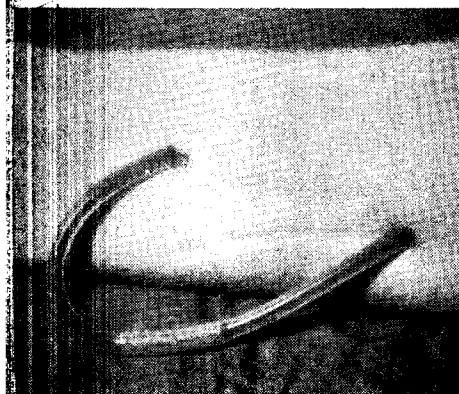


FIG. 2

Book Reviews

Documentation from Cradle to Grave

Medical Record Linkage. By E. D. Acheson, M.A., D.M.(Oxon.), M.R.C.P.(London). (Pp. 213+xviii; illustrated. 25s.) Published for the Nuffield Provincial Hospitals Trust by Oxford University Press, London, 1967.

Nowadays, as we travel from birth to death, we leave behind us a vast accumulation of personal information about our changing health and social circumstances. This information is recorded in separate places and at different times in the files of dozens of different medical and social agencies. A national system for piecing together the more important and reliable fragments of this scattered medical and social information in a series of personal, cumulative files would undoubtedly advance our knowledge about the aetiology and progression of many

diseases. The revolution in data-processing techniques that has taken place since the war has removed one major obstacle in the way of achieving such a national system of medical record linkage, but there remains the formidable problem of how to standardize the recording of the information and how to gather it in from its widely scattered sources.

Dr. Acheson, Reader in Medicine at Oxford University and director of the Oxford Record Linkage Study, is a pioneer in this field—so important to the future of epidemiological

research. He has convincingly demonstrated that routine record linkage is feasible at the regional level, and his experiment has already yielded research dividends in a series of papers in scientific journals. In this important book he traces the historical origins of our ideas about record linkage, gives a detailed technical account of the Oxford experiment, and makes sensible and practical suggestions about how a national scheme might be introduced. On the way he discusses the issues of breach of medical confidence, possible abuse by the State, and the general distrust in Britain of national registration, with its echoes of wartime restrictions, Buchenwald horrors, and Orwell's 1984.

C. R. LOWE.

Shock

Diagnosis and Treatment of Shock. By Max Harry Weil, A.B., M.D., Ph.D., F.A.C.P., and Herbert Shubin, A.B., M.D., F.A.C.P. (Pp. 391+xxvii; illustrated. 96s.) Edinburgh: E. & S. Livingstone. 1967.

This comprehensive book on shock has benefited greatly from the new emphasis in America during the last five years upon clinical rather than animal studies. It combines the mature views of many leading authorities with the recent experience of the Shock Research Unit at Los Angeles County General Hospital, where there is a wealth of clinical material. The classical sequence of pathophysiology, diagnosis, and treatment is adopted and the links between these stages can be much more securely based now that the guesswork between what is true of the dog and what of man has been largely eliminated.

A very strong team of authors, for instance M. I. Gregersen on volume relations, E. C. Bradley on haemo-dynamic aspects, and S. M. Levenson on metabolic changes, makes the section on pathophysiology particularly impressive. In the diagnostic section a variety of types of shock is distinguished. Among these, those due to blood loss, fluid loss, and infection are classical. Shock due to myocardial infarction, vascular obstruction, hypersensitivity, anaesthesia, and drugs are valuable additions to this section, but the inclusion of shock due to endocrine failure seems somewhat outside the usual scope. The section on treatment is based both on the research studies and on the practical lessons of a busy clinical department.

Throughout the book there is a wealth of diagrams and illustrations, many of them very clear and informative. Attention is drawn to a number of new studies—for instance, the value of comparisons between central and capillary haematocrits as an index of peripheral blood flow.

In considering the value of blood volume determinations, a good point is made that a convenient, rapid technique for estimation of fat-free body weight, and hence the expected

normal volume, would be more helpful than further improvements in blood volume estimation. However, no mention is made of the improved estimates of the expected normal blood volume which can be obtained by combining knowledge of height and weight.

The new clinical details of the different types of shock largely derive from recent improvements in monitoring. Though several pitfalls and hazards of these techniques are pointed out, Dr. Weil looks forward to further advances whereby computer analysis will not only give continuous information on the state of the patient but will automatically make appropriate adjustments to treatment. Whether or not this is a true prophecy, the book is a good guide to what can be done now.

J. P. BULL.

Cellular Chemotherapeutic Problems

Experimental Chemotherapy. Vol. 4. Chemotherapy of Neoplastic Diseases. Part 1. Edited by R. J. Schnitzer and Frank Hawking. (Pp. 670+xxii. £10 16s.) New York and London: Academic Press. 1966.

This book is the fourth of a series of volumes on experimental chemotherapy, and the title is interpreted in its widest possible sense. Previously issued parts have been concerned with the agents used in protozoal, fungal, and bacterial infections, and about 200 pages of the present book are supplementary to the previous three volumes, expanding them and introducing the results of recent research. This is a most valuable service to owners of the previous volumes, and J. Hill's account of modern developments in the chemotherapy of malaria and Jillian M. Bond's chapter on antibiotics used in the chemotherapy of bacterial and fungal infections are of particular interest.

The main part of the book, however, is

composed of material and subjects quite new to the series. At first it was surprising to me to find cancer chemotherapy and the therapy of infections dealt with in the same book. On reflection, however, the logic of the editors in considering cellular chemotherapeutic problems as a whole emerges triumphantly. A short introductory chapter by L. A. Elson serves to focus the reader's attention on this unity of chemotherapy. V. M. Rosenoer very fully discusses the problems of drug evaluation and the special aspects of experimental design. The statistical treatment of data is well discussed and a very full bibliography of recent papers is included.

The next 300 pages are a *tour de force* by J. A. Stock, who gives a splendid account of the antimetabolites and the antitumour antibiotics. The content of his chapters is absolutely up to date and well documented. An exhaustive bibliography follows each of the two sections. Tumour inhibition, pharmacology, and metabolism of the drugs is described in detail, together with mechanisms of action, drug resistance, and clinical applications. It is a revelation of how well a mass of information can be analysed and presented. Many of the drugs which are described have been evaluated and found wanting in human clinical use. The cautious approach of Stock is emphasized in his comment on mitomycin, when he says "the discrepancy (between clinical and experimental results) provides a good illustration of the danger of a too eager extrapolation of results in the experimental animal."

The authors have done excellent justice to their subjects, and in this Anglo-American series the British reader may feel reflected pride in the literary and scientific performance of Elson, Rosenoer, and Stock, all of whom hail from the Chester Beatty Institute. This series has a place of great value in the medical libraries of the world and further volumes will be eagerly awaited. The book can be enthusiastically recommended both on its own and as part of a larger project.

P. S. BOULTER.

Disorders of the Heart and Circulation

Disorders of the Heart and Circulation. Symposium, Edinburgh, 1965. Royal College of Physicians of Edinburgh. (Pp. 162; illustrated. Paper 25s.) Edinburgh: Royal College of Physicians, 1966.

The good symposiast should really do his task twice over, first for the listener and then for the reader. Certain learned societies ordain that papers be spoken and not read, and if we are listeners we owe them a debt. But the transcribed tape-recording will then make hard reading, and the slide, so evocative in the lecture, is bleak and silent on the printed page. Two versions is the only answer.

The seven symposiasts convened by the Royal College of Physicians of Edinburgh took their task to heart and have set out their ideas in an engaging way in this little volume. Sir John McMichael's George Alexander Lecture "Some Observations on the Micro-circulation" is a neat summary of the Hammersmith work on the applied physiology of the small pulmonary blood vessels in mitral stenosis and the retinal changes in hypertension and diabetes. The surgical treatment of aortic valve disease from the viewpoint of the physician (Dr. R. W. D. Turner) and the surgeon (Mr. A. Logan) is fairly weighed up. The authors' anxieties and travails in the early days of cardiopulmonary bypass surgery will sound a sympathetic note in the breasts of many of their colleagues outside Edinburgh.

The cardiomyopathies find Professor J. F. Goodwin on a favourite theme. At best, the term is a diagnostic waste-paper basket. It has no more specificity than "infectious fever," but it is the best we can manage at present. Professor Goodwin popularized the designations "congestive," "constrictive," and "hypertrophic obstructive" which helped by distinguishing the three main groups. Each of them can mimic the clinical picture of well-known diseases of entirely different nature. For instance, constrictive cardiomyopathy and non-calcific constrictive pericarditis can defy differentiation by the most enlightened clinician. Yet the latter is curable and the other is not. Professor Goodwin's Sydney Watson Smith lecture, reproduced here in full, is the best available summary of the subject. Endomyocardial fibrosis (Dr. D. Emslie-Smith) and viral cardiomyopathy (Professor N. R. Grist) complete a useful survey of these mysterious conditions.

WALTER SOMERVILLE.

A Dermatopathologist's Lifetime

Dermatopathology. In two volumes. By Hamilton Montgomery, M.D. (Vol. 1: pp. 650+viii+index. Vol. 2: pp. 651-1247 +vi+index; illustrated. £24 set of two vols.) New York: Harper & Row, 1967.

Every doctor has at some time heard that dermatology is more art than science. Why has this idea persisted for so long? Perhaps because so many of its physical signs depend more on visual appreciation than on the other senses. Another reason has certainly been the inability of dermatologists and pathologists to apply the analytical methods of

other branches of medicine to the study of the skin. All analysis of skin disease must start with pathology, but medical students and trainee dermatologists are too often allowed to pass through their teachers' hands with but little knowledge of its histopathology.

At the Mayo Clinic students of dermatology have long been taught that their best friend is the microscope, and credit for this must largely go to Dr. Hamilton Montgomery and his pupils. His standard textbook with the late Dr. Ormsby on diseases of the skin is already in its ninth edition; he has now satisfied those who have long hoped that he would write a purely histological work as a companion to it. His *Dermatopathology* is large and covers about 1,300 pages in two volumes weighing ten pounds (4.5 kg.) and costing sixty dollars. It is written in his own personal style and appears in places to be almost autobiographical. One wonders how some phrases will read in five to ten years' time. "This is discussed further in the forthcoming 9th Edition of *Diseases of the Skin*, by H. Montgomery" (p. 383); "my colleague at the Mayo Clinic, S. A. Muller, is preparing a monograph on herpes simplex in all its aspects" (p. 531).

The arrangement of the book is conventional with preliminary chapters on definitions, biopsy, normal structure, and histochemistry (the latter two by R. K. Winklemann). Inevitably there will be some omissions, considered culpable by some readers, but books such as this are not intended to be encyclopaedic.

The very personal style with its free use of the first person singular may irritate, but the book is not really so egocentric. Other views than the author's are expressed and discussed. The references to cases shown on papers presented at various conferences and congresses and colleagues' slides sent to him make it more vivid and personal; it is, as it were, an account of a dermatopathologist's lifetime. For those who have met him, or admired his work, or lived through his time, this book will be intensely interesting. On almost every page one feels that the lines can only have been written by "Ham" Montgomery.

C. D. CALNAN.

Malnutrition in Primitive Countries

The Assessment of the Nutritional Status of the Community. By Derrick B. Jelliffe, M.D., F.R.C.P., F.A.P.H.A., F.R.S.H., F.A.A.P. (Pp. 271; illustrated. 30s.) Geneva: World Health Organization. London: H.M. Stationery Office, 1966.

The author of this useful book, who directs the Caribbean Nutrition Institute in Jamaica, has compiled his text in consultation with 25 of the world's leading nutritionists. Its purpose is to give guidance and practical advice to those responsible for the detection of signs of malnutrition, in all its various forms, in those parts of the world in which it occurs most frequently.

Its chapters cover: direct nutritional assessment of human groups, indirect nutritional assessment of human groups, assessment of ecological factors, nutrition surveys, and social problems in different groups. Subdivisions

of chapters deal with topics such as the clinical signs of malnutrition, nutritional anthropometry, biochemical tests, and biophysical methods. Perhaps its most important feature is its wealth of photographs—many in colour—of patients suffering from malnutrition, including close-ups of the outward parts of their body which are affected. Thus there are excellent photographs of the eyes in vitamin-A deficiency, of the gums in scurvy, and of the skin in pellagra. A photograph to illustrate ecological factors shows a group of Eskimo children sitting for a picnic meal on the kitchen floor, tended by their mother and entertained by an older brother strumming his guitar.

To aid the worker in the field, specimen forms are included, with spaces in which ticks can be placed against those signs of malnutrition present in the subject under examination. Details are given of the best ways of measuring heights, weights, arm circumferences, and skinfold thicknesses in children, and an annex tabulates standard values with which these measurements can be compared. Biochemical tests are recommended for assessments of the nutritional status in regard to protein, ascorbic acid, thiamine, riboflavin, niacin, iron, folates, and iodine. About 300 references to the literature are cited, and a good subject index is included.

A minor criticism is an occasional tendency to ascribe to modern workers findings made many years ago. Thus the discovery of the effect of acute infections in lowering vitamin A in the blood, ascribed to McLaren in 1966, was reported by Lindqvist in 1937, and has been frequently confirmed since then. But the purpose of the book is to help the worker in the field, and not to contribute to the history of nutrition. For those whom it is primarily intended it will be invaluable. Many others, however, will doubtless learn with interest and profit about the many practical problems to be faced in the assessment and correction of malnutrition.

T. MOORE.

Strike in Saskatchewan

'Doctors' Strike. Medical Care and Conflict in Saskatchewan. By Robin F. Badgley and Samuel Wolfe. (Pp. 201+xiii. \$6.50.) New York: Atherton Press, 1967.

Robin F. Badgley is a lecturer and specialist in public health administration. Samuel Wolfe, now the medical director of a group practice in Saskatoon, Saskatchewan, was a commissioner of Saskatchewan's medical care plan. These collaborators, by writing a lengthy account of previous medical and political squabbles in Saskatchewan and by dwelling on much detail in the conflict between the politicians and the doctors, have produced this book.

The Government's medical care plan caused the "strike" in 1962, but the doctors made emergency health services available. The dispute was largely settled through the wisdom and advice of Lord Taylor, who was sent by the British Government, on the invitation of the Prime Minister of Saskatchewan, to act as mediator. He succeeded in obtaining concessions from both sides, peace was made, and the "strike" ended. At the time it caused general interest, but it was less epoch-making than the authors would imply.

A summary is given of Britain's National Health Service and other health organizations now being considered in Canada and the United States. Much attention is paid to political direction of health services, but the doctor-patient relationship and medical ethics receive less attention in spite of their fundamental importance.

ARTHUR S. MACNALT. Y.

Human Behaviour

An Introduction to Psychopathology. 2nd edition. By D. Russell Davis, M.A., M.D., F.R.C.P., D.P.M. (Pp. 158+x. 16s.) London: Oxford University Press. 1966.

The first edition in 1957 was an expansion of the author's psychopathology lectures at Cambridge; now the text has been entirely rewritten to include more clinical and experimental findings at the expense of theoretical discussion. The result is a very clearly written, readable book. It was originally designed to tempt the experimental psychologist out of his laboratory and into the clinic, and at the same time to get the clinician thinking about possible psychosocial explanations of disturbed behaviour in his patients. While still fulfilling this function, it should also be of interest to anyone with a flexible mind who is interested in human behaviour.

The first chapters are devoted to various models which might help to generate useful hypotheses about abnormal behaviour. These include laboratory models such as the sensory deprivation situation, and naturally occurring models such as the reaction to earthquakes, bereavement, or brainwashing. One of the highlights is the description of the author's own well-known experiments with the Cambridge Cockpit. Presented with a machine which they could not make to work, under conditions of high drive, the subjects manifested a degree of psychopathology which is unusual in the laboratory situation.

Some became anxious, others aggressive; many became curiously inert or talked repetitively about details of the task; and a few went out drinking. It is surprising that this experimental design has not been used much in recent years; certainly the frustrations of real life are coming more and more to resemble the laboratory situation.

After a critical chapter on inheritance, the various mental disorders are discussed with particular reference to possible causative factors in the family and social environment. A full and varied section on the psychosocial causes of mental subnormality may be a surprise to some. Recent work on the families of schizophrenics is dealt with leniently, and the reader unfamiliar with the literature may get the impression that there is good evidence that the parents' behaviour plays a part in causing schizophrenia. Concerning disorders in adult life, the author writes "there is little systematic evidence on which to base a discussion of the psychosocial causes of mental illness. . . ." Nevertheless, the discussion ranges over possible factors such as widowhood, retirement, and the departure of children from the home. The final chapter on psychotherapy gives some idea of how the psychological models may be used in the planning of treatment.

The book makes no claim to comprehensiveness. Even so, in such a short space, many topics get only a brief mention; I would willingly have forgone the section on congenital malformations to learn more about the effect of separating mother and child shortly after birth. In his new department at Bristol University Professor Russell Davis is well placed and well qualified to apply the hypothetico-deductive method and experimental technique of psychology to the difficult problems of family pathology. There is certainly a great need for such a rigorous approach in this field of inquiry, and it is to be hoped that the book will encourage others, both psychologists and clinicians, to join him in the task.

JOHN PRICE.

N. R. GRIST.

Books Received

Review is not precluded by notice here of books recently received.

Dinamica Proceselor Cerebrale. By A. Kreindler. (Pp. 229. 16.50 Lei.) Bucarest: Editura Academiei Republicii Socialiste Romania. 1967.

Lehrbuch der Psychiatrie. By Professor Hans Heinrich Wieck. (Pp. 414+xvi. illustrated. DM. 44.) Stuttgart: F. K. Schattauer. 1967.

What is Allergy? A Guide for the Allergic Person. By Raymond T. Benack, M.D. (Pp. 158+xiii. \$6.75.) Springfield, Illinois: Charles C. Thomas. 1967.

Introduction to Dental Anatomy. 5th edition. By James Henderson Scott, D.Sc., M.D., F.F.D. R.C.S.I., and Norman Barrington Bray Symons, M.Sc., B.D.S., F.F.D. R.C.S.I. (Pp. 422+x; illustrated. 55s.) Edinburgh and London: E. & S. Livingstone. 1967.

The African Witch. With Particular Reference to Witchcraft Beliefs and Practice among the Shona of Rhodesia. By Michael Gelfand, C.B.E., M.D., F.R.C.P., D.P.H. (Pp. 227+xvi; illustrated. 30s.) Edinburgh and London: E. & S. Livingstone. 1967.

Clinical Virology. By R. H. A. Swain, M.A., M.D., F.R.C.P.Ed., F.C.Path., F.R.S.E., and T. C. Dodds, F.I.M.L.T., F.I.I.P., F.R.P.S. (Pp. 318+xii; illustrated. 75s.) Edinburgh and London: E. & S. Livingstone. 1967.

Venen-Fibel. 2nd edition. By Dr. F. Haid-Fischer and Dr. Helmut Haid. (Pp. 218+xv; illustrated. DM. 19.80.) Stuttgart: Georg Thieme. 1967.

Micro-Vascular Surgery. Report of First Conference, 1966. Mary Fletcher Hospital, Burlington, Vermont. Edited by R. M. Peardon Donaghy, M.D., and M. Gazi Yasargil, M.D. (Pp. 171+xii; illustrated. DM. 48.) Stuttgart: Georg Thieme. 1967.

Die Krankheiten der Schilddrüse. By K. Oberdisse and E. Klein. (Pp. 595+xv; illustrated. DM. 148.) Stuttgart: Georg Thieme. 1967.

The Mechanics of Healing. By Parnell Bradbury, D.O., M.R.O., M.B.N.O.A. (Pp. 141; illustrated. 37s. 6d.) London: Peter Owen. 1967.

Cerebrovascular Disorders. By James F. Toole, M.D., and Anel N. Patel, M.D. (Bombay), M.R.C.P.(Edin.). (Pp. 280+xv; illustrated. No price given.) New York: McGraw-Hill. 1967.

Viral Ecology

The Natural History of Viruses. By C. H. Andrewes. (Pp. 237+viii; illustrated. 55s.) London: Weidenfeld & Nicolson. 1967.

From the fluent pen of Sir Christopher Andrewes comes yet another highly readable, entertaining, and informative book. This one deals with viruses from a broad biological point of view, as organisms involved in the complex interactions of living things which form the stuff of ecology (which anthropocentric medical men so often treat as mere "epidemiology").

A general introduction to viruses and their interactions with metazoan and bacterial hosts is followed by the main section dealing with transmission of viruses. Examples are drawn freely from man, other animals and plants, from the jungles, the tundras, and Wiltshire. Representative chapter-headings are "Influenza, Ringer of Changes," "Mosquitoes, Herons, and Pigs," and "Boots, Worms, and Fungi."

The final section deals with more speculative aspects of ecology, such as latency, congenital infections, and tumours, and concludes with a brief consideration of the ways in which man might try to influence viral ecology for his own benefit.

The book is well illustrated and has useful appendices, bibliography, and a glossary. The latter, together with the lucid and entertaining style, makes this book suitable for the intelligent layman and general student of biology as well as for the undergraduate in medicine. All medical men interested in the interplay of living things should enjoy the stimulating ideas and up-to-date background information it provides for those concerned with communicable diseases at patient or community level. Virologists and those concerned in teaching virology will appreciate the broad approach and wealth of detail of this fascinating book.

Cancer in Pregnancy. By Larry McGowan, B.S., M.D. (Pp. 142+xi. \$7.50.) Springfield, Illinois: Charles C. Thomas. 1967.

The Rays are not Coloured. Essays on the Science of Vision and Colour. By W. D. Wright, A.R.C.S., D.Sc. (Pp. 154+x. 35s.) London: Adam Hilger. 1967.

Salisbury 200. The Bicentenary of Salisbury Infirmary. 1766-1966. By Members of the Hospital Staff. (Pp. 162; illustrated. 12s. 6d.) Salisbury: Salisbury General Hospital. 1967.

"Instinct and Intelligence." The Science of Behaviour in Animals and Man. By S. A. Barnett. (Pp. 250+xiii; illustrated. 45s.) London: MacGibbon & Kee. 1967.

Ausgewählte Internationale Bibliographie. 1952-1963. Zur Verkehrsmedizin. By Hermann Hoffmann. (Pp. 192. No price given.) Munich: J. F. Lehmanns. 1967.

Speech Handicapped School Children. 3rd edition. Edited by Wendell Johnson and Dorothy Moeller. (Pp. 562+xiv. No price given.) New York: Harper & Row. 1967.

Marvels of Medical Engineering. By Norman Carlisle and Jon Carlisle. (Pp. 144; illustrated. 27s. 6d.) London: Oak Tree Press. 1967.

Middle Articles

CONFERENCES AND MEETINGS

Chemotherapy of Tuberculosis in Developing Countries

[FROM A SPECIAL CORRESPONDENT]

A symposium on the chemotherapy of tuberculosis in developing countries was held at the Royal College of Surgeons of England on 25, 26, and 27 September.

Economics of Tuberculosis Control

With Dr. WALLACE FOX (London) in the chair, the first session began with a paper by Dr. H. T. WAALER (Oslo) on the economics of tuberculosis control, which was read in his absence. He emphasized the need to allocate resources to produce the maximum reduction of a disease problem per unit of expenditure. This principle applied at every level, from the Government to the director of health services, the tuberculosis services, and the individual clinician. At some levels there was a choice in allocating resources to one disease or another; at other levels a choice between approaches to the actual disease had to be made. Dr. L. MOKHTARI (Algiers) reported that 92% of the budget on tuberculosis in Algeria was spent on sanatorium beds, 7% on the clinic services, and 1% on B.C.G. vaccination. It was current policy to reduce the number of beds from 7,000 to approximately 5,500 to permit expansion of the other sectors. Dr. P. W. KANT (Nairobi) said that in East Africa there was a striking gap between the 80% or more cure rates achieved in the treatment of patients in controlled clinical trials and the 50% achieved by the general tuberculosis services in the same area. He favoured concentrating therapy exclusively on the effective use of standard drugs rather than dissipating resources on failure patients. He advocated diagnosis by smear and culture examination in patients producing sputum, and B.C.G. vaccination on school entry. Dr. K. M. CARRON (London) summarized the currently available regimens and their cost, recommending one year of treatment as the first priority, and the use either of thiacetazone plus isoniazid, if possible with an initial streptomycin supplement, or twice-weekly intermittent streptomycin plus high-dosage isoniazid. Dr. F. POLANSKY (Prague) reported that in the central Bohemian region over the five-year period 1958 to 1962 the expenditure on the tuberculosis outpatient facilities was 25% of that on hospitals and sanatoria. The total expenditure on 6,500 patients who were being treated for active tuberculosis on an outpatient basis was less than the expenditure on a sanatorium with 325 beds. Mr. D. E. SEYMOUR (Welwyn Garden City) reminded the audience of the formidable expenditure involved in testing new drugs. The cost to prepare a new drug for clinical trial was rarely as low as £100,000.

Drug Trials

At the second session, chaired by Dr. J. R. BIGNALL (London), Dr. J. FRIMODT-MÖLLER (South India) reported on a chemotherapy project in six small towns in India, in three of which the patients were treated with isoniazid and in three with isoniazid plus P.A.S. At the end of one year 45% of the patients who were initially smear positive had become culture negative, as had 63% of those initially smear negative but culture positive. There was a marginally higher prevalence of drug resistance in the study population at the end of the survey than at its start. Dr. J. F. HEFFERNAN (London) summarized the results of the series of East African/British Medical Research Council controlled clinical trials, which had established thiacetazone 150 mg. plus isoniazid 300 mg. in a single tablet as a standard regimen in East Africa, supplemented initially, when possible, by two months of daily streptomycin. Dr. D. H. SHENNAN (Newcastle) reported the results of a controlled trial in Rhodesia which demonstrated that thiacetazone plus isoniazid was as effective as streptomycin plus P.A.S., 76% of 58 patients compared with 84% of 55 being culture negative at six months; streptomycin plus thiacetazone was substantially inferior, for only 46% of 58 patients were culture negative. Dr. N. K. MENON (Madras) summarized a trial in Madras. In South Indian patients thiacetazone plus isoniazid was therapeutically as effective as P.A.S. plus isoniazid, but rather more toxic. Dr. P. A. L. HORSFALL (Hong Kong) reported the results of a controlled trial which showed that thiacetazone plus isoniazid in the Chinese in Hong Kong was somewhat less effective than P.A.S. plus isoniazid in terms of culture negativity at one year and the emergence of isoniazid resistance.

Drug Resistance

At the third session on thiacetazone sensitivity and resistance, chaired by Dr. N. RISØ (Paris), the chairman reminded the audience that pretreatment strains of tubercle bacilli type W and H37Rv behaved differently from strains from patients with acquired thiacetazone resistance in Europe and North Africa, whereas in South India the behaviour of many pretreatment strains resembled European strains with acquired resistance. Dr. D. A. MITCHISON (London) described differences between the pretreatment thiacetazone sensitivity of strains in different parts of the world. In East Africa and Madras a substantial proportion of strains were thiacetazone-resistant, associated with low virulence and susceptibility to hydrogen peroxide. In Hong Kong there was often

thiacetazone resistance with full virulence. He reviewed animal studies which showed that the decreased pretreatment thiacetazone sensitivity influenced the response to treatment with thiacetazone. He discussed anomalies in the differences in the response to treatment with thiacetazone plus isoniazid from one area to another, for the regimen was effective in East Africa and India, but less so in Hong Kong. A lively discussion ensued on whether or not a laboratory finding of natural resistance resulted in a failure of clinical response to thiacetazone-containing regimens.

Dr. J. GROSSET (Algiers) had found that pretreatment Algerian strains resembled British strains in being fully sensitive to thiacetazone, unlike strains from Hong Kong and Madras, and that the sensitivity to ethionamide was the same in all four groups of strains. He further reported that there was some correlation between acquired resistance to ethionamide and thiacetazone, but not true cross resistance. Dr. P. R. J. GANGADHARAM (Madras) had studied the pretreatment thiacetazone sensitivity of Indian tubercle bacilli in a survey in 10 large cities in India. There were differences from centre to centre, the northernmost city (Amritsar) having strains as sensitive as those from Britain, the sensitivity progressively decreasing until Madras, the most southern city, which had the most highly resistant strains.

Drug Toxicity

At the fourth session, with Dr. J. PEPYS (London) in the chair, thiacetazone toxicity was discussed. Dr. A. B. MILLER (London), in a general review, summarized the early experience which led to the abandonment of thiacetazone in the early 1950s. Its safety in combination with isoniazid was established in a series of controlled trials in East Africa. Subsequently, widely divergent reports on toxicity from different parts of the world led to a co-operative blind investigation by the Medical Research Council into the incidence of thiacetazone side-effects in 14 countries. This suggested there were genuine differences between countries, Czechoslovakia, Hong Kong, and Pakistan having the highest levels, Cyprus and India the lowest. The differences might be due to racial, dietary, or climatic factors or differences in observing and reporting side-effects. A second study was investigating these factors further, and also the claims of benefits from vitamin and antihistamine additives. The world literature suggested that jaundice was not more common in regimens containing thiacetazone 150 mg. than in control regimens, but there was evidence that the increase in haemoglobin,

which normally occurs during treatment, was less in patients on thiacetazone-containing regimens. The incidence of cutaneous hypersensitivity was very variable, and in some areas exfoliative dermatitis was encountered. There was evidence that thiacetazone could potentiate streptomycin toxicity. Sister M. AQUINAS (Hong Kong) reported a high incidence of side-effects with thiacetazone plus isoniazid in a study in Hong Kong, particularly cutaneous and haematological. Although 37% of 150 patients had rashes, about half generalized and some with stomatitis or a purpuric element, there had been no case of exfoliative dermatitis. The haemoglobin fell on average from 11.9 g./100 ml. pretreatment to 11.5 g./100 ml. at a year, in contrast to a rise from 11.9 to 13.3 g./100 ml. in the control group on P.A.S. plus isoniazid.

Dr. H. RADENAC (Morocco) summarized differences observed in toxicity in four centres in Morocco to thiacetazone plus isoniazid. In Rabat toxicity, notably cutaneous hypersensitivity, was common, whereas side-effects were very uncommon in Marrakesh and were intermediate in frequency in Meknes and Tangier. Women had more toxicity than men. Finally, Mr. K. TATTERSALL (London) reported on a laboratory evaluation of the antituberculous activity of thiacetazone and ethionamide.

Experimental Study of Intermittent Regimens

In session five, under the chairmanship of Dr. D. A. MITCHISON (London), the experimental basis of intermittent regimens was discussed. Dr. J. M. DICKINSON (London) described an in-vitro technique for exposing cultures of tubercle bacilli to chemotherapeutic agents for differing periods of time and studying the influence of such exposure on the growth of the cultures. Streptomycin could be expected to be highly effective when used in intermittent regimens, followed by ethionamide, isoniazid, and ethambutol. Pyrazinamide and cycloserine were in a doubtful category, thiacetazone and thiocarlide were unlikely to be useful, and P.A.S. gave variable results. She also reported in-vivo findings in the guinea-pig, which she considered a particularly good model for man, provided note was taken of species differences in drug metabolism. Dr. J. C. BATTEN (London) reported experiments with streptomycin plus isoniazid in murine tuberculosis. Both streptomycin and isoniazid were effective intermittently, but as the interval between doses increased the streptomycin effect was maintained but isoniazid was impaired. He pointed out that isoniazid is particularly rapidly excreted in mice.

Dr. G. CANETTI (Paris) described his mouse model, emphasizing that treatment was started after two weeks' delay when 10^4 bacilli were present, so that in effect the situation resembled a medium-sized cavity. Only certain drugs could be studied in mice, which were not suitable for cycloserine, P.A.S., and thiacetazone. It was important to use a murine strain which was highly susceptible, young animals, a highly virulent

bacillary strain, and a standardized inoculum. The three important factors in the response were the frequency of administration of drug, the dose, and the duration of an initial period of daily chemotherapy. Bacillary resistance was frequent in long-term intermittent chemotherapy, especially if the residual population exceeded 400 viable units. The mouse was an excellent model but unsatisfactory for studying relapse, since organisms almost invariably grew out after stopping chemotherapy, and, also, reversion from resistance towards sensitivity both with streptomycin and isoniazid commonly occurred.

Clinical Aspects of Intermittent Regimens

The sixth session, with Professor J. G. SCADDING (London) in the chair, considered clinical aspects of intermittent regimens. Dr. N. K. MENON (Madras) reported a comparison of streptomycin 1 g. plus isoniazid 14 mg./kg. body weight twice weekly (S.H.T.W. regimen) with the same combination once weekly (S.H.O.W. regimen). The S.H.T.W. regimen achieved quiescence in 92% of patients at a year compared with 71% on the S.H.O.W. regimen, a highly significant difference. The S.H.T.W. regimen was uninfluenced by the inactivation rate of isoniazid or the dosage of streptomycin (1 g. or 0.75 g., which had also been allocated at random). In the S.H.O.W. regimen 82% of the slow compared with 60% of the rapid inactivators had quiescent disease—a significant difference, but there was a smaller difference between the two streptomycin dosages. In a second phase two further regimens were added, making a four-regimen concurrent comparison. In one regimen (S.H.Z.O.W.), pyrazinamide 90 mg./kg. was added to the once-weekly streptomycin plus isoniazid, and in the other (S.H./S.H.O.W.) the once-weekly 2-drug combination was preceded by one month of daily streptomycin plus isoniazid. At one year quiescent disease was achieved in 95% of the S.H.T.W. patients, 88% of the S.H./S.H.O.W. patients, 75% of the S.H.Z.O.W. patients, and 66% of the S.H.O.W. patients. Although the S.H./S.H.O.W. regimen achieved a high level of success, there was evidence that it, like the two once-weekly regimens, was affected by the inactivation rate of isoniazid. Only the twice-weekly regimen was really robust. Dr. S. P. TRIPATHY (Madras) reported on the bacteriological findings from the same study, which showed that the emergence of isoniazid and streptomycin resistance in the four regimens approximately paralleled their efficacy, and that in the S.H.O.W. regimen the isoniazid was inadequate in the rapid inactivators and the streptomycin was inadequate in the low-dosage streptomycin group. Adding the third drug, pyrazinamide, in the S.H.Z.O.W. regimen made up for the streptomycin deficiency in the low-dosage streptomycin group but not for the isoniazid inadequacy. The addition of the initial intensive phase of chemotherapy in the S.H./S.H.O.W. regimen corrected the deficiency of streptomycin in the low-dosage streptomycin group.

Dr. P. CHAULET (Algiers) reported the use of streptomycin plus high-dosage isoniazid twice weekly in 135 patients in Algiers, in 26 from the start of treatment, in 41 after one month, in 36 after two months, and in 32 after three or more months daily chemotherapy. All four regimens achieved a high level of success; overall 95% had quiescent disease at 12 months. In contrast, Dr. F. J. M. BURZONI (Morocco) reported unsatisfactory results with streptomycin 1 g. plus isoniazid 750 mg. combined in a large single intramuscular injection twice a week. The study was uncontrolled and the losses were high, but of 64 patients remaining for analysis 29 were classified as failures of chemotherapy. There was no obvious explanation for these findings which did not fit either the experimental or the other clinical reports. Dr. P. STRADLING (London) had satisfactory results with supervised continuation chemotherapy with streptomycin 1 g. plus isoniazid 650 mg. three times a week after an initial three months of standard triple daily chemotherapy. Of 139 patients 88% completed one year and 80% the planned 18 months. There was only one failure.

In the seventh session, under the chairmanship of Dr. R. GOULDING (London), the quality control of drugs for tuberculosis was discussed. Professor A. H. BECKETT (London) gave a general survey of what quality control entailed. Dr. H. STOTT (London) reported the striking deterioration of tablets and capsules of cycloserine in Madras. A current batch of 250-mg. tablets was found on assay to have a mean cycloserine content of 76 mg. at the time of issue to patients. Investigation showed that in the high tropical temperatures the humidity was particularly dangerous and that tablets dispensed in paper envelopes and kept in the patients' homes rapidly had less than the lower *British Pharmacopoeia* limit—within a matter of days—namely, in one experiment an average content of 41 mg. at 10 days and in another 21 mg. at 56 days. Dr. Stott emphasized the importance of care, not only in the manufacture, packaging, and in transit, but in storage in the tropics and dispensing for outpatients. Routine checks for potency were also necessary. Mr. Y. RICE (Basingstoke) discussed the quality control of cycloserine, Mr. T. E. V. HORSLEY (Ulverston) of streptomycin, and Mr. B. W. MITCHELL (Gilston Park) of P.A.S.

Laboratory Methods

In the last session of the symposium a discussion was held under the chairmanship of Professor J. W. CROFTON (Edinburgh) on the role of the laboratory in the chemotherapy of tuberculosis in developing countries. The panel members agreed in principle that simple methods were essential, but disagreed widely on the frequency with which smears, cultures, or sensitivity tests should be performed, and in which patients. Radiography was agreed to be less valuable than bacteriology, especially during treatment.

The symposium was sponsored by Smith and Nephew Associated Companies Ltd.

European Views on Liver Disease

[FROM A SPECIAL CORRESPONDENT]

The second meeting of the European Association for the Study of the Liver was held at Gothenburg, Sweden, on 22-24 September under the presidency of Professor Sheila Sherlock and with Professor S. Bengmark acting as local secretary.

Treatment of Infectious Hepatitis

Dr. U. P. HAEMMERLI (Zurich) reported an analysis of 471 consecutive admissions with acute infectious hepatitis to two public hospitals in Zurich. In one hospital the patients were treated routinely with corticosteroids, in the other they were not. Corticosteroid therapy lowered the serum bilirubin and transaminase levels but did not shorten the period of hospitalization. The mortality was 2.4% in the group treated with corticosteroids, due to ulcer complications, as compared with 0.7% in the untreated group. There was also an increased incidence of relapse after discharge from hospital in those given corticosteroids.

Dr. G. TYTGAT (Louvain) reported generally unfavourable results from the use of exchange transfusion in hepatic coma due to acute infectious hepatitis. This was also the experience of Professor Sherlock (London) and Dr. J. P. Benhamou (Clichy). Dr. R. FRISSIG (Berne) reported recent experimental studies in dogs with canine hepatitis, in whom the survival rate had been improved by exchange transfusion. Hyperimmune serum given intravenously had also been effective, and he and his colleagues had started a controlled trial on the use of gammaglobulin in severe hepatitis.

Dr. B. HARVALD (Copenhagen) reported the latest results of the Copenhagen controlled study of long-term prednisone therapy for cirrhosis. This trial had been initiated in 21% of 122 first-degree relatives of 42 histologically verified cases. Prednisone produced a temporary symptomatic and biochemical improvement, but to date had not improved the overall survival rate. A beneficial effect on survival might, said Dr. Harvald, be found in females with active non-alcoholic cirrhosis and high gamma-globulin levels, though the difference in survival was as yet of borderline statistical significance.

Dr. D. MÜTING (Homburg/Saar) gave an account of studies of the long-term effect of lactulose and *Bacterium bifidum* on protein metabolism in 27 patients with chronic liver disease. In a number of these tolerance had been improved to food protein, and blood ammonia level, the free serum amino-acids, and the free serum phenols had been reduced to normal. In the subsequent discussion Dr. J. P. HAEMMERLI (Zurich) stressed the importance of titrating the dose of lactulose

according to the response of the patient. Initially 20 g. daily should be tried, this being increased to 30-40 g. daily given in divided doses. The pH of the stools should be kept below 6.

Bilirubin Metabolism

Dr. A. BAKKEN (Oslo) opened a discussion on bilirubin metabolism. He had found that erythroblastotic infants had conjugated bilirubin in their sera at birth if their mothers had been heavily immunized during pregnancy. He postulated that the maternal bilirubin induces bilirubin glucuronyl transferase activity in the foetal liver, and this had been confirmed experimentally in rats. Dr. V. DESMET (Louvain) had studied the distribution of conjugated and unconjugated bilirubin in the liver in different varieties of cholestasis using selective histochemical stains. He had found that the bilirubin in bile thrombi was predominantly conjugated, whereas pigment accumulation in the cells was partly of the conjugated and partly of the unconjugated type. The presence of the latter might be due to deconjugation of conjugated bilirubin by β -glucuronidase, suggested Dr. Desmet. The concentration of this lysosomal enzyme had been shown to be increased in cholestatic jaundice.

Dr. G. ACOCCELLA (Milan) produced further evidence in favour of deconjugation of conjugated bilirubin in the liver. He had studied the distribution of bilirubin administered in conjugated form to Gunn rats after ligation of their bile ducts. Serum levels of unconjugated bilirubin rose, and this, together with the finding of an increased β -glucuronidase activity in the liver, suggested that the conjugated bilirubin was being deconjugated in the liver.

Dr. B. H. BILLING (London) reported that she had found a raised serum bilirubin level in 21% of 122 first-degree relatives of 42 patients with Gilbert's syndrome (idiopathic unconjugated hyperbilirubinaemia). She concluded that the disorder was inherited as an autosomal dominant with incomplete penetrance. Of interest was the considerable variation in serum bilirubin levels found in the probands. In 33% the serum bilirubin level had been on one occasion within the normal range.

A new syndrome of hereditary recurrent cholestasis was described by Dr. O. AAGENAES (Oslo). He had studied 16 patients, all related, with this condition. The patients had varying degrees of cholestatic jaundice from birth to between 1 and 6 years of age. After the cholestatic period development had been satisfactory apart from a tendency to leg oedema; but later cholestatic episodes recurred. Liver biopsy during the attacks showed a giant cell hepatitis. Seven of the patients had died in infancy of bleed-

ing, so early recognition of the disease permitting treatment with vitamin K was important.

Dr. A. SCOTT (London) drew attention to "the stagnant bile syndrome." The presence of bacteria in large numbers in the bile in patients with partial biliary obstructions and cholangitis leads to bacterial overgrowth in the small intestine with suboptimal B_{12} absorption and other features which mimic the intestinal "blind loop syndrome."

Iron Metabolism

Dr. M. BARRY (London) reported that he had found that desferrioxamine and diethylenetriamine penta-acetic acid differed in their relative affinities for the various chelatable iron pools in the body. Increased desferrioxamine chelatable iron did not necessarily indicate an increased total body iron; high values were found, for instance, in cholestatic jaundice. Dr. V. HOENIG (Prague) said that the administration of ethanol caused increased absorption of iron from a bivalent iron salt in cirrhotic patients but not in normal subjects. This effect could be prevented by simultaneous administration of pancreatin and to a lesser extent by intravenous pancreozymin.

Dr. R. WILLIAMS (London) described the clinical features of the specific arthropathy of idiopathic haemochromatosis. This had been present in 16 of 32 patients examined. Radiographs showed chondrocalcinosis due to deposition of calcium pyrophosphate, which was also responsible for acute episodes of crystal synovitis. Increasing age of the patient and duration of iron overload were important factors in the pathogenesis.

Pancreatic Disorders

Dr. G. A. MARTINI (Marburg/Lahn), using the pancreozymin secretin test, had found abnormal pancreatic function in more than half of 70 patients with proved chronic liver disease. Abnormalities were found as frequently in cryptogenic cirrhosis and active chronic hepatitis as in alcoholic cirrhosis. The characteristic high volume low bicarbonate concentration juice seen in haemochromatosis was also found in some patients with cirrhosis. Dr. W. CREUTZFELDT (Göttingen), in discussing the cause of the increased incidence of diabetes in cirrhosis (12-14%), reported further studies showing elevated plasma insulin levels in the fasting state, after glucose loading, and after intravenous tolbutamide in patients with cirrhosis. These findings were consistent with endogenous insulin antagonism as the most important factor in the impaired carbohydrate tolerance.

Correspondence

Letters to the Editor should not exceed 500 words.

Psychotropic Drugs

SIR,—The letter of Dr. P. Leyburn and others (14 October, p. 108) is misleading enough to require answering, since it both ignores and oversimplifies the problems facing psychiatrists today.

The term depression is open to misunderstanding. It is employed in different ways, and there is no one accepted classification or terminology. Depressive illness is probably not a single entity. Clinically there are several recognizably distinct forms, responding differently to different treatments.

The M.R.C. trial was a valuable one. It was carried out on patients suffering from what traditionally would be called endogenous depression, with symptoms of self-depreciation with a morbid sense, sleep disturbance, hypochondriasis, retardation of thought and action, and agitated behaviour. These are patients of the type likely to respond to E.C.T., and known since 1960 to respond to tricyclic antidepressants such as imipramine. Early on in our investigations of the actions of antidepressant drugs we recognized that patients with endogenous depression would not generally respond to monoamine oxidase inhibitors, and could indeed be made worse by them. The M.R.C. trial therefore confirmed these early findings.

The monoamine oxidase inhibitors are particularly useful in cases of reactive depression. Here phobic anxiety symptoms are sometimes prominent, and the clinical picture often resembles that of anxiety hysteria. In other patients tiredness and lack of energy are the main complaints, similar to what in the past was called "neurasthenia." Somatic symptoms are apt to arise and become a focus on to which the patient's anxiety is displaced. Vicious circles of this type were difficult to break before the advent of the monoamine oxidase inhibitors, and no amount of investigation and reassurance would convince the patient that he was not afflicted by some fatal illness. A similar vicious circle may arise during or following a somatic illness, when anxiety and depression will perpetuate symptoms. It is this type of patient, so common in general practice and general hospital out-patients departments, who responds so well to the monoamine oxidase inhibitors. To confuse these patients with those with endogenous depression who require admission to a mental hospital is only adding confusion to an already confused subject. Dr. Leyburn and his colleagues write that there are many clinicians who have become doubtful of the value of monoamine oxidase inhibitors. I know of no physician or psychiatrist, dealing frequently with reactively depressed patients described above, who has become "doubtful of their value." That these drugs need to be given skilfully and discriminatingly goes without saying, but when used properly their value is considerable.

By all means let us have controlled clinical trials, but Dr. Leyburn and his colleagues can surely have little idea of the practical difficulties and time involved if they can write that "they should have little difficulty in carrying out a properly controlled trial to demonstrate this" (the value of monoamine oxidase inhibitors in psychosomatic conditions). The psychiatric departments of general hospitals today are already over-stretched in their commitments. If the M.R.C., or some other organization, will provide money for research units to be attached to psychiatric departments, then the controlled trials and proof for which Dr. Leyburn and his colleagues ask will be forthcoming.—I am, etc.,

P. DALLY.

Department of Psychological Medicine,
Westminster Hospital,
London S.W.1.

SIR,—In the point of view expressed by a Morpeth group of psychiatrists (14 October, p. 108) regarding Dr. William Sargent's advocacy of certain drugs in psychosomatic illness (30 September, p. 861) perhaps the reason for the variable results obtained in different parts of the country lies not so much in either the symptoms or the drugs but in the patients' constitutions, which have developed in response to differing climatic and social variants.

I recall a Scottish psychiatrist who observed that sodium amytal gr. 6 (0.4 g.) produced only a mild sedative effect in certain of his Edinburgh patients, but his similar patients in Northumberland just went to sleep on that dosage.

Psychosomatic (or preferably somato-psychic) patients are very sensitive. The lady quoted as eventually dying after eating cheese while taking iproniazid may on that occasion have had some other unnoticed or unknown factor which had a catalytic or cumulative terminal effect.

Similarly, patients who fall ill in climates or circumstances different from those in which they spent their earlier years may show an unexpected response to drugs which have been found satisfactory in the native community.—I am, etc.,

Bristol

G. M. LANGHAM-HOBART.

Future of the Regional Hospitals

SIR,—The National Health Service has much to be proud of in the improvement that has been achieved in the vast majority of regional hospitals. The future of these hospitals, whether old or new, however, is open to grave misgivings unless staffing and facilities within them is not a good deal more imaginative than is provided at present.

Public interest and money is being spent on building new hospitals, equipping intensive care units, coronary care units, renal units, etc., but unless they are properly staffed, not only by senior staff but with appropriate assistants, with accommodation for doing the work necessary to keep their departments really alive, they will never be first-class. At present little or no accommodation for discussion in departments is provided. Junior medical staff and secretarial help is kept at a minimum, no official link is made with teaching schools in the region, and senior staff are bogged down by overwhelming routine.

Much emphasis is laid on study leave for all grades of staff, but, important though this may be, attending courses is no substitute for an active department with a spirit of inquiry at the hospital in which the doctor works, whether he is senior or junior, and no teaching is as useful as the bedside teaching and informal discussion in a room attached to the department.

The number and seniority of junior medical staff in a department should not depend on numbers of beds but on what work should be done in the department. Difficulty in obtaining junior staff is put forward as a reason for not having them, but keen junior staff can always be obtained for a really active hospital, and hospitals that are static do not deserve any better help.

It is probably no fault of regional boards or management committees that they cannot provide what is necessary to keep our hospitals as proper medical centres, and senior staff from getting frustrated, as they are tied by finance and the decisions of committees. Could not the Ministry of Health take positive steps to combine the resources of our teaching schools with our regional hospitals, and set up joint medical committees from both, to arrange that their teaching and research work shall be complementary to each other?

Many of the senior medical staff of teaching schools and regional hospitals have for a long time recognized this situation, and in many cases there is such good will between them that semi-private arrangements for interchange of junior medical staff and sometimes medical students has been arranged at their instigation, albeit with the somewhat reluctant approval of their official governing bodies. The time has now come for such arrangements as these to be part of the normal programme which the National Health Service as a whole should recognize. Furthermore, some recognition to the staff of regional hospitals who assist with teaching would not come amiss, as they give a lot of extra time for the benefit of both those they teach and to maintaining a high standard in the hospitals. Unless the universities, the Ministry of Health, boards of governors and regional boards can produce some scheme to accomplish this the regional hospitals are likely to become second-class, and the junior staff and students at the teaching schools are in danger of losing a lot that would help them have a wider training.—I am, etc.,

Hitchin, Herts.

P. J. W. MILLS.

Pyloric Stenosis in Turner's Syndrome

SIR,—The prevalence of congenital hypertrophic stenosis in the general population is estimated to be about 2 to 5 per 1,000 live births,^{1,2} and Carter was able to demonstrate that the sex ratio for this malformation amounted to 5:1, boys being more affected than girls.³ Benson and King have drawn attention to a possibly high prevalence of this condition in patients with Turner's syndrome.⁴ We have investigated a series of 43 patients with Turner's syndrome and found two patients with congenital pyloric stenosis.⁵

The diagnosis of Turner's syndrome in Case 1 was established at the age of 19 years on the following criteria:

- (1) Sexual infantilism with primary amenorrhoea, infantile external and internal genitalia, and absence of breast development.
- (2) Dwarfism: height 143 cm.
- (3) Extragonadal malformations: short neck without webbing, low implanted and malformed ears, scoliosis, clinodactyly, striking brachymetacarpism of the fourth and fifth fingers of the right hand, and of the fourth finger of the left hand, oedema of the fingers and feet, hypoplastic nails, hallux valgus, shortening of the first metatarsal, and multiple pigmented naevi.
- (4) The sex chromatin was found to be negative in the buccal smear, and the karyotype in the peripheral blood was 45-XO.

The patient was the youngest of a family of four children, and weighed 2.65 kg. at birth after a pregnancy lasting 38 weeks. Persistent vomiting started seven weeks after birth. No information could be obtained about gastric peristalsis or a palpable gastric tumour, but the diagnosis was radiologically confirmed. Surgical intervention was proposed, but refused by the parents. Conservative treatment, however, was successful, and the vomiting stopped by the age of 7 months.

The diagnosis of Turner's syndrome in Case 2 was established at the age of 12 years on account of:

- (1) Dwarfism: height 128 cm.
- (2) Extra-gonadal malformations: short neck with webbing and low hairline, low implanted and malformed ears, hypoplastic and retrognathic jaw, shield-shaped chest with widely spaced nipples, clinodactyly, oedema of both fingers and feet, and multiple pigmented naevi.
- (3) The sex chromatin in the buccal smear was negative and the karyotype in the peripheral blood was 45-XO.

The patient was the first-born of a family of two children, and the duration of the gestation was probably 44 weeks. The birth weight was 3.5 kg. Between the fourth and eighth week of pregnancy unsuccessful attempts to procure a miscarriage with drugs were made. Persistent vomiting started from the first week after birth. Gastric peristalsis and tumour were noted, and the diagnosis was radiologically confirmed. Conservative treatment was successful, and the vomiting stopped at the age of approximately 6 months, at which time the child weighed 3.3 kg.

The prevalence of hypertrophic pyloric stenosis in our series of 43 patients with Turner's syndrome amounts to 46 per 1,000, which is the same as found by Benson and King.⁴

Turner's Syndrome and Pyloric Stenosis

Author	Number of Patients with Turner's Syndrome	Number of Patients with Pyloric Stenosis	Prevalence
Lindsten ⁷	57	1	18/1,000
Benson and King ⁴	65	3	46/1,000
This study	43	2	46/1,000

According to Benson and King this incidence of 46 per 1,000 is significantly different ($P < 0.01$) from that found in the general population, the incidence for girls being 1 per 1,000, for boys 5 per 1,000. Further evidence is thus added to the hypothesis that the incidence of hypertrophic pyloric stenosis in Turner's syndrome might be higher than in the general population, and might be comparable with the incidence among sibs in cases with familial pyloric stenosis.—I am, etc.,

H. VAN DEN BERGHE.

Department of Human Genetics,
University of Leuven,
Belgium.

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Medical and Surgical Vagotomy and Intrinsic Factor Secretion

SIR,—In the interesting report by Dr. J. F. Adams and others (19 August, p. 473) on the effect of medical and surgical vagotomy on the gastric secretion of intrinsic factor, these authors cite one of our papers on this subject.¹ We should like to correct a slight misunderstanding concerning the concept "reduction." We expressed the postoperative values in per cent of the preoperative values—that is, the values are reduced to x% not reduced by x%. Thus the intrinsic factor output after operation was reduced to 44%, or reduced by 56%. According to our data the values for volume, acid, and intrinsic factor output,¹ though somewhat higher than the values given by Dr. Adams *et al.*, did not differ significantly from the results recorded by these authors.

It seems then well established that the histamine stimulated intrinsic factor secretion after vagotomy and a drainage procedure is reduced to about half the preoperative values.^{1,2} It is therefore interesting that medical vagotomy does not lead to a significant reduction in intrinsic factor output. This finding is supported by the result of Dotevall *et al.*³ and our own study⁴ on the effect of optimal effective doses of L-hyoscyamine on gastric secretion. In the accompanying Table are shown the mean secretory values in the posthistamine hour for a series of duodenal ulcer patients before and after surgical vagotomy and drainage,¹ and in

	Volume	Acid	Intrinsic Factor
Surgical vagotomy			
Before ..	408	40.4	27.8
After ..	217 (53%)	15.0 (37%)	12.2 (44%)
L-Hyoscyamine treatment			
Before ..	391	43.8	27.2
During ..	284 (73%)	30.8 (70%)	24.3 (89%)

Mean values of volume (ml./hour), acid (mEq/hour), and intrinsic factor (kilo units/hour) in posthistamine hour for male duodenal ulcer patients, before and after surgical vagotomy and drainage, and before and during treatment with optimal effective doses of L-hyoscyamine.

another series of male duodenal ulcer patients before and during anticholinergic treatment.⁴ After surgical vagotomy the output of volume, acid, and intrinsic factor was significantly reduced. During treatment with L-hyoscyamine the values of volume and acid were significantly lower than the pretreatment values, while no significant difference was found for the intrinsic factor secretion.—We are, etc.,

POUL M. CHRISTIANSEN.

Surgical Department A,
Bispebjerg Hospital,
Copenhagen.

PAUL RØDBRO.

Medical Department F,
Glostrup Hospital,
Copenhagen.

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Human Infection with Porcine Ascaris

SIR,—Drs. R. F. Phillipson and J. W. Race (30 September, p. 865) have drawn timely attention to the fact that the pig *Ascaris* can infect man. Some years ago we pointed out¹ that work in this laboratory supported by the Medical Research Council of Ireland suggested that the pig was a source of human ascariasis. Later we concluded² that no biochemical differences could be found between the porcine and human forms of *Ascaris*.

Recently³ we have reviewed the evidence for regarding *A. lumbricoides* and *A. suum* as separate species and shown that there is evidence (for example, Lysek⁴ and Moskalev⁵) that *A. suum* can develop as readily in man as in the pig. Apart from the infection of the gut, porcine *Ascaris* may cause Loeffler's syndrome in man⁶ and sensitivity to the helminth occurs not uncommonly in laboratory workers.⁶—I am, etc.,

FERGUS J. O'ROURKE.

Department of Zoology,
University College, Cork.

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Insulintropic Action of Secretin

SIR,—Drs. D. R. Boyns, R. J. Jarrett, and H. Keen in their recent study (10 June, p. 676) were unable to enhance the serum insulin response to an oral or intravenous glucose load in normal subjects by simultaneous duodenal acidification with citric acid. They have therefore suggested that secretin may not play a physiologic role in the regulation of glucose metabolism.

Since the intraluminal duodenal pH of fasting normal subjects may be acid, however, exogenous acidification of the duodenum in these subjects may not stimulate further

secretin release. For this reason we have chosen to study the fasting serum insulin and blood glucose response to duodenal acidification in four subjects unresponsive to maximal histamine stimulation in the presence and absence of an intravenous glucose load.¹ The secretin mechanism in these patients may be presumed intact since (a) they did not have any clinically evident impairment of pancreatic function; and (b) a number of substances other than gastric hydrochloric acid, such as amino-acids and fatty acids, cause the release of secretin.²

Our results support and extend those of Boyns, Jarrett, and Keen.³ Duodenal acidification in all four subjects in the absence of an intravenous glucose load failed to cause a rise in serum insulin or a fall in blood glucose. In three of these subjects duodenal acidification was carried out in the presence of an intravenous glucose load, and in all three there was no rise in serum insulin or consistent enhancement in the rate of glucose disappearance over that observed with the control ingestion of neutralized saline. In addition, the shapes of the individual serum insulin response curves were striking in that while variations existed from patient to patient, in each individual patient the shape was practically identical following either acid or saline. These observations together with those of Boyns, Jarrett, and Keen suggest that the intestinal factor responsible for the more rapid blood clearance of an oral glucose load does not appear to be endogenously released secretin.

In contrast to their findings and those of Dupré, Curtis, and Beck,⁴ however, we were able to demonstrate an increase in fasting serum insulin levels of 54 to 115% with pancreozymin when injected intravenously into two fasting normal subjects. This difference may be explained by the fact that we sampled venous blood within one minute of injection and at closely timed intervals thereafter. Since the peak increase in serum insulin occurred within one minute and subsided within 10 minutes, this transient response may not have been detected by these previous investigators. In view of our preceding findings with endogenously released secretin, however, we feel that this effect of exogenously administered pancreozymin, like that of secretin, is probably of pharmacologic rather than physiologic significance.—We are, etc.,

RICHARD J. MAHLER.
HERBERT WEISBERG.

New York Medical College,
Flower and Fifth Avenue Hospitals,
New York, U.S.A.

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Oculogyric Crises after Phenothiazines

SIR,—It was interesting to see a report from Drs. E. C. B. Keat and P. J. Toghill (30 September, p. 867) on side-effects from the use of phenothiazine. These bizarre effects were first brought to my attention in 1962¹ and were then described as the

"grimacing syndrome." I reported two further cases,² both occurring in early pregnancy, after the use of prochlorperazine (Stemetil) for vomiting of pregnancy.

A review of the literature was published in January 1962,³ with two further case reports where perphenazine (Fentazin) and trifluoperazine (Stelazine) were the drugs concerned. Bush⁴ reported two cases following Fentazin, one in pregnancy, in 1963. Since then I have seen two further cases, in one of which the resemblance to epilepsy in pregnancy led to initial advice to refrain from holding a driving licence. This advice was reversed when the facts were later reviewed, and the patient remains well five years later. In the second case it was again noticeable that an inability to protrude the tongue when requested was the main diagnostic sign in a middle-aged woman who had had prochlorperazine.

I would join Drs. Keat and Toghill in sounding a note of caution in the use of this useful group of drugs, and this should perhaps apply to their use in pregnancy more than at other times. It should also be added that the recognition of this condition is of the greatest importance, as, if misdiagnosed, it may lead to the patient being labelled as an epileptic or at least submitted to unnecessary diagnostic procedures.—I am, etc.,

Worcester.

J. B. ROGERS.

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Vital Decision

SIR,—The recent correspondence about the resuscitation notice in Neasden Hospital leads one to suppose that not many doctors are aware of the concern of the nursing profession over the whole question of the resuscitation of patients in hospital. Nor do some of our medical colleagues seem to appreciate the extent to which nursing staff are involved in initiating resuscitation in patients suffering from cardiac arrest.

It is the nursing staff who more often than not start to resuscitate the collapsed patient in the "ordinary" wards of a hospital—that is, in other than special areas such as intensive therapy units, recovery units, cardiac-thoracic units, operating-theatres, etc. It is one thing for a citizen to give the "kiss of life" to a dying person in the street—and more and more of the general public are being trained to meet this sort of emergency—but it is quite another thing for an inexperienced junior member of the nursing profession to exercise judgement about which patient (who may already be seriously ill in bed) should be subjected to heroic resuscitation measures. A nurse's instinct is to help to prolong life, but there is understandable reluctance to do so at the expense of more unnecessary suffering on the part of patients and relatives.

The Royal College of Nursing has asked the medical profession to give guidance for each individual patient on the very difficult issue of deciding which patients should be allowed to end their days in dignity and peace because of their medical condition. A survey (see below) which the Hospitals Department of the R.C.N. undertook in July

1966 to find out the extent of the nurse's involvement in initiating resuscitation, and the guidance and instruction given on action to be taken in such circumstances, showed, among other things that in more than half the cases reported in 302 wards in the hospitals where the survey was conducted it was junior student nurses on night duty who initiated the resuscitation.

The results of the survey were published in the *Nursing Times* of 11 November 1966, and were referred to in the *B.M.J.* (*Supplement*, 8 April, p. 15). The fact that other hospitals have similar criteria (though not publicly displayed) to those issued at Neasden seems to have gone unnoticed.—I am, etc.,

CHRISTINE BROWN.

Secretary,
Hospitals Department,
Royal College of Nursing.

London W.1.

SIR,—I hope that the composers of this "soothing syrup" (30 September, p. 814) will not consider the following comments hysterical or ill-informed or be offended by them, as that is not their purpose. A patient who is really dead cannot be revived. If he can be revived he can't be dead, and no one can be certain if he is alive or dead until appropriate measures have been tried and failed. Perhaps this may seem pedantic, but the point I want to make is that *only* the patient has the right to decide for or against attempts at resuscitation and *no one else*.

A doctor's duty in observance of his Hippocratic Oath is to maintain life as long as possible by every means in his power. Furthermore, as euthanasia is still illegal, doctors have no legal right to deprive any patient of appropriate treatment to resuscitate him. We doctors are far from infallible, so every patient, whatever his age or disease (unless he doesn't wish to be resuscitated), should be resuscitated if possible, no matter what his doctor may think about its desirability. No Government or Ministry has the right to saddle doctors or anyone else with this responsibility. To leave the question of life or death to man-made decisions is to open the road to disrespect for the sanctity of life, murder, or even mass murder, as in Hitler's Germany.—I am, etc.,

Gosport, Hants.

G. W. FLEMING.

Paget's Disease in a Family

SIR,—I was very interested to read the paper on Paget's disease by Drs. J. Verrier Jones and Mervyn F. Reed (14 October, p. 90).

I have a patient aged 54 on my list who was one of eleven children. He had five brothers and five sisters. Two of his brothers are now dead; both were incapacitated by Paget's disease.

The remaining brothers are also sufferers from Paget's disease. One of the sisters has the disease to a marked degree. The others appear to be mildly affected. Between them they have seven children, all free from any abnormalities. Also there is no evidence of Paget's disease in parents, grandparent, uncles, aunts, etc.

It appears from the above that only one generation has been affected (all members

having Paget's disease in some form or other).
—I am, etc.,

Sutton-in-Ashfield,
Notts

G. STEIN.

Gritti-Stokes Amputation

SIR,—Mr. Peter Martin and his colleagues' (30 September, p. 837) series of Gritti-Stokes amputations for vascular disease is unrivalled. Their primary healing rate is probably superior to any other reported series of amputations in the elderly atherosclerotic patient.

Knowing of their results, and, like them, disappointed with the through-knee disarticulation in this type of patient, we have tried to combine the benefits of early healing with satisfactory weight-bearing when pylons and permanent prostheses are fitted. To this end it seemed desirable to provide as flat and large a weight-bearing surface as possible, and therefore it was proposed to section the femur just above its condyles (as it is in the true Gritti operation), but to supplement this with a patellar enucleation. Patellar enucleation not only provides better end bearing, but also prevents slipping, avascular necrosis or non-union of the patella, and provides a painfree stump.

We have now carried out this operation on 15 patients, with primary healing in all but two. One patient whose arterial tree was blocked up to the aorta suffered a 1-in. (2.5-cm.) localized loss of his anterior flap. The other, owing to technical faults, suffered a superficial skin loss of his posterior flap.

The patients can often be discharged home, walking on their pylons, three weeks after amputation.—I am, etc.,

St. Bartholomew's Hospital,
London E.C.1. F. E. WEALE.

SIR,—We were delighted to read the recent article by Mr. P. Martin and his colleagues (30 September, p. 837) in which they record their favourable experience with the Gritti-Stokes amputation for the ischaemic limb. There seems to have grown up an unjustifiable prejudice against the Gritti-Stokes amputation, and we have been frankly puzzled by reports^{1,2} condemning the amputation, since to us it seems to possess all the attributes the authors of these reports seek in other amputations. The alternatives they suggest seem far less favourable, and we have concluded that there must be wide differences in the manner of performing a Gritti-Stokes amputation. The paper by Messrs. Martin, Renwick, and Maelor Thomas is timely, since it redresses the balance and focuses attention again upon an excellent form of amputation which has been in danger of being discarded for less satisfactory operations.

Our experience with approximately 100 patients over the last five years accords well with that of Mr. Martin. The operative technique we use is slightly different from that described by him. The first step is to divide all structures behind the lower end of the femur, and this is easily accomplished from either the medial or the lateral aspect. The incision for the anterior flap divides the ligamentum patellae and the quadriceps expansions so that a flap of patella and associated tendon is turned up; the undersurface of the patella is removed with a saw, and the

skill with which this is done is decisive in determining the success of the amputation. Admittedly this requires a knack, but after correct removal of its articular surface the flat face of the patella is very stable upon the cut end of the femur; a few catgut stitches between the ligamentum patellae and the investing fascia of the thigh posteriorly are sufficient to prevent its subsequent displacement. We do not find it necessary to dislocate the knee joint at any stage, since it is removed, together with the leg, when the femur is divided. The quadriceps expansions are sutured to the deep fascia posteriorly and to the various hamstring tendons. With careful haemostasis it is unnecessary to drain, and of course firm bandaging is avoided—only loose dressings are applied.

Perhaps surgeons, uncertain about the best general-purpose amputation for the elderly, will give fresh thought to the Gritti-Stokes amputation.—We are, etc.,

DAVID M. ESSENHIGH.
DAVID J. TIBBS.

Radcliffe Infirmary,
Oxford.

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Railroading in Retinal Vessels

SIR,—I was interested in the report of the above condition by Dr. P. J. Tomlin (16 September, p. 722).

The late Dr. Ernest Bulmer, who achieved great distinction in the Birmingham area and also nationally, was house-physician to the then professor of medicine Dr. Lovell Gullund in Edinburgh Royal Infirmary around 1922. It was Bulmer's habit when a death occurred in his ward to rush off immediately with his ophthalmoscope to examine the eyes of the patient. Primarily he did this because of the good view of the retina afforded by the dilated pupils of death. He noted the curious appearances of the retinal vessels, changes which he had never seen in life, and regarded these changes as conclusive signs of death. His discovery of these phenomena were known to his friends and colleagues, and he waxed so enthusiastically about them that, rather irreverently, they were called "Bulmer's breaks."

Whether he ever recorded them in writing I do not know, but as the ordinary signs of death were accepted at that period I am sure no attempt was made to resuscitate anybody who showed these retinal changes. I know that Bulmer, then a young man, regarded them as a confirmatory and most conclusive sign of death.—I am, etc.,

Broughton,
Lanarkshire.

A. C. GILLIES.

Demonstration Aerosol Inhalers

SIR,—Many patients for whom aerosol inhalers are prescribed do not use them properly, despite the instructions printed on the containers or in the leaflet accompanying it. The only way the doctor can ensure that his patient knows how to use the inhaler effectively is to watch him using it, and if necessary to give him a demonstration. Such a demonstration is likely to be more effective, and to occupy less time, if the doctor can

take an inhalation himself, but most doctors would prefer not to inhale a drug such as isoprenaline.

It would therefore be useful if the manufacturers of pressurized aerosol preparations would provide "demonstration" inhalers, containing only an inert propellant. Doctors and nurses in general practice and in hospital could then use their own personal demonstration inhalers as often as needed for teaching patients how to inhale correctly.—I am, etc.,

A. HERXHEIMER.

Department of Pharmacology,
London Hospital Medical College,
London E.1.

Thymic Structure

SIR,—In your leading article "Thymic Function and Disease Processes" (19 August, p. 447) it is stated that the normal thymus contains no lymph follicles with germinal centres.

I would like to refer you to my findings¹ in a survey of 928 necropsy thymus glands. This included a group of 71 apparently healthy subjects killed in accidents in which the incidence of follicular structures with germinal centres was 50% if all age groups are considered, or 70% if only those subjects falling into the 0-39 years' age group are considered. This figure (70%) is identical with that quoted by Castleman² for the incidence of follicular structures in the thymuses of myasthenic patients without thymomas who had a thymectomy. Most such patients fall into the 0-39 years' age group. Although the follicles found in myasthenic patients are usually more numerous than those found in apparently normal subjects, this is not always the case.¹ Some accident victims had follicles just as numerous and as large as have been seen in the most florid myasthenic thymuses.

The overall incidence of follicular structures with germinal centres in 714 hospital deaths was 5%. This increased to 31% if only those patients (58) who died within three days of the onset of their illness were considered.

The implication in your leading article that follicular structures with germinal centres in the human thymus are significant of autoimmune disease is misleading. Thymic follicular structures with germinal centres do occur in a high proportion of healthy human subjects. The incidence decreases with advancing age and with illness.—I am, etc.,

G. MIDDLETON.

Department of Pathology,
University of Queensland,
Brisbane, Australia.

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Facial Palsy

SIR,—Therapeutic nihilism can be carried too far. It is well known that Bell's palsy usually recovers spontaneously, and therefore treatment is unnecessary (30 September, p. 815). Nevertheless, in the residual 10% who do not recover there are some who will benefit from decompression of the facial nerve if it is done in time. This small fraction of all cases of Bell's palsy is usually identified

through patients having a complete paralysis, usually of six or more weeks' duration, with normal electrical conductivity of the nerve, and clinical evidence that the lesion is sited in the descending portion of the Fallopian canal. When regular tests show commencement of progressive deterioration of electrical conductivity then decompression of the grossly oedematous nerve is promptly carried out in order to facilitate survival of the remaining nerve fibres with normal electrical conductivity.

The infrequency of this clinical situation makes a random control series impossible, but the repeatedly observed fact by different observers that prompt partial recovery sometimes follows decompression in the situation described above should not be simply dismissed.—I am, etc.,

Hedon, Yorks.

R. G. WILLIAMS.

"Geriatric Emergencies"

SIR,—Dr. D. F. C. Deacon's letter on the subject of emergency admissions for the elderly (7 October, p. 53) raises important issues regarding the function of the acute medical ward in general and particularly in relation to the elderly.

The function of the average acute medical ward is multifarious. Many patients who are admitted, such as those for investigations, or with peptic ulcer, or diabetes for stabilization, fulfil the useful function to the ward of diluting demands on the nursing staff. Nevertheless, as a result of tradition the nurse/patient ratio of such wards is relatively favourable, varying in different hospitals between 2:1 and 1:1. One is a fortunate patient indeed to be admitted to such wards, particularly if one is in the age group mentioned by Dr. Deacon.

On the other hand, the patient admitted into the geriatric assessment unit, however well organized, has to compete for the attention of a nursing staff under continuous demand from other helpless patients. However, it must be pointed out to Dr. Deacon that the modern geriatric assessment unit does not present the picture of the old chronic-sick ward, inasmuch as there are side wards for the dying patient and also provision for the acutely confused patient, either in small psycho-geriatric units attached or in side-rooms. Furthermore, the resources of the fully evolved geriatric unit are geared more adequately to the rehabilitation of the elderly patient both socially and physically. This is particularly true of the hemiplegic, who in the average acute medical ward runs the danger of being relegated to one corner with a label of chronic sick very early in his ward life. Furthermore, the nursing staff of a fully developed geriatric unit, by virtue of specialized training in geriatric nursing, is particularly more attuned to the prevention of the dreadful bedsores than the staff of the average general medical ward.

It is unfortunate, of course, that many geriatric units are relegated to the worst type of accommodation instead of to the best and that an inadequate amount of financial resources from the National Health Service has been devoted to the treatment of this group of the community. It is interesting to note, for example, that the cost to a regional hospital board of an operation on a "blue baby" is about £5,000, although the results are in doubt and even successful results do

not necessarily mean that the baby will grow up into a productive member of society. On the other side of the scale, a member of the community who has been a taxpayer all his life and has never had an illness until he reaches the age of 76 who suddenly develops a stroke or an acute confusional state due to illness runs the risk of being admitted into an inferior type of accommodation where the nurse/patient ratio is grossly inadequate owing to maldistribution of nursing resources. These are the factors which lead to the frustration experienced by Dr. Deacon.

What is urgently needed is a complete re-assessment of work load factors of various departments in the hospital service. These work load factors should be assessed by an industrial team, so that nurse/patient ratios are not determined by indefinables such as pre-existing establishment or status. It is quite obvious that the hospital of the future will have as its centre a main block of beds containing geriatric assessment units and intermediate and long-stay wards for the elderly, and that grouped on its periphery will be small units for other specialties, including day wards for patients who were previously admitted for investigation. In this way nursing staff will be deployed more efficiently, so that the present contradictions so well outlined by Dr. Deacon may in future be avoided.—I am, etc.,

W. FINE.

Liverpool 25.

Lithotomy Position for Forceps

SIR,—I should like to offer support to Dr. A. H. Morley in his indictment of the lithotomy position for forceps delivery (30 September, p. 862). The fact that deaths are still occurring from inhalation of gastric contents shows that the practice still continues.

The hazards often develop unexpectedly. I recall an instance where a patient was sent to the theatre for a forceps delivery, and, as the anaesthetist, I received a message that the operator might proceed to do a caesarean section. One therefore expected the patient to arrive fully prepared for a major operation, and this to include having an empty stomach. She vomited copiously in the early stages of the induction, thus proving the point in the *Confidential Enquiries*: "The only safe assumption in any parturient woman is that the stomach is full." One is tempted to add, "in spite of all assurances to the contrary."

I attribute this patient's fortunate survival to two circumstances. Firstly, a sucker in working order was immediately to hand. Secondly, shortly before I left the hospital common-room for the theatre a fellow-resident with anaesthetic experience told me that when vomiting occurred in an obstetric patient the lithotomy position was "a death trap." This put me on my guard and was a reference to the fact that the lithotomy stirrups, by anchoring the legs, prevent the patient from being turned on her side to prevent inhalation of vomited material.

In such an emergency it is essential that the anaesthetist be given authority to remove the stirrups without question and without delay. Sterility at this point is irrelevant. Indeed, the question should be asked whether in any case of forceps delivery under general anaesthesia stirrups should be allowed to be

used. The legs could be held by two attendants, who could then give valuable assistance under the anaesthetist's instruction should vomiting occur.—I am, etc.,

Huddersfield,
Yorks.

P. DRANSFIELD.

REFERENCE

¹ *Report on Confidential Enquiries into Maternal Deaths in England and Wales, 1961-63*, H.M.S.O.

Fallacies in Four Fevers

SIR,—I read with great interest the article by Professor R. S. Illingworth entitled "Fallacies in Four Fevers" (7 October, p. 41). His article does much to banish the old-fashioned concepts of the treatment and management of infectious disease, and confirms the impressions held by many general practitioners in the course of their work. His comments concerning the keeping of children home from school following infectious illness should be given to every general practitioner and local school authorities throughout the country.

Unfortunately in practice it is not always easy to persuade parents and teachers that in fact the child is perfectly able to go to school after a short period of time, as suggested by Professor Illingworth. Only this week I had a child sent home from school nine days after the onset of chicken-pox, despite the fact the child was clinically well and well out of the period of infectivity. This was because the regulations concerning the return to school after infectious disease were last drawn up in 1956 and have never been amended since.

It is to be hoped that this article will abolish once and for all the illogical and absurd treatment and management of these common conditions.—I am, etc.,

Bristol.

JEREMY P. TELLING.

SIR,—Professor R. S. Illingworth's article "Fallacies in Four Fevers" (7 October, p. 41) brought a breath of fresh air to the subject of exclusion from school in the common infectious diseases.

Most local education authorities and their school medical officers follow the advice on periods of exclusion contained in a memorandum issued jointly by the Ministry of Education and the Ministry of Health. The latest edition of this memorandum, that of 1956, suggests the following periods of exclusion:

Measles: 10 days after the appearance of the rash if child appears well.

Rubella: 7 days from the appearance of the rash.

Mumps: 7 days from the subsidence of all swelling.

Chicken-pox: 14 days from the date of appearance of the rash.

While there is room for some divergence of opinion on the question of how many days each disease is communicable, it is clear that these officially recommended periods of exclusion give a wide safety margin, up to seven days in some cases.

So far there have been editions of the memorandum in 1909, 1925, 1927, 1942, and 1956, and each successive edition has reflected changes in medical opinion, and the periods

of exclusion advised have become progressively shorter. Perhaps the time is now ripe for a further revision, to take account of newer knowledge of periods of communicability. Uniformity of practice in excluding children from schools is very desirable, and difficulties arise when doctors follow their own individual fancies in this matter. In a school where the children are patients of different doctors one can imagine the confusion that can occur in a chicken-pox epidemic when Dr. A. excludes children for one week after the appearance of the rash, while Dr. B. keeps them off school until every last scab has fallen off. Teachers and parents who favoured Dr. B's approach would not hesitate to ascribe the natural progress of the disease through the school to Dr. A's "negligence" in letting the children return to school "too soon."

School medical officers being naturally cautious souls, we tend to fall back on the advice given in the Ministry memorandum when consulted about this matter. There is real need for an authoritative up-to-date guideline on periods of exclusion from school.—I am, etc.,

J. M. MORFITT.

Spalding Urban District Council,
Public Health Department,
Spalding, Lincs.

REFERENCE

- ¹ Ministry of Education Memorandum on the Closure of Schools and Exclusion from School on Account of Infectious Illness, 1956. H.M.S.O., London.

Fatal Constipation in the Aged

SIR,—The triad of cardiac failure, constipation, and confusion is well known in geriatric practice; hence rectal examination has come to be regarded as a routine and imperative procedure in the aged. The complications of constipation in the aged are numerous and may sometimes prove fatal. The following report illustrates the point.

Miss A, aged 87, was admitted complaining of constipation and abdominal distension, discomfort, and pain. There was a history of recurrent episodes of these symptoms over two and a half months. In the past she also suffered from coronary thrombosis and had periods of confusion. The present attack of abdominal symptoms was followed by melaena and a clinical picture of colonic obstruction. As she was unfit for surgical intervention, she was treated conservatively. However, three days after admission she died.

Necropsy showed a peritonitis of short duration due to stercoral perforation of a pelvic colon grossly overfilled (1,195 g.) with impacted faecal matter. No new growth was found.—We are, etc.,

D. B. RAO.

M. S. KATARIA.

St. Francis's Hospital,
London S.E.22.

Haemoglobin Levels and Dietary Iron

SIR,—The paper by Drs. R. H. Davis, A. Jacobs, and Rosa Rivlin on haemoglobin levels and dietary iron (16 September, p. 711) is most interesting because it provides experimental evidence for some deductions that have so far been rather tenuous.

It is curious that in some recent surveys the amount of anaemia among women is remarkably similar, although the surveys have been conducted in areas which might be

expected to have differing dietary habits and social composition.

Surveys in rural Wensleydale,¹ industrial Birmingham,² and suburban Beckenham³ have nearly all shown a degree of anaemia among women of childbearing age close to 25%, and with the mean haemoglobin levels showing little change since the M.R.C. survey of 1943.⁴ Other surveys give different figures for the incidence of anaemia or mean haemoglobin levels, but without revealing any obvious cause for this in terms of social or geographical factors.⁵⁻⁷

It is known that menstruation plays an important part in this because the incidence of anaemia decreases after the menopause, but dietary anaemia is not uncommon in infancy, adolescence, and in the elderly. Yet the influence of dietary variations is not so far reflected in a detectable form in the haemoglobin surveys mentioned. If the relationship between diet and haemoglobin is as variable as the authors have demonstrated then this absence of correlation is not surprising.

It is, of course, very difficult to obtain an accurate estimate of dietary intake,⁸ those with the poorest intake giving the least reliable results. Moreover, McCance's⁹ tables measure total iron and not absorbed iron. These two may not be equivalent, as has been shown by the radioactive iron studies of Moore.¹⁰

The only survey of haemoglobin levels showing a regional variation is that in the Perinatal Mortality Survey of 1958,¹¹ where haemoglobin levels are lowest in Scotland and the north, and highest in the south-east. The only factor in the Ministry of Agriculture Food Survey of 1961¹² which shows a consistent geographical distribution is that of green vegetables, whose intake is least in Scotland and greatest in the south-east. Whether this is cause and effect is an interesting speculation.—I am, etc.,

Cambridge.

R. H. MORGAN.

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- ⁹ McCance, R. A., and Widdowson, E. M., *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, 1960, No. 297.
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- ¹¹ Butler, N. R., and Bonham, D. G., *Perinatal Mortality*, 1963, p. 78. Edinburgh.
- ¹² National Food Survey Committee, 1963. *Domestic Food Consumption and Expenditure: 1961*, p. 17. H.M.S.O., London.

M.A.O. Inhibitor Headache

SIR,—Any patient who is put on to the monoamine oxidase inhibitor drugs should be advised to avoid eating cheese, Marmite, and other substances which combine with the drugs to give a violent and dramatic headache, clinically comparable with a subarachnoid haemorrhage. Cooper *et al.*¹ described the syndrome as a hypertensive crisis. They found that in their series the mean resting level of the blood pressure rose from 125/75 to 180/120 mm. Hg.

I wish to record that in the last two cases seen by me soon after the onset of the

symptoms there was no marked rise in the blood pressure. Mrs. A. B., aged 50, who was on Parstelin (tranlycypromine and trifluoperazine), came home from a meeting and had a large cheese sandwich. Soon afterwards she developed a very severe headache, which she described as if something had struck her on the back of the neck. I was at the bedside within half an hour of the onset of the pain, and I took her blood pressure several times. It varied between 160/90 and 140/80. The latter figure was the norm for this patient. The headache lasted for a week, and kept her in bed most of the time. Her blood pressure after the first day varied from 120/60 to 140/80. This incident took place in 1963, before I realized that cheese was a factor in the problem. Last week I saw a Mrs. C. D., who had been given Parstelin by one of the doctors on our rota. In spite of warnings about cheese, she had had a meal of it, and within half an hour she was laid low with the typical headache, which made her feel sick. I had no prior record of her blood pressure, but when I took it within an hour of the onset of the symptoms it was only 120/80. This is a painful and alarming drug reaction, and in my experience it is not always accompanied by a marked rise in arterial tension.—I am, etc.,

Ibstock,
Leicestershire.

C. A. H. WATTS.

REFERENCE

- ¹ Cooper, A. J., Magnus, R. V., and Rose, M. J., *Lancet*, 1964, 1, 527.

Mercury Perchloride in Surgery

SIR,—The assumption behind the use of mercury perchloride solutions in cancer surgery is that, in addition to a mechanical wash-out action, they have a cancerocidal effect on cells not washed out; or, to use a more modern idiom, that the harmful effects on the cancer cell outweigh the harmful effects on the normal tissues. This half-century-old assumption has not to my knowledge been put to the test. Dr. George E. Moore, whose group at Roswell Park Memorial Institute has intensively investigated the question of local chemotherapy in cancer surgery, informs me that he too does not know of any accurate evaluation of mercury perchloride (personal communication). If such is the case, has not the time come for an accurate evaluation?—I am, etc.,

London W.1.

DAVID PATEY.

Cantharides Intoxication

SIR,—The interesting item in Medical Memoranda (7 October, p. 33) under the heading "Cantharides Intoxication" states that only four cases have been reported in the English medical literature in the past 25 years.

I would mention a short report entitled "Catharidin Poisoning Due to a 'Blister Beetle'" in the *British Medical Journal*, 1960.¹—I am, etc.,

S. G. BROWNE.

The Leprosy Study Centre,
London W.1.

REFERENCE

- ¹ Browne, S. G., *Brit. med. J.*, 1960, 2, 1290.

Advantages of Health Centres

SIR.—Dr. E. V. Kuenssberg (14 October, p. 108) seems to have read into our letter much that was not there and to have missed the points we intended to make. We were neither criticizing nor underestimating privately financed health centres, merely pointing out the high costs involved, which we felt was an intolerable burden on the young doctor who has recently come into general practice. This was not an armchair criticism, as we have had this information from visitors to the William Budd Health Centre and, in discussions at conferences, from the doctors working in privately owned centres. Certainly there is no possible interpretation in our letter which might infer that we regard private health centre schemes as "hare-brained"; on the contrary we even suggested how these could be run with advantage.

Furthermore, we are well aware of the various conferences on health centres (one of us attended and spoke at the M.P.U. conference earlier this year), but our primary object is to have a conference of health-centre doctors and *not* a conference on health centres.—We are, etc.,

H. I. HOWARD.
E. J. LACE.

William Budd Health Centre,
Bristol 4.

Interview Board for North America

SIR.—The Minister of Health is to send out a team whose unenviable task it will be to try to win back a proportion of medical emigrants (30 September, p. 873). Since conditions are so unsatisfactory here it seems probable that some special incentive will have to be offered if this scheme is to meet with any success at all. But if it does meet with a measure of success who will be the most likely to return—the able enthusiast, who has established himself in a new country, or the disappointed emigrant who has found himself no less a misfit in his new surroundings than he did in this country?—I am, etc.,

North Shields,
Northumberland.
DENIS V. CASHMAN.

"Total Family Care" and Fees

SIR.—As one of the "pre-Whittaker" prodigals returned from the more commercial side of the Atlantic, I take some comfort in the vague signs of rescue from one's financial entanglements in the shape of the faltering steps of our ministerial masters into the thorny jungle of "fee for service." At the same time, however, the very tentative nature of these steps does I believe cause some difficulty in the conscientious application of the two opposing principles under which we are expected to operate.

In an attempt to provide what I regard as total family care I am happy to include advice and practical assistance in family planning, a subject which I feel strongly falls squarely within the court of the family doctor, as opposed to the more impersonal health clinic. That I may charge my patients a fee for the initial examination, fitting, and supply of a suitable device or tablet is clearly understood by both doctor and patient. So far so good. I also feel thereafter under a professional obligation to maintain regular checks upon the patient so serviced. But

here the dividing line between my responsibilities under the N.H.S. and those as private medical adviser becomes somewhat less differentiated, and, in common with other objects of an undifferentiated nature, a source of possible future danger. Indeed, to pursue the analogy a step further, in the course of time, and in the light of the very proper encouragement of preventive medicine, this lack of differentiation may deteriorate to frank malignancy. Further I would add that if I am any judge of the expected reaction of patients, at least in my part of the country, I am quite confident that they would be content to pay a moderate fee for this service of aftercare. This willingness to pay for a recognizably useful "check-up" service is a matter which I feel is kept too well concealed in the political undergrowth of the Elephant and Castle.

If I might be allowed to encroach one further inch upon your valuable space, it would therefore be to suggest that we should be allowed to charge any patient over school age, who so requested, a reasonable and agreed fee for one annual "complete physical examination," without fear of contravening our terms and conditions of service. That this fee should be paid by the Ministry as for the other items so covered (though one would hope with less complicated paperwork) is of course a most laudable ambition, which would bring the N.H.S. in line with most if not all the provincial insurance schemes in Canada.—I am, etc.,

Alcester,
Warwicks.

A. F. MADGE.

More Forms

SIR.—It appears that to get a refund of selective employment tax in respect of part-time employees it will now be necessary to make two applications—one to the Ministry of Social Security and one to the executive council.

Bureaucratically this may be excellent, but it makes one wonder whether all the value for direct payments for ancillary staff is not going to be eaten up by the fact that the staff are going to be employed in producing more and more forms for the Ministry and less and less help for the general practitioner.—I am, etc.,

Wolverhampton,
Staffs.

R. S. V. MARSHALL.

Overseas Registration and Seniority

SIR.—I graduated from Punjab University in April 1941, and was registered with the Punjab Medical Council in May 1941. I was eligible for full registration with the General Medical Council, London, from that date, as confirmed by a letter from the G.M.C. dated 9 February 1967.

I have been a principal in the N.H.S. continuously from July 1958. I applied for the first seniority payment and was refused by Birmingham Executive Council on the ruling they received from the Ministry of Health that full registration means registration with the G.M.C. London only. I then applied direct to the Ministry on 9 March 1967 explaining that my registration was equivalent to full registration with the G.M.C. (as confirmed by their recent letter), and that the period should be counted from 15 May 1941. I received a reply in May

1967 telling me that full registration means actual registration by the G.M.C. and that registration with overseas bodies did not count for the purpose of determining eligibility for seniority payment.

While I was awaiting the above reply the Ministry issued a circular, paragraph 2 of which says that registration with the Registration Council of the Republic of Ireland is now recognized for seniority payment.¹ This came into effect from October 1966. While congratulating Irish colleagues on their well-deserved success in obtaining justice, one wonders if it is because the Ministry realizes the absurdity of not recognizing overseas registration, or is it that Eire is still regarded as a British possession?—I am, etc.,

Aston,
Birmingham.

G. MURTAZA.

REFERENCE

¹ E.C.N. 594 (E.C.L. 17/67), Ministry of Health.

Points from Letters

Sales Promotion

Dr. H. G. MORRIS-JONES (Dyserth, Flintshire) writes: I was interested to read Dr. J. R. Caldwell's letter on sales promotion (16 September, p. 741). It reminded me of a visit by a young representative some months ago—not knowing that I had retired some seven years ago. In the course of the conversation he said that he knew of two doctors who refused to see travellers, and he wondered how they managed to carry on their work. Such was his opinion of general practitioners. I told him that they probably gave better treatment because they were not bothered with representatives pushing their drugs.

Drinking Doctors

Dr. R. A. DE K. GLOVER (West Horsley, Surrey) writes: Many doctors enjoy, deserve, and feel all the better for a drink or two after a hard day's work. . . . But they have no real idea about how much is required to push their individual blood readings up beyond legal limits. I therefore suggest that they invest in a few breathalysers, and, on a few duty-free evenings, test themselves hourly (for say three or four hours) after one, two, and three drinks of their normal tippie on (a) an empty stomach, and (b) a full one. This would give them some idea of their legal capacity and prevent a great deal of worry or reluctant abstinence.

Melanoma, Halothane, and Liver Necrosis

Mr. M. WHITING (London W.1) writes: The two cases described by Mr. G. S. W. Organe and Dr. G. L. B. Thurston (7 October, p. 49) resemble in some respects those which used to be called "delayed chloroform poisoning" or "post-anaesthetic acidosis."

I had seen two cases of this condition, both in children aged 4 and 7 respectively, who were operated on for acute appendicitis. The anaesthesia was relatively short, 15 minutes for the first, and 30–35 minutes for the second, which had an appendix abscess. Both patients appeared to be doing well the morning after operation, but each later in the day became very restless and vomited frequently. One had a high temperature of 105–106° F. (41° C.), but the other only a moderate temperature of 101° F. (38.5° C.), which became normal next morning. Death took place in each case 36 hours after operation.

Post-mortem examination in the younger patient showed extensive fatty degeneration of the liver; in the older one the liver was yellow and mottled, with fatty degeneration, and the kidneys were pale and enlarged, and microscopically fat was seen in the cells of the convoluted tubules.

These cases differ in some respects from those of Mr. Organe and Dr. Thurston, which were, however, adult patients.

Obituary Notices

F. E. STABLER, V.R.D., M.D., F.R.C.S., F.R.C.O.G.

Mr. F. E. Stabler, senior obstetrician and gynaecologist to the United Newcastle upon Tyne Hospitals, died on 13 October after returning home by car on a stormy night from Southport, where he had been adjudicating in a nurses' contest. He had borne ill-health and pain for many years with remarkable fortitude, and had achieved his avowed object of carrying out his full professional commitments until the day of his retirement on 23 September. He was 65.

Francis Edward Stabler was born on 23 September 1902, and received his medical education at the University of Durham, graduating M.B., B.S. in 1925. He proceeded M.D. in 1928, and was awarded a gold medal; in the following year he took the F.R.C.S. After holding resident appointments in the skin, gynaecological, and general surgery departments at the Royal Victoria Infirmary, Newcastle upon Tyne, he was appointed assistant obstetrician at Princess Mary Maternity Hospital. He later became consultant obstetrician and gynaecologist at the Royal Victoria Infirmary, and consultant at Princess Mary Maternity Hospital. During the second world war he served in the R.N.V.R., and spent a considerable part of his time practising general and traumatic surgery at Chatham, Sherborne, and Trincomalee, attaining the rank of surgeon commander. He was elected Fellow of the Royal College of Obstetricians and Gynaecologists in 1945.

As a member of Council of the Royal College of Obstetricians and Gynaecologists, and as an examiner for the Membership of the College, Stabler concerned himself with the wider field of his subject, while in Newcastle he was an active committee member. He was recently vice-chairman of the House Committee, and chairman of the Medical Staff Committee, of the Princess Mary Maternity Hospital, and of the Medical Staff Committee of the Royal Victoria Infirmary. He was an ex-president of the North of England and Newcastle upon Tyne Obstetrical and Gynaecological Societies, where his lively comments stimulated spirited discussion. In 1957 he was vice-president of the section of obstetrics and gynaecology at the Annual Meeting of the British Medical Association.

Frank Stabler was a very determined man, frank by nature, forthright and outspoken in discussion, and sincere in his opinions. His direct approach and puckish humour made him a popular teacher to students and nurses, in whose education and welfare he always took a keen personal interest. In his professional work he was sound, down to earth, and practical, and reluctant to adopt new techniques until he, personally, was satisfied that they had been proved to be safe and were practicable. However, he strongly supported well-planned research programmes and adequately controlled clinical trials. He was one of the original small team of obstetricians who introduced and operated the Newcastle Emergency Obstetric Service—the "Flying Squad"—in 1935, of which until

recent months he was an active and enthusiastic member.

In private life he had many diverse interests. He loved to visit his cottage in Swaledale, or to fish the waters of the Tyne or Colt Crag reservoir, and he was an enthusiastic wildfowler who, undeterred by adverse weather conditions, would happily spend many cold, wet hours in his punt, stalking duck on the sandy flats between Holy Island and the North Northumberland coast. He was chairman of the Northumberland and Durham Wildfowling Association for some years, and, in addition, with his great interest in bird life and deep concern for nature conservation, he was active in the formation of the Lindisfarne National Nature Reserve, and became committee chairman. In quieter moments of relaxation he became absorbed in the interpretation and working of intricate patterns of tapestry, in which he was very proficient and which gave him great satisfaction.

He will be greatly missed in Newcastle and in many other places where he was a welcome visitor. We extend our deep sympathy to his widow, daughter, and two sons.—W. H.

W. PATRICK, T.D., M.B., CH.B.

F.R.F.P.S.GLASG., F.R.C.S.ED.

F.R.C.S.GLASG.

Mr. W. Patrick, surgeon and director of accident services at Glasgow Royal Infirmary, died suddenly on 14 October as he was playing golf at Turnberry, Ayrshire. He was 66.

William Patrick was born on 5 July 1901, and was educated at the High School and University of Glasgow, graduating M.B., Ch.B. in 1924. After serving early resident appointments at Glasgow Royal Infirmary he joined the staff in 1928. In 1931 he was elected Fellow of the Royal College (then Faculty) of Physicians and Surgeons of Glasgow, and the following year Fellow of the Royal College of Surgeons of Edinburgh. In 1936 he became first assistant to the late Professor J. A. G. Burton, St. Mungo professor of surgery in the University of Glasgow. He served during the second world war in the R.A.M.C. as lieutenant-colonel in charge of a surgical division. He was sent overseas, and was mentioned in dispatches. He was also the holder of the Territorial Decoration. After demobilization he returned to Glasgow Royal Infirmary, and in 1953 he was appointed consultant surgeon. Some years later he became surgeon and director of accident services at the infirmary. In 1962 he was elected Fellow of the Royal College of Surgeons of Glasgow. He retired in 1966.

H. H. P. writes: There will be many sad hearts at the news of the sudden death of Bill Patrick. Patients, colleagues, and a

multitude of friends will mourn the loss of a skilful and decisive surgeon, and a loyal and well-loved companion on every and any occasion. During his school and university days Bill proved himself something of a "natural" at ball games—rugby, cricket, and golf in particular—and indeed at any activity which demanded what is generally called "a good pair of hands." His "Blue" at Glasgow University was gained as opening bat in the cricket eleven, and probably only attention to his medical work, then and thereafter, prevented his achievement of higher honours in this game. It was not surprising therefore that he should follow his father's path, and spend his distinguished medical career as a surgeon. It is, however, of his other qualities that I write here, and of these his modesty takes pride of place. Never from him would one discover the wide spectrum of his medical activity and achievement, or the many facets of his life outside his professional duties. In hospital and out of it Bill Patrick was a perfectionist, demanding always of himself the highest standards in duty and behaviour. Conscientious and considerate for others, he was justifiably intolerant of those who failed to measure up to his standards—for him to undertake a task was to ensure that it was well done.

For many years, and especially since his retirement a year ago, his main recreation was golf, at which he was a stylish and able performer. He founded the active golf club of his infirmary, a conception which has brought relaxation and happiness to many colleagues within and without the hospital. Only his closest friends, of whom there are many, are aware of his pride in the talents of his devoted family. Such friends, and a host of admirers, extend to his wife, son, and two daughters their deepest sympathy in their bereavement.

Major-General F. J. O'MEARA

A.M.S.(RTD.), C.B., M.A., M.D., F.R.C.P.I.

D.T.M.&H.

Major-General F. J. O'Meara died suddenly on 15 October at Ledbury, Herefordshire. He was 67.

Francis Joseph O'Meara was born into a medical family at Skibbereen in the County of Cork on 4 July 1900. He received his medical education at Trinity College, Dublin, and at Sir Patrick Dun's Hospital, where he graduated M.B., B.S., B.A.O. in 1923, and was awarded the Haughton medal and the prize in clinical medicine. He was commissioned into the Royal Army Medical Corps in the same year, and was almost immediately posted to Egypt, where he was to serve for the next six years. During his leave in 1926 he took the M.R.C.P.I., and was elected to the Fellowship in 1928. On his return to England in 1930 he passed the medical specialists' course at the Royal Army Medical College, and obtained the D.T.M.&H. in 1932. From 1935 to 1939 O'Meara

served as medical specialist to Meerut District in India, after which he returned home to join the British Expeditionary Force to France. He was a prisoner of war in German hands from June 1940 to May 1944. Two years after his release he returned to Germany and served as consulting physician to the headquarters at B.A.O.R., where he was very active in touring the hospitals and giving his support to younger medical specialists. From 1950 onwards until his retirement O'Meara was called upon to fill a series of posts in rapid succession: consulting physician to the Far East Land Forces in 1950; officer commanding Queen Alexandra Military Hospital, Millbank, in 1951; deputy director of medical services, British Forces in Korea, in 1952; assistant director of medical services, London district, in 1953; director of medical services, Middle East Land Forces, in 1954; and deputy director of medical services, Western Command, from 1956 to 1959. He was appointed C.B. in 1956, and was honorary physician to the Queen from 1955 to 1959.

O'Meara possessed many fine attributes, both physical and mental, not commonly found in others. Tall, broad-shouldered, dignified, and with a commanding personality he stood out in any company. He had firmly held opinions, which he expressed clearly and forcibly and with no hint of compromise. His somewhat forbidding manner made him a difficult person to know, but once his reserve had been penetrated a warm personality was revealed. The softer side of his nature was readily apparent to young medical officers, who could call on him unreservedly when in need of support. O'Meara was probably at his best and happiest at Millbank Hospital, and many of the patients and staff who knew him in those days will remember him for his wise direction, his firmness, his justice, his staunchness, and for those sudden flashes of humour which were so entirely unexpected.

To his widow and three children, one of whom is a medical officer in the Royal Navy, we extend our sympathy.—R. J. G. M.

I. W. GALLANT, M.D., M.R.C.P., D.C.H.

Dr. I. W. Gallant, a former consulting physician to the Birmingham (Dudley Road) group of hospitals, died suddenly on 27 September. He was 67.

Ian Wolfe Gallant was born on 19 September 1900, and received his medical education at University College Hospital, qualifying with the Conjoint diploma in 1922 and graduating M.B., B.S. in 1925. He held early appointments at the Miller General Hospital and the Evelina Hospital for Children in London and at West Kent General Hospital, Maidstone. In 1927 he took the M.R.C.P. He became assistant medical superintendent at the West Middlesex Hospital, Isleworth, and was clinical assistant at the Hospital for Sick Children, Great Ormond Street, and the Royal Chest Hospital, London. During the second world war he served overseas with the R.A.M.C., and after receiving severe injuries in a road accident in North Africa was invalided out shortly before the war ended. In 1945 he took the D.C.H. and proceeded M.D. in 1949. At the beginning of the National

Health Service he was appointed physician to St. Chad's Hospital and Dudley Road Hospital, Birmingham, where he remained until his retirement at the end of 1965.

L. N. writes: Ian Gallant was basically rather a shy man, shunning the limelight and hiding his true worth. He had had a long schooling in general practice in London before coming into consulting practice after the second world war. Miraculously he survived a serious accident when he was knocked down by an Army lorry, but because of a slight residual disability he was disinclined to the more active pursuits. He was a prodigious reader, and a glance at his bookshelves indicated a catholic taste in literature. But most of all he enjoyed travelling abroad, and during his holidays he could be found somewhere in Europe or further afield. In fact, it was on a trip to Africa immediately after his retirement that he became ill, and he was never really well since that time. The deepest sympathy of his many colleagues will go out to his wife and son.

I. F. ROSE, M.B.E., M.A., B.M., B.CH. F.R.C.S.

Mr. I. F. Rose, deputy surgeon at Manor House Hospital, London, died on 12 October after a long illness. He was 54.

Ian Falconer Rose was born on 3 December 1912, and was educated at Oriel College, Oxford, graduating B.A. in 1935. For his clinical studies he went to St. Bartholomew's Hospital, London, where he graduated B.M., B.Ch. in 1937, and took the Conjoint diploma the same year. After holding early resident posts at St. Bartholomew's Hospital he took the M.A. in 1938. At the outbreak of the second world war he was commissioned in the R.A.M.C. in No. 131 Field Ambulance. Promoted to captain in 1940, he was taken prisoner in Belgium. He spent the next five years caring for British and Allied sick in German prison camps. In 1945 he led 1,200 British prisoners of war from a prison camp in Danzig westward to be liberated by the 7th Armoured Division. On demobilization he spent some months in hospital before returning to surgery. He was appointed M.B.E. for his wartime services.

He held appointments at St. Andrew's and the Metropolitan Hospitals, and became a Fellow of the Royal College of Surgeons in 1947. After an appointment as surgical registrar at Hillingdon Hospital, he became senior registrar at St. Peter's Hospital for Stone, and later at the Royal Marsden Hospital. From 1954 to 1958 he was senior surgical registrar at Chase Farm Hospital, Enfield, before becoming deputy senior surgeon at Manor House Hospital. He filled this post with distinction. He came to Manor House when it was expanding. The hospital acquired some of its consulting staff largely owing to his personal contacts. In particular its urological service was extended by him. The illness of Sir John Nicolson placed an extra burden on him, which he shouldered magnificently. He did two people's work with willingness, humanity, and accuracy. He inspired not only the confidence but the love of his patients and of all who knew

him. In June 1964 he was injured by a car, and soon afterwards he was overtaken by the disease which was to prove fatal. He spent nearly a year in hospital before returning to serve his patients for six months, despite being in constant pain and walking only with the aid of a stick. This was a great blow to one whose abiding passion was walking in the countryside, especially his beloved Cairngorms.

For Ian Rose medicine was a vocation. He devoted his life to his patients, and the Manor House was fortunate in having such a man on its staff. He leaves his wife, who nursed him devotedly, and to whom we offer our sympathy in her grievous loss.—N. S. P.

R. T. PAYNE, M.D., M.S., F.R.C.S.

Mr. R. T. Payne, a well-known consulting surgeon and an authority upon diseases of the salivary glands and on varicose veins, died at his home in London on 20 October, aged 71. He had been ill for many months, but had fought gallantly against increasing pain and disability, and had continued in practice in Harley Street up to the date of his death. The end came suddenly at a time when his health seemed much improved after a short holiday in Somerset.

Reginald Theobald Payne was born on 15 March 1896 at Northampton, where his father had a furniture business. The eldest of four brothers, he had an unusual upbringing, which he described very movingly in his remarkable autobiographical novel *The Watershed*, published in 1961. He was a careful and conscientious surgeon, a man of great sensibility, of considerable artistic talent, and very widely read. His parents had been Unitarians, teetotallers, and vegetarians; and his father was for many years strongly opposed to the tenets of orthodox medicine and surgery, in place of which he favoured a highly personal form of hydrotherapy. Reginald thus came into headlong conflict with his father's ideas at the time when, after grim and illuminating experiences during the first world war, he decided to take up medicine. It is a tribute to the characters of both men that they remained on good terms. Payne qualified with the Conjoint diploma at St. Bartholomew's Hospital in 1923, and was successively house-surgeon and chief assistant to a surgical unit there. He also held appointments as clinical assistant at St. Peter's Hospital, and registrar at the Royal National Orthopaedic Hospital. He was elected Fellow of the Royal College of Surgeons of England in 1925, and graduated M.B., B.S. in 1927. In 1932 he took the M.S., and proceeded M.D. two years later. He was Hunterian Professor of the Royal College of Surgeons of England in 1929 and 1932, and again in 1936 and 1938, and was Erasmus Wilson lecturer in 1931.

Payne was a great individualist and did not work easily—outside the operating-theatre—as a member of a team, but his patients and friends will always remember him for his kindness and humanity, and for his richly stored mind, which made him a delightful companion.

He was married and had two sons, the elder of whom is a pathologist at Glasgow, and the younger a clergyman.—F. H. K. G.

A. S. JARRETT, M.Sc., M.D.

Dr. A. S. Jarrett, who became director of the Royal Naval Physiological Laboratories at Alverstoke nine days before his death, died in London on 10 October. He was 35.

Antony Smith Jarrett was born on 10 May 1932, and received his education at University College, London, graduating B.Sc. in physiology in 1953 and M.B., B.S. in 1957. After an appointment as assistant lecturer in physiology at University College in 1960 he became a surgeon lieutenant-commander in the Royal Navy. From 1962 to 1965 he held an appointment at the R.A.F. Institute of Aviation Medicine at Farnborough. His work there led to an appointment in the Royal Navy as specialist in physiology. He proceeded M.D. in 1965 and took up an appointment as medical director of Syntex Pharmaceuticals, which involved him in a good deal of travel to various parts of the world. In October 1967 he was appointed director of the Royal Naval Physiological Laboratories at Alverstoke.

He leaves a widow and two sons.

D.M.D. writes: Tony Jarrett's interest in the problems of escape from submerged aircraft and of respiration on immersion began in 1962, when he took part in experiments that measured the rate at which modern aircraft sink under water. The following year, in association with Dr. "Cam" Wright, he carried out important work estimating the physiological tolerance to underwater ejection. This was succeeded by "live" trial ejections from Buccaneer and Vixen aircraft. The remainder of his time at the R.A.F. Institute of Aviation Medicine was spent studying the effects upon respiration of partial and deep submersion. This work was published as his M.D. thesis, "Breathing at Increased Ambient Pressures." He was regarded as one of the most talented and colourful scientists to pass through the institute, and will be greatly missed.

D.M.M. writes: It is particularly sad that this most likable young doctor should have died when he had just achieved his long-standing ambition of becoming director of the Royal Naval Physiological Laboratories. His growing authority on medical matters, brilliantly demonstrated at the symposium on breast cancer which he organized for 150 consultants in Caius College, Cambridge, in September of this year, would have ensured the Navy of international leadership in physiology problems for many years to come.

**K. S. MAURICE-SMITH, M.R.C.S.
L.R.C.P.**

Dr. K. S. Maurice-Smith, a well-known general practitioner in East Anglia, died peacefully on 15 October, at the age of 66 years.

Kenneth Samuel Maurice-Smith was born on 28 November 1900. He studied medicine at St. Bartholomew's Hospital, London, qualifying with the Conjoint diploma in 1924. He was appointed resident medical officer at Gravesend and North Kent Hospital, and later became a surgeon to the Blue Funnel Line. In 1928 he entered general practice and settled in Ely. For some 30 years he was medical officer of health for the Ely

urban and rural districts, and held additional appointments as Treasury medical officer to the Tower Hospital, Ely, and honorary medical officer of the Ely Palace Convalescent Hospital. He took a great interest in the St. John Ambulance Association and Brigade. During the second world war this involved intensive lecturing and travelling at a time of increased practice commitments. He became County Commissioner of the Brigade in Cambridgeshire. In 1951 he was made a Knight of the Order of St. John.

Until a year ago he was a member of the General Medical Services Committee and chairman of the Infectious Diseases Subcommittee. For the past 25 years he was the elected representative at the Annual Conference of Local Medical Committees. He was chairman of the Cambridge and Isle of Ely Local Medical Committee, vice-chairman of the Cambridge and Isle of Ely Executive Council, and a member of many other committees. An active member of the British Medical Association, he was chairman of the Isle of Ely Division in 1938-9, 1951-2, and again in 1960-61 and 1962-3, and was president of the Cambridge and Huntingdon Branch in 1957-8, and had for many years served as a representative at the B.M.A. Annual Meeting.

His interests included hockey, climbing, rally-driving, and photography. He was commodore of the Ely Sailing Club, and a past-president of the amateur dramatic society. He had a great interest in boxing, and was president of the boxing club. Of special concern to him was the provision of guide dogs for the blind. He was held in high regard not only by his colleagues in the profession but by all sections of the community as well. His great interest was the British Medical Association, and he was always conversant with the many and varied issues of the day. He was very concerned that all doctors should understand these issues before making a decision. Those who sought his help were always sure of friendly advice. He will be remembered for the vast amount of work he put in on behalf of his colleagues. Our sympathy goes out to his widow and to his son, who was in practice with him at Ely.—G.L.K.

**E. A. ANDRADE, M.B., B.S.
D.OBST.R.C.O.G.**

Dr. E. A. Andrade, a general practitioner in Hereford, died after a motor accident on 10 October. He was 45.

Edward Anthony Andrade, son of Professor E. N. da C. Andrade, F.R.S., was born in London on 14 May 1922, and was educated at St. Paul's School. He received his medical education at University College Hospital, where he was awarded the McGrath scholarship in obstetrics, and graduated M.B., B.S. in 1944. After an obstetric house-surgeon's post at his teaching hospital he served for two years as surgeon lieutenant in the R.N.V.R. During the next four years he held several resident appointments, and took the D.Obst.R.C.O.G. before going into general practice in St. Martin's, Guernsey. In 1960 he moved to Hereford, and went into partnership with Dr. Cyril Francis. He also held the appointment of clinical assistant at St. Mary's Hospital, Burghill, Hereford.

A member of the British Medical Association, he was chairman of the Guernsey and Alderney Division in 1958-9, and secretary of the Division in 1959-60.

B.E.M. writes: Tony Andrade was outstanding both as a doctor and for the wide range of his pursuits. To his fluent French and Spanish were added a useful knowledge of Greek and a recent "O" level pass in Russian. He was widely travelled. His special interests were art, music, and photography. It is as a family doctor that he will best be remembered. His patience and sympathy were inexhaustible, and he was particularly successful with patients whose social and psychiatric problems seemed to others to be insoluble. Somehow he always found time to attend postgraduate courses and meetings, and his standards in obstetrics and medicine were exceptionally high. He was a man of great charm and modesty whom all his patients will mourn as a friend.

Our sympathy goes out to his widow and family.

C.F. writes: Dr. Andrade came to me in April 1960 as an assistant, and within three months he became a partner, which position he held until his untimely death. He proved himself to be a very quiet, deep-thinking, and conscientious worker, with a great interest in all he undertook. By his calm manner, perseverance, and thorough work he soon gained the confidence of the patients. Apart from his profession he took a great interest in languages, speaking French and Spanish fluently; more recently he undertook a course in Russian, which enabled him to spend his recent holiday in Russia. He had resumed work only the week before his tragic death.

He will be missed by many, and the sympathy of his patients and of his friends will go out to his wife and stepdaughter.

**G. J. MURRAY, M.D., M.R.C.P.
D.T.M.&H.**

J.B.R. writes: When Gerry Murray (obituary, 9 September, p. 686) came to Hexham in 1950 he set to work to build up an efficient medical department from its very early beginnings, and within a few years had succeeded fully in that aim. For a number of years he bore a responsibility which weighed heavily on him at times as the sole consulting physician to the Hexham group of hospitals. I was closely associated with him from his early days in Hexham, at first as medical registrar, and valued deeply the friendship which grew up between us through the years. He was always keenly interested in the welfare of the medical and nursing staffs of his department, and never hesitated to support them when the need arose. He was a good clinician with a great understanding of patients as people, and many of his former patients expressed their deep concern during his long final illness. In difficult cases his common-sense approach usually led him to a correct diagnosis through a careful examination, when others might have been misled through the results of equivocal or conflicting investigations. Despite the illnesses of his later years his sense of humour never left him and enlivened many a ward round. Those of us who knew him well will not easily forget him.

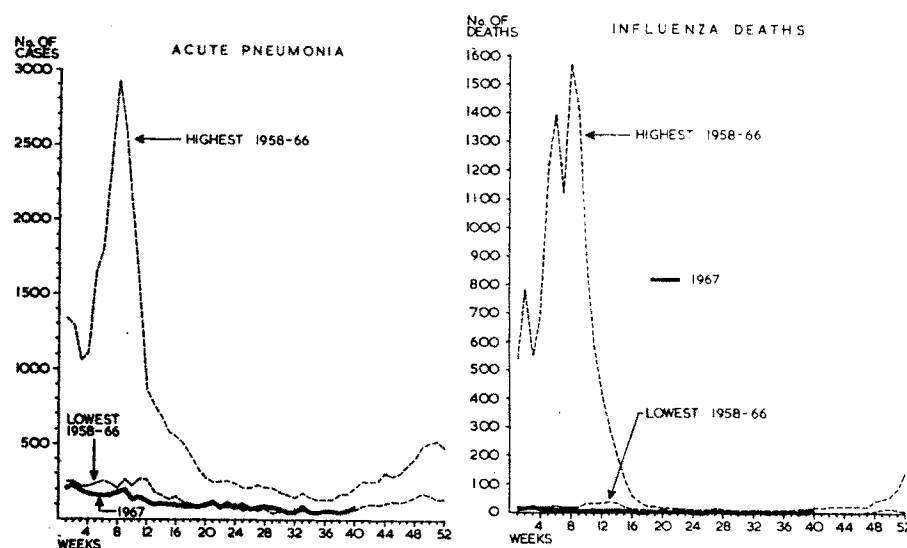
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of acute pneumonia and deaths from influenza in England and

Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending	
	6 Oct.	13 Oct.
Dysentery		
Greater London ...	43	28
Lancashire ...	34	28
Surrey ...	4	12
Warwickshire ...	37	22
Yorkshire West Riding ...	17	41
Glasgow ...	67	52
Edinburgh ...	14	20

Typhoid Fever		
Aylesbury M.B. (Bucks)	0	1
Croydon (London) ...	0	1
Ealing (London) ...	1	1
Lewisham (London) ...	0	1
Richmond (London) ...	0	1
St. Albans R.D. (Herts)	0	1
Northampton C.B.	0	1
Kingston upon Hull C.B.	0	1

Paratyphoid Fever		
Moray County ...	1	3

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 7 October (No. 40) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0				1	0	
Dysentery ..	223	43	116	8	1	306	35	100	16	4
Encephalitis, acute..	0	0		0		4	1		0	
Enteric fever:										
Typhoid ..	6	3	0	0	1	6	2	0	0	
Paratyphoid..	3	2	1(B)	0	0	3	1	0	0	1(B)
Food-poisoning	141	17	9	0		120	25	25	6	
Infective enteritis or diarrhoea under 2 years				32	44				17	93
Measles*	1,023	53	12	26	19	4,408	449	124	85	94
Meningococcal infection ..	4	0	2	0		10	1	1	0	
Ophthalmia neonatorum..	14	1	0	0		9	1	0	0	
Pneumonia† ..	83	10	58	8	3	66	7	101	1	
Poliomyelitis, acute:										
Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic	0	0	0	0		0	0	0	0	
Puerperal fever‡	88	27	1	0		123	56	3	0	
Scarlet fever ..	218	56	30	10	4	268	50	14	8	10
Tuberculosis:										
Respiratory ..	214	56	29	4		198	61	47	8	
Non-respiratory	34	6	4	1		37	8	13	3	
Whooping-cough	720	84	63	11	28	499	88	53	5	6

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..			0	0	0	0		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	0	0	1	1	0	3	0	0	0	2
Influenza ..	5	2	0	1	0	3	0	0	1	1
Measles ..	0		0	0	0			0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	568	96	11	14	6	607	103	16	13	7
Poliomyelitis, acute..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0			0		0
Tuberculosis:										
Respiratory ..	25	3	5	0	1	38	4	7	0	1
Non-respiratory				0	0				0	0
Whooping-cough	0	0	0	0	0	2	0	0	0	0
Deaths 0-1 year	239	42	23	5	15	269	50	20	7	5
Deaths (excluding stillbirths)	9,269	1486	515	89	169	9,661	1592	542	117	169
LIVE BIRTHS	16,389	2730	944	263	411	16,534	2752	937	276	486
STILLBIRTHS	243	40	17			260	30	11		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

‡ Includes puerperal pyrexia.

Eire in Second Quarter

The birth rate in Eire during the second quarter of 1967 was 23.1 per 1,000 population, and was 0.2 above the rate for the second quarter of the previous year. The infant mortality rate was 25 per 1,000 registered births, the same as in the previous June quarter. The neonatal mortality rate was 17, which was 1 above the rate for the preceding June quarter. The death rate, at 10.9 per 1,000 population, was 1.8 below the rate for the second quarter of 1966.

Sixty-three deaths were attributed to respiratory tuberculosis and eight to other forms of tuberculosis. These deaths were 13 fewer and 1 more, respectively, than in the pre-

ceding June quarter. Deaths from infectious diseases included 42 from gastroenteritis under 2 years, 32 from influenza, 4 from measles, and 2 from whooping-cough. Of the 1,279 deaths attributed to malignant neoplasms 527 were due to growths of the digestive system and 208 to growths of the respiratory system.

Accidents at Work

In 1966 in Great Britain 18,533 accidents were reported under the Offices, Shops, and Railway Premises Act, 1963. Of these accidents 29 were fatal. The total number

of accidents was 7.7% higher than in 1965, but the fatal accidents were fewer than the 34 in 1965, and the proportion they comprised of total accidents also fell from 0.19% in 1965 to 0.15% in 1966. The increase in total number of accidents is thought to arise from a greater awareness of the need to notify them. Of all classes of premises inspected under the Act railway premises were found to be the least satisfactory.

In the enforcement of the Act the authorities relied generally on advice and guidance, but during 1966 there were 147 prosecutions involving 300 charges, of which 276 ended in conviction.—*Report by the Minister of Labour for the year ended 31 December 1966, 1967, H.M.S.O.*

MEDICO-LEGAL**Cautionary Tales**

[FROM OUR LEGAL CORRESPONDENT]

It is a little depressing to be reminded by the annual reports of the Medical Protection Society and the Medical Defence Union that the complaints of retained swabs or instruments, and of operations on the wrong side or wrong part of the body, still form a substantial part of the defence societies' work. Mishaps arising from the misuse of intravenous plastic catheters also continue to be reported, though there can be little doubt that the warnings given of the precautions required are having some effect.

Inadequate Premises

A bad system or inadequate premises may be as important a contribution to a mishap as momentary aberration of a practitioner. When a man attended an outpatients department with an indecipherable general practitioner's letter, he was noted in that department as having a left inguinal hernia. On admission, the accuracy of that entry was not properly checked and not altered, and the operation was made on the left side instead of on the right as in fact required.

In another case the personal error of the surgeon (following careful preoperative discussion) was corrected by the anaesthetist but not before a right loin incision had been made when exploration of the left kidney was intended. In another hospital the absence of a proper recovery ward contributed to the death of a patient recovering from a ureterolithotomy. Representations had been made to the hospital authority before this fatality, and following it a recovery ward was provided. But when the dangers involved in carrying women in labour (often anaesthetized) down two flights of narrow stone stairs from the labour ward to the operating-theatre were pointed out to another hospital authority action was delayed pending alterations in two years' time, on the ground that no untoward incident had as yet occurred. Whatever the prospects of resultant activity hospital practitioners would be well advised to make representations

regarding inadequacies of system or premises.

The Medical Protection Society expresses grave concern at doctors' failure to read radiologists' reports, either deliberately or because "sometimes the hospital system almost seems to be designed to prevent a radiologist's report from being seen." For example, a doctor discharged a patient from a casualty department after failing to detect any bone injury on the wet film provided after an x-ray taken because of a history of falling through a skylight. A radiologist's report delivered the following day drew attention to a fracture of the medial malleolus, but in the absence of any system of bringing the report to the attention of a clinician the report was filed away. Four doctors saw the patient in the ensuing month without being aware of the radiologist's report of the fracture.

Accidental Infection

Accidental infection may occur in various ways. One patient contracted a blistered hand and cellulitis of the forearm from vaccinia infection incurred during pinprick testing on the hand (with a needle taken from a box on the practitioner's desk). Another patient, a long-haired young woman, contracted a tetanus infection from a hairpin which had found its way under a full body plaster applied to correct a severe idiopathic scoliosis of the lower thoracic spine. The infection nearly killed her and required premature removal of the plaster rendering that treatment useless. Before further treatment in another hospital, the surgeon insisted that the patient's hair must first be cut short, and the need for the hairpins removed.

Drug addiction will no doubt cause increasing trouble in future years. A much publicized case in which a legally aided patient who sued his doctor after becoming addicted to the Omnopon prescribed for him has been settled. The publicity given to this case may well encourage others of a similar nature. Balancing the risk of addiction

against the benefits to be gained from a drug will often call for difficult decisions, which will not be held negligent merely because with hindsight they may appear mistaken.

But simple human carelessness continues as a major cause of injuries to patients. For example, the Medical Protection Society points out that every year a number of claims are made arising from the use of trichloroacetic acid, "and perhaps no other topical application is responsible for such extensive demands on the Society's finances, as such claims are usually indefensible."

Third Party Insurance

Insurance with a medical defence society remains a best buy for doctors. But it is not enough. In addition third party insurance of surgery and consulting-room premises is desirable in case of accidents to patients. And personal accident and sickness insurance should be considered to guard against loss arising out of an accident suffered by the doctor, for example when driving his car, or when being driven in one of the fashionable "flying squads."

The Medical Defence Union's report refers to "a barrister" who is alleged to have consulted a Fellow of the Royal College of Physicians and then declined to pay his fees, relying on the College's by-law which prevents Fellows from suing for their fees. This paragraph caused considerable dismay among members of the Bar, and the Bar Council asked the Medical Defence Union for the name of the barrister. Although it is said that the physician had employed debt collectors to try to recover the debt, he is apparently unwilling to disclose the name of the barrister concerned to the Bar Council and no complaint has been made to the Bar Council. In a letter to *The Times*, the Chairman of the Bar Council has said that he could not believe that the barrister concerned was a practising member of the Bar. At a time when relations between the professions are improving, it is a pity that such allegations should be made in general terms without particulars. If a complaint were laid before the Bar Council (or any other professional body, one would think) disciplinary steps would certainly follow.

PARLIAMENT

Key Amendments Reversed in Abortion Bill

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The passing of the Abortion Bill was assured after yet another long debate in the House of Lords on 23 October. On both the contentious issues which had resulted from amendments made by the House of Lords last July—the condition that one of the doctors whose opinions were to authorize the termination of a pregnancy should be a Health Service consultant, and the vote to remove the risk of injury to existing children of the pregnant woman—the Lords surprisingly reversed their previous decisions, and so removed the possibility of conflict with the majority in the House of Commons that had passed the Bill.

One final alteration, in the form of a manuscript amendment by VISCOUNT DILHORNE, was left for the Commons to decide. This would permit a third medical man, after the other two had given their opinion, to perform the operation. While LORD KENNET saw a difficulty here, that the doctor who actually did the operation could not be prosecuted, LORD SILKIN was disposed to accept it, at least to give the Commons an opportunity to consider it, but he did not want it to become a constitutional issue if the Commons did not agree.

The amendment was agreed to, and so the Bill reached the end of its course through the Lords and appeared safely set on the way to the Statute Book.

Restriction on Practices

LADY STOCKS (Lab.) moved the amendment to Clause 1 to delete the requirement that one of the two doctors giving an opinion in favour of termination on the stated grounds must be a Health Service consultant or a doctor approved by the Minister of Health.

Her reasons were that consultants were few and far between, and it might be difficult for a woman in a rural area to find such a consultant. She added there would be a tendency to push distressed women into the hands of the back-street abortionist.

The clause would also have an effect on private practice. It was not the business of the Bill to restrict the area of private practice, but the clause if passed unamended would have that effect.

If the clause was unamended, she feared it would wreck the Bill. It would not be accepted in the Commons. Those who were anxious to rationalize and legalize the present position would have to start all over again with a new Bill in both Houses.

VISCOUNT DILHORNE said the House had already debated this question and expressed its opinion in no uncertain words. The words which it was now proposed to delete from the Bill had been put into it by a vote of 167 to 116.

There was far less risk of collusion and of the Harley Street racket developing throughout the country if there was the requirement that one of the two opinions must be that of a consultant employed in the Health Service.

It was better to keep this provision in the Bill than leave it wide open for newly called doctors to engage in a racket.

LORD BROCK said there were nearly 9,000 consultants in the National Health Service; nearly 6,000 of them were part-time. There was therefore no restriction on choice. The amendment would ensure a higher standard of advice and treatment to the pregnant woman.

VISCOUNT WAVERLEY said the amendment would not only check collusion between two doctors in practice together but would ensure expertise in the treatment of the pregnant woman.

LORD SOPER (Lab.) said that he was not concerned with promiscuous girls of 15 or 16 or frivolous married women who were pregnant by a man other than their husbands, but with the other 80% of abortion cases involving women for whom another pregnancy was an intolerable prospect.

He had great difficulty in reconciling what had been said about the number of consultants available and figures which had been published, and which indicated there were 740 consultants available unevenly distributed throughout the country.

If the provision were allowed to remain in the Bill there would be delay, and delay in the early stages of pregnancy was a devastating experience for a woman, especially one faced with the intolerable prospect of another child. It was in order to reduce suffering that he thought the amendment should be accepted.

The ARCHBISHOP OF CANTERBURY said that when he supported the insertion of the words Lady Stocks proposed to delete he did so for two reasons: to help prevent a racket by some doctors, and to ensure the highest standard in connexion with abortions. These reasons still seemed to stand.

Not for the first time, but more forcibly, it was suggested that consultants were so scarce or so inaccessible that women would resort to back-street abortions. But were consultants inaccessible?

Was it beyond the power of the Ministry of Health to see that if the Bill were passed in its present form the necessary provisions were made? Was it not the duty of the Government to see that what the Bill asked for was provided? Was it possible to have a social reform of the kind envisaged without a commensurate action on the part of the Government to see that it worked?

Collusion Discounted

LORD SILKIN (Lab.) said that at present it was possible for an abortion to take place quite lawfully with only one doctor. This Bill provided for two doctors as a safeguard. Most people felt there should be a second opinion. The issue was what the nature of the second opinion should be.

Much had been made of the danger of collusion, but what was meant by that? Was it that two partners in practice would start

a racket of freely giving authority for abortions? But a panel patient could not be charged, and it would be quite unlawful to ask for a fee for performing an abortion. The paying patient was not the problem—she would be able to find her way to Harley Street. Surely if doctors could not charge a fee there was no incentive for collusion.

He asked the House to reconsider its vote on the last occasion and to vote for the amendment.

LORD KENNET, Parliamentary Secretary, Ministry of Housing and Local Government, said that last year there were 521 obstetric and gynaecology consultants in England and Wales. He could not say that no bottleneck would be introduced by the enforced employment of these consultants.

In the gynaecological departments of N.H.S. hospitals the average delay in getting an operation in non-emergency cases was about six weeks at the moment. No Minister of Health had ever arrogated to himself the right to say that one class of doctor should carry out a surgical operation and another should not. The present Minister was unwilling to be the first to arrogate that right to himself. On the question of collusion and rackets, he said that one could not be certain that a consultancy indicated a superior degree of morality and social conscience.

Although this was very much a question for the House, in the Government's view the amendment was quite acceptable.

LORD SEGAL (Lab.) said there was no use in obtaining a second opinion if it was to be given by a doctor with the same qualifications as the first doctor, and who would merely rubber stamp what had already been said.

There was a list of general practitioners skilled in midwifery. It was a list approved by the medical bodies. Those on it had certain qualifications in midwifery. There was therefore no need for the Minister to draw up such a list.

The amendment was carried by 113 votes to 79—majority 34.

Effect on Existing Children

LORD SILKIN moved an amendment to restore to the Bill the words "or any existing children of her family," thus permitting an abortion if there was a risk of injury to any existing children from the birth of another child.

He said the amendment dealt with what had become known as the social clause, a term which was quite wrong. It was a provision that in considering the circumstances of the pregnant woman the doctor had to take account of her total environment or of the circumstances of the existing children.

There were cases, few in number, where the injury to the existing children would be severe and ought to be taken into account by the doctors who were going to decide whether an abortion should take place.

LADY SUMMERSKILL (Lab.) said they were concerned with the masses of people who lived in the industrial areas of the towns: the slums, where adolescents slept in the same

room and where families were kept awake at night by a crying child.

We plead, she said, for those families where the family is already so big that the wife is harassed and where the husband is so bad-tempered that he stays out at night in the public-house, arrives home drunk, has sexual intercourse, and produces another child.

LORD STONHAM, Minister of State, Home Office, said he could think of many cases where another pregnancy could affect the health of existing children. There were cases where the social circumstances of the family might be worsened by an addition to the family. There could be cases in which the doctor's knowledge of the family circumstances enabled him to form an opinion.

The ARCHBISHOP OF CANTERBURY said he was always ready to change his mind in the light of new evidence or facts. In the earlier debate that evening he had asked for information about matters that were obscure, and the information forthcoming sufficed to tilt the balance of argument in his mind.

On this amendment he was ready to hear anything to cause him to change his mind, but he had heard nothing to lead him to think it was right that the House should reverse the decision made a few months ago.

THE MARQUESS OF SALISBURY (Con.) said that Lord Silkin and his friends in all sincerity asked the House to take a far-reaching step. It was a very dangerous one.

It was one thing to say that an abortion was justified because the birth of a child

would involve risk to the health of the mother. That was a question of medical opinion. The decision to allow an abortion on further social grounds was a very different thing. Who was qualified to judge what would endanger the health of one or more of the existing children?

If there was a referendum, and he sometimes thought there was a case for a referendum on such issues as this, he believed it would be decisively defeated.

Decision Should be Free

LORD CARRINGTON (Con.) said he hoped members would not be influenced in the way they voted because of the fear of a constitutional crisis. He did not think it should, or could, arise on this Bill.

If ever there was a Bill on which peers should vote according to their consciences this was it. There should be no threats, he said, by the newspapers, the Government, or anybody else, which should deter them from doing what was right.

LORD STONHAM repeated that the Government were neutral. The people were not concerned about the constitutional issue. They and most members of the House wanted their discussions to result in a viable Bill.

The amendment was carried by 86 votes to 69—majority 17.

The Bill was agreed to on third reading, and was finally passed without a division.

Ban on Cigarette Coupons

The MINISTER OF HEALTH told the Commons on 23 October of his decision to ban cigarette coupon and other promotional schemes, and to limit expenditure on advertising cigarettes.

Last month, he said, in answer to a question by Dr. JOHN DUNWOODY (Falmouth and Cambourne, Lab.), the manufacturers had told him of their failure to reach a voluntary agreement. Two of the firms would agree to the ending of coupon schemes and to the limitation of mass media advertising expenditure on a basis agreed between them. The third firm would not agree to the ending of coupon schemes, though they would have been prepared to control their development and to limit advertising.

After more than a year of negotiations, he continued, it was now clear that no further progress was possible by voluntary agreement. Cigarette-smoking was a serious danger to health and a major cause of preventable deaths. In view of this the Government had decided to introduce legislation in due course to take powers to ban coupon gift schemes in relation to cigarettes, to control or ban other promotional schemes, to forbid or limit certain forms of cigarette advertising, and to limit expenditure on advertising of cigarettes.

Mr. B. WHITAKER (Hampstead, Lab.) asked him whether he would now take steps to compel all cigarette manufacturers to print on their packaging and advertising a warning of the danger to health. Mr. ROBINSON: Not at present.

MEDICAL NEWS

Professor in Experimental Pathology

The title of professor in experimental pathology has been conferred on Dr. LYNNE REID by the University of London in respect of her work at the Institute of Diseases of the Chest, Brompton Hospital, London.



Dr. Lynne Reid graduated in 1946 at the University of Melbourne. After various clinical appointments she became a member of the Royal Australian College of Physicians, and was appointed a research fellow of the National Health and Medical Research

Council of Australia in 1949. In 1951 she joined the Brompton Hospital as a research assistant, and became a member of the Royal College of Physicians in 1952. In 1955 she joined the Institute of Diseases of the Chest when she started the research department of morbid anatomy and experimental pathology, becoming full-time senior lecturer and reader. In 1964 she was elected a fellow of the Royal Australian College of Physicians. She is honorary consultant to the Brompton Hospital, a foundation member and fellow of the College of Pathologists,

and a member of the Medical Advisory Committee to the Cystic Fibrosis Foundation. The work of her department has been particularly concerned with the morbid anatomy of chronic bronchitis, cor pulmonale, and emphysema.

Royal College of Obstetricians and Gynaecologists

The President of the Royal College of Obstetricians and Gynaecologists, Sir JOHN PEEL, presided over a large company at the annual dinner of the college on 18 October, held for the first time in the college's own premises. Sir JOHN WOLFENDEN, Chairman of the University Grants Committee, proposed the toast of the college. The PRESIDENT replied. The toast of the guests, proposed by Mr. ANTHONY ALMENT, was responded to by Mr. GILBERT EDGAR.

Joint Consultants Committee

Sir JOHN RICHARDSON was elected chairman and Mr. WALPOLE LEWIN was elected vice-chairman of the Joint Consultants Committee at the Royal College of Physicians and Surgeons of Glasgow on 24 October. Warm tributes were paid to Sir THOMAS HOLMES SELLORS, who had been chairman for nine years.

General Practice Teaching Unit

The Nuffield Foundation has given the sum of £33,000 to Guy's Hospital Medical School to establish a general practice teaching unit based on Thamesmead. This sum is additional to the £35,000 given by the

Foundation in 1964 to establish the general practice research unit at Guy's to develop the Thamesmead health services project. Dr. ROBERT SMITH, until recently seconded from the Wellcome Foundation to head the Guy's G.P. Research Unit, has been appointed director of the general practice teaching unit, attached to the department of medicine.

Postgraduate Medicine, 1967

A series of six weekly programmes for doctors has been produced jointly by Scottish Television and Tyne Tees Television in association with the Glasgow Postgraduate Medical Board and the Organization for Postgraduate Medical Education, Newcastle upon Tyne. The first title, with time of transmission, is announced under "Coming Events" (p. 247), and the announcements will be continued each week.

Postgraduate Medical Education

For the next year the offices of the Central Committee on Postgraduate Medical Education (Great Britain) will be at the Royal College of Physicians, St. Andrew's Place, London N.W.1.

Research into Mental Retardation

An institute to co-ordinate and promote research into mental retardation has been established under the sponsorship of the National Society for Mentally Handicapped Children. It will provide an information service, and plans to organize conferences, symposia, and study groups. A scientific

library, initially for reference, is being built up. The chairman of the institute is LORD FRANCIS-WILLIAMS and the vice-chairman Dr. DAVID MORRIS. Its address is 5 Bulstrode Street, London W.1.

Club for Doctors and Engineers

Doctors and engineers in the Manchester area have formed a medical-engineering club to encourage the use of engineering techniques in medicine. Some 50 members of the staffs of Manchester University and Salford University as well as consultant surgeons are said to have applied for membership. Professor J. H. KELLGREN, professor of rheumatology at Manchester University, is president of the club. The secretary is Dr. JAN SKORECKI, senior lecturer in mechanical engineering at the University of Manchester Institute of Science and Technology.

Dr. Raymond Hoffenberg

A deputation from Cape Town University was received by the Minister of Justice, Mr. PETRUS PELSER, on 19 October and discussed the case of Dr. RAYMOND HOFFENBERG, senior lecturer in the department of medicine, who has been served with a banning order (see *B.M.J.*, 26 August, p. 512). It consisted of Dr. J. P. DUMINY, principal of Cape Town University, Mr. HARRY OPPENHEIMER, the Chancellor, Mr. CLIVE CORDER, chairman of the university council, and Professor JOHN F. BROCK, head of the department of medicine.

Overseas Students in Universities

Clinical medicine ranked highest as a field of study among overseas students enrolled at British universities 1966-7, according to a report by the Association of Commonwealth Universities. The figures were undergraduate (504) and postgraduate (790). Altogether there were 17,659 full-time overseas students in universities at the beginning of the academic year. More than half (9,584) were Commonwealth students. The countries from which the largest numbers of students came were U.S.A. (1,991), India (1,711), Pakistan (952), and Nigeria (904). Copies of the report can be obtained from the association's office at 36 Gordon Square, London W.C.1.

Nobel Prizewinners

A Swede, Professor RAGNAR GRANIT, and two Americans, Professor HALDAN KEFFER HARTLINE and Professor GEORGE WALD, share this year's Nobel Prize for medicine. Their work is referred to on page 185.

Artificial Kidney

With the support of the National Research Development Corporation a research group at Leeds University, under the direction of Professor G. G. HASELDEN, is attempting to produce a disposable plastic kidney. Professor Haselden describes the project as follows:

The short-term aim is to produce a low-cost sterilized dialyser which may be disposed of after use, thus reducing infection hazards and labour requirements in hospital units. In terms of function it is hoped that the new unit will perform in a way similar to that of the Kiil dialyser, while offering the advantages of disposability at present restricted to the several designs based on the twin coil kidney. The unit has been designed with the prime objective of forming a cheaper, more convenient, and safer substitute for the Kiil, without any loss in dialyser performance. It will be quite compatible with existing monitor units.

The long-term aim is to produce a self-contained dialyser which does not depend on an external source of dialyser fluid. The present dispensers of dialysis fluid and associated monitoring devices represent the major capital cost of the entire artificial kidney machine and inevitably present servicing problems which use scarce labour. The self-contained dialyser will use a small volume of fluid contacting a bed of adsorbent and ion exchange resin. Work at present is concerned with the evaluation of suitable adsorbent materials.

Occupational Medicine

An exhibition of various aspects of occupational medicine is being held in the Claire Wand Gallery, B.M.A. House. Organizations represented include the M.R.C. Pneumoconiosis Research Unit, Group Industrial Health Services, London Transport Medical Service, Steel, Peck and Tozer (medical department), and the Scottish Occupational Health Laboratory Service Ltd. The exhibition will be open to members during library hours until 10 November.

M.R.C. Fellowships and Training Awards

For the academic year 1967-8 the Medical Research Council has awarded 23 junior research fellowships and 466 training awards. The fellowships are intended for medical and dental graduates with some research experience or for science graduates holding a postgraduate degree. Scholarships for training in research methods and awards for further education in the medical sciences enable young graduates with medical, dental, or science degrees to continue training beyond a first degree. The training awards also include awards for intercalated courses. These are intended for medical and dental students who have completed the second M.B. and B.D.S. examinations and who wish to undertake a course in a biological science before proceeding to their clinical studies.

Coming Events

British Medical Association.—"The Effectiveness of Television in Medical Education," lecture by Professor I. R. MERRILL, of the University of California, 16 November, 5 p.m., B.M.A. House, London W.C.1.

Postgraduate Medicine, 1967.—"Intra-uterine Growth," Scottish Television and Tyne Tees Television: 31 October (1.15 p.m.), repeat 5 November (10.15 a.m.).

Mental Health Research Fund.—Public meeting, "The Promotion of Psychiatric Research," by Sir GEOFFREY VICKERS, 7 November, 5 p.m., Edward Lewis Theatre, Middlesex Hospital Medical School, London W.1.

St. Thomas's Hospital Medical School.—Old Students' Dinner, 10 November, 7 p.m. for 7.30 p.m., Savoy Hotel, London (entrance Victoria Embankment). Ladies welcome. Price of dinner, exclusive of drinks, £2 10s.

Chelmsford Medical Education and Research Trust.—Gynaecological seminar, 11 November, Chelmsford and Essex Hospital. Fee £1. Applications to St. John's Hospital, Chelmsford, Essex.

Royal Free Hospital Old Students' Association.—Clinical meeting, 16 November, 12.30 p.m. Hospital and Medical School Dinner, 7.15 p.m. for 7.45 p.m., Savoy Hotel. Details from Dr. J. R. M. GIBSON, 90 Bromley Common, Bromley, Kent.

Developmental Neurophysiology and E.E.G. in Paediatrics.—Course on problems of developmental neurophysiology and E.E.G. in paediatrics, 16-18 November, Hospital for Sick Children, Great Ormond Street, London W.C.1. Details from Dr. G. PAMPIGLIONE, department of clinical neurophysiology at the hospital.

Institute of Urology.—Week-end course on "Essentials of Urology," 17-19 November. For details see advertisement on p. xxxiii.

Biochemical Society.—Meeting, 18 November, Medical Research Council Laboratories, Carshalton. Programme includes colloquium on "Toxic Substances and Brain Metabolism." Further details from Executive Secretary, Biochemical Society, 7 Warwick Court, Holborn, London W.C.1.

St. John's Hospital, Lincoln.—Annual day conference on psychiatry, 19 November, 10.15 a.m.

Symposium on Carbenoxolone Sodium.—20 November, 9.40 a.m., Royal Society of Medicine, 1 Wimpole Street, London W.1. Open to all members of the profession. Tickets may be obtained, free of charge, from Mr. W. D. D. LEWIS, Berk Pharmaceuticals Ltd., Godalming, Surrey.

National Heart Hospital.—The St. Cyres Lecture, which was to have been given on 31 October at the Royal College of Physicians, will now take place.



Professor Ragnar Granit.



Professor Haldan Keffer Hartline.



Professor George Wald.

Societies and Lectures

For attending lectures marked ● a fee is charged and a ticket is required. Applications should be made first to the institution concerned.

Monday, 30 October

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Dr. J. H. Gough: Angiocardiography in Congenital Heart Disease.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Dr. V. Goodhill (Los Angeles): Some Crucial Problems in Case Selection and Surgical Technique in Tympanoplasty.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. D. C. O. James: Pathology of Trauma—Blood Loss; 6.30 p.m., Dr. A. Bold: Aspects of Homeostasis—Calcium Metabolism.●

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in pathology by Dr. N. A. Mitchison: Control of the Immune Response.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. Peter Bishop: Sex Chromosome Anomalies and Intersexual States.

Tuesday, 31 October

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. J. R. Tata: Hormonal Control of Protein Synthesis.

CHARTERHOUSE RHEUMATISM CLINIC.—At Royal Society of Medicine, 5.30 p.m., Gilbert Scott memorial lecture by Mr. G. K. McKee: The Development and Present Status of Total Prosthetic Replacement of the Hip Joint.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. I. Sarkany: Physiology of Itching.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 2 p.m., Mr. R. A. Tennent: Induction of Labour.●

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in pathology by Professor G. Bras (West Indies University): Degenerative Diseases and Neoplasms as Influenced by Nutrition—an Experimental Study.

NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., clinical meeting by Dr. A. John.

ROYAL COLLEGE OF GENERAL PRACTITIONERS: SOUTH LONDON FACULTY.—At Board Room, King's College Hospital, 8.15 p.m., Dr. H. L'Etang: Great Men and Their Illnesses.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Professor A. K. Basu: Non-cirrhotic Portal Fibrosis with Portal Hypertension.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Professor R. B. Welbourn: Nutritional Aspects of Gastric Surgery.

ROYAL STATISTICAL SOCIETY: MEDICAL SECTION.—At Mansion Theatre, London School of Hygiene and Tropical Medicine, 5 p.m., Dr. M. C. Pike: Detection of Low Intensity Epidemics—an Extension of Knox's Model and Some Applications.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. E. A. Nieman: clinical demonstration.

Wednesday, 1 November

ASSURANCE MEDICAL SOCIETY.—At Medical Society of London, 5 p.m., Sir John Richardson: The Connective Tissue and its Disorders.

PSYCHOMETRIC SOCIETY: BRITISH REGION.—At Wellcome Building, Euston Road, London N.W., 2.30 p.m., Professor J. F. Scott: Investigation of a Psychological Syndrome by Multivariate Analysis.

BOOK GENERAL HOSPITAL.—8 p.m., Sir Terence Cawthorne: Vertigo—its Diagnosis and Management.

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

INSTITUTE OF DENTAL SURGERY.—5 p.m., Wilkinson lecture by Sir John McMichael, F.R.S.: Science and Practice.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. R. W. Riddell: Diseases Caused by Fungi.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. W. D. W. Brooks: The Lungs in Systemic Disease.

OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Professor T. Stamey (Stanford University): Reinfections of the Urinary Tract—Studies on the Portal of Entry.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., urology lecture by Mr. J. Cosbie Ross: The Neurogenic Bladder.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. G. L. Nardi (Boston): Surgery of Pancreatitis.

ROYAL MICROSCOPICAL SOCIETY.—At Edward Lewis Building, Middlesex Hospital Medical College, 5.30 p.m., Dr. A. Klug: Interpretation of Electron Microscope Images of Negatively Stained Biological Particles.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conferences by Dr. G. F. Joplin: Myelomatosis; Dr. J. G. Azzopardi: Amyloidosis. (2) 2 p.m., Renal Unit, urology seminar. (3) 2 p.m., Dr. A. C. Allison: Immunity Against Viruses and Tumours.

STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. V. E. Lloyd-Hart: clinical cases. (2) 6 p.m., Group Captain R. Mortimer: Malaria.

WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Professor J. G. Scadding: Sarcoidosis of the Lungs.

Thursday, 2 November

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Mr. D. P. Burkitt: A Study of Cancer Patterns in Africa.

DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Professor W. St. C. Symmers: Opportunistic Infections.

HONYMAN GILLESPIE LECTURE.—At Surgery Lecture Theatre, Edinburgh Royal Infirmary, 5 p.m., Professor G. Smith: Ischaemic Neuropathy associated with Atherosclerotic Disease in the Lower Limbs.

LONDON UNIVERSITY.—(1) At Royal Society of Medicine, 5 p.m., Semon lecture by Mr. D. H. Patey: Diseases and Disorders of the Salivary Glands in Relation to General Physiology and Pathology. (2) At Physiology Lecture Theatre, University College, 5.30 p.m., special university lecture in biophysics by Dr. B. Chance (Pennsylvania): Electron and Ion Transport in Mitochondrial Membranes.

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.—7 p.m., Dr. J. G. Dare: A Brief Survey of Australian Pharmacy.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Aris and Gale lecture by Mr. B. L. Whitaker: An Investigation into Factors Affecting the Blood Supply of the Descending Colon and Rectum.

ROYAL PHOTOGRAPHIC SOCIETY: MEDICAL GROUP.—7 p.m., informal discussion of problems in medical photography.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 4 p.m., Mr. P. Martin: Reconstructive Arterial Surgery. (2) 5 p.m., lecture on medical history by Dr. E. S. Clarke: Disease in Graeco-Roman Antiquity.

RUNWELL HOSPITAL.—At Wickford, Essex, 8 p.m., general medicine in relation to psychiatry by Dr. R. Brown: Cardiac Failure.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Mr. M. D. Cameron: Postoperative Management of Gynaecological Operations.

Friday, 3 November

KINGSTON-UPON-THAMES MEDICAL CENTRE.—8.15 p.m., clinicopathological conference by Dr. J. B. Harman.

NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 8.15 p.m., Professor S. Shuster: Skin and the Gut.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Mr. F. B. Cockett, Mr. W. G. Fegan, Mr. Hugh Jones: Profile on Varicose Veins. (2) 4 p.m., Professor J. G. Scadding: Sarcoidosis—History and Definition.

WEST MIDDLESEX HOSPITAL.—4 p.m., Dr. C. Barnes: Non-toxaemic Hypertension in the Pregnant Woman.

Saturday, 4 November

PRINCESS ALEXANDRA HOSPITAL, ESSEX.—At lecture room, 2 p.m., symposium: Recent Advances in Rheumatic Diseases.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—9.30 a.m., anaesthetic teaching meeting: Mechanics of Ventilation during Anaesthesia.

Sunday, 5 November

EDGWARE POSTGRADUATE MEDICAL SOCIETY.—At Edgware General Hospital, Middx., 10.30 a.m., Dr. A. M. Joekes: Investigation of the Renal Tract.

Universities and Colleges

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the College held on 18 October 1967, the following candidates who passed the requisite examinations were admitted Fellows:

M. M. A. A. Abdallah, M. M. Abdul-Hadi, C. B. T. Adams, M. L. Adiga, W. Ahmad, Maung Than Aung, S. C. Bagchi, K. Balasingham, B. Balgobin, S. C. Basu, A. Baxter, A. R. Bean, I. S. Begg, S. E. Benjamin, T. Bhaduri, W. M. Bowden, D. P. Byrnes, D. C. Carter, J. P. Chacko, J. Chamberlain, Chung Chun Chan, Wing Fook Chan, R. K. Chatfield, B. Chatterjee, A. B. Chaudhary, Z. U. Chaudhry, A. Constantinou, O. St. J. Da Costa, B. Dean, A. H. B. De Bono, A. N. Dey, T. S. Dogra, J. A. Dormandy, N. St. J. P. Dwyer, E. I. Efrong, H. W. Elcock, A. S. H. El-Ghorab, A. A. El Mannan, Marina D. Fakirbhai, G. Farago, G. H. Foster, J. W. Fowler, P. M. Fullman, J. N. Gangopadhyay, Siraj-Ul-Iqbal Z. Ghazali, G. S. Ghorpade, S. K. Ghoshal, E. S. Glen, H. F. Godfrey, G. Gordon, M. Abdel-Hamid, M. Gouda, W. E. G. Griffiths, A. Grover, A. J. Haddadin, Mg. M. T. Han, B. S. Heer, M. T. Hlaing, L. A. Holbrook, R. M. Honner, E. C. Horan, A. K. House, M. J. Hunter, Z. Huc, A. Hussain, Z. Iqbal, Md. A. Jalil, A. G. Jatoti, R. V. Jeffreys, W. G. Johnston, M. Kanagalingam, S. N. Kapoor, A. A. Kareim, P. Kakati, H. B. Kennedy, G. D. Kerr, I. A. Khan, R. C. Khosla, L. Krogh, R. B. Lea, Yiu-Ting Lee, Chun-Kuen Leung, A. B. Lockhart, F. I. Low-A-Chee, W. Lloyd-Jones, B. St. C. McCormick, I. J. A. Macfarlane, A. B. MacGregor, S. T. D. McKelvey, R. D. W. McLean, A. Mahmud, A. Majekodunmi, S. P. Malhotra, G. S. Mangat, C. E. Marshall, J. P. Matthews, D. P. L. May, G. M. Memon, P. B. M. Menon, A. H. Mike, R. N. Mohapatra, W. B. Molloy, S. H. Mong, M. L. Mulcahy, A. A. Nada, G. Neil-Dwyer, A. N. Nicolaides, K. N. Oji, Saw Young Ong, P. J. O'Rourke, G. A. A. Oyemade, B. J. Parakh, D. J. Parker, A. Patel, S. P. Payne, T. Y. Pemba, C. N. Pillay, B. Prakash, K. Prasad, S. P. Puri, J. M. Quilter, M. Rahman, E. W. Ramsey, W. R. Roney, P. B. Roy, E. A. Saad, I. Scott-Findlay, Pramila B. Sehgal, D. K. Sen, H. J. Shah, B. Shahi, M. Shamm, U. C. Sharma, J. M. Shennan, M. A. T. Siddique, D. C. Simpson, I. S. Smith, V. I. Sreenivas, T. E. Steven, Mrudula A. Talwalkar, P. A. Tan, J. F. Tattersfield, J. T. Taylor, N. P. Tendolkar, H. K. D. Thakore, M. Thambirajah, I. W. Thomas, Marjorie P. Thomas, P. Thompson, O. N. Tikki, G. S. Tucker, A. P. Tynan, D. W. Walters, J. M. Watts, J. H. Wheeler, J. H. White, E. Whitehead, P. J. R. Zelas.

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 1967.

Volume 21, No. 4. Yearly subscription (4 numbers) £3 3s., abroad £3 10s.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitology*, London W.C.1. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 4 NOVEMBER 1967

Pointers

Intensive Care: Description of organization and results in a respiratory unit set up after a preliminary survey to assess the need for such a unit in Glasgow (p. 255).

Visuo-motor Handicap: Poor school performance in spite of average I.Q. in a number of healthy children explained by visuo-motor defect. Some of these children had a history of perinatal abnormality (p. 259).

Aspirin and Chronic Urticaria: Aspirin-containing drugs caused exacerbation in some patients with chronic urticaria. This action may be due to enhancement of effect of histamine in the skin (p. 262).

Salicylates in Rheumatoid Arthritis: Trial to demonstrate clinical assessment of anti-inflammatory properties of rapidly acting drugs shows that high dosage of salicylates produced measurable reduction in joint size (p. 264). Leader at p. 251.

Relief from Angina: Comparison of aerosol and sublingual administration of glyceryl trinitrate in a double blind trial showed tablets still to be the treatment of choice (p. 268). Leader this page.

Treatment of Septicaemia: Intravascular coagulation caused by *Cl. perfringens* successfully treated by exchange transfusion and heparin (p. 271).

Topical Corticosteroids: Comparison of commonly used preparations shows betamethasone 17-valerate ointment to be significantly better than fluocortolone in patients with eczema and psoriasis (p. 275).

Case Reports: Charcot joints in early adolescence (p. 277); Coarctation of aorta complicated by subarachnoid haemorrhage (p. 278); True heartburn (p. 279).

Dyspepsia: Diagnosis, medical management, and indications for surgery of duodenal ulcer (p. 281).

Is There an Alternative? Review of B.M.J. booklet on the Health Service (p. 285).

Obstetric Services: National postal survey of general-practitioner maternity units reveals that almost half of them are more than ten miles from consultant units, and lack formal arrangements for consultant visiting (p. 287).

Council: Report of meeting (*Supplement*, p. 29).

Central Committee for Hospital Medical Services: Report (*Supplement*, p. 36).

Surrey Public Health Appointment: Call for inquiry (*Supplement*, p. 41).

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Treatment of Myocardial Ischaemia

Anginal pain is felt when the myocardium's demand for oxygen outstrips the available blood supply. Relief stems from improvement in the flow of coronary blood or from reduction in cardiac work.

Until recently the rationale of anti-anginal drugs has been to improve blood flow, but observation of the sort of disease commonly present at necropsy suggests that attempts at pharmacological coronary dilatation must be futile. Though dilatation of healthy parts of the main coronary arteries can be observed during cine-angiography,¹ no coincident improvement in blood flow has been detected.² Indeed, dilatation of healthy arteries could well divert blood away from ischaemic areas supplied by the more rigid diseased vessels.

The undoubted benefits of nitrites in the treatment of angina are almost certainly owed to peripheral rather than coronary vasodilatation, a reduction in cardiac size and work following a decrease in the venous return and arterial pressure.^{3,4} When taken before pain-provoking exercise, glyceryl trinitrate both prevents the pain and reduces the electrocardiographic changes of ischaemia. But it has not been shown to be effective in relieving established attacks,⁵ though widely used for this purpose. Apparent benefit from it in those circumstances may result simply from the expectation of relief, and indeed the brevity of the ordinary attack makes it difficult to assess the effect of any anti-anginal drug except in prophylaxis. Natural improvement also frequently occurs and makes the efficacy of therapy still harder to judge.

A different approach to treatment came with the introduction of β -adrenergic blocking drugs such as propranolol (Inderal), which block the cardiac actions of adrenaline.⁶ The demand of the myocardium for oxygen is roughly proportional to the heart rate,⁷ and probably the most important benefit from propranolol lies in the prevention of tachycardia during exertion or emotion.⁸ β -Adrenergic blockade also reduces the wastage of oxygen that can result from an adrenaline-induced increase in vigour of contraction. Coronary flow is facilitated by a longer diastolic filling period, and anxiety is relieved through the patient's awareness of a slower heart beat. Other lesser benefits may be a slight fall in blood pressure and the suppression of exercise-induced ventricular ectopic beats.

Propranolol can be of great therapeutic value in preventing angina provided a sufficiently high dose is prescribed and the contraindications to its use are observed. Less than 150 mg. of the drug daily in divided doses is rarely of benefit and even 250 mg. may be needed. Left ventricular failure is a complete contraindication, and signs of incipient failure should be carefully sought while the dose is being gradually increased. Removal of the support that the patient derives from adrenaline is the reason why patients with heart failure are extremely sensitive even to small doses, why the drug is largely contraindicated in cardiac infarction, and why overt heart failure may be precipitated by its use in patients with impaired myocardial performance.

No. 5574, page

By slowing the heart, not the man, β -adrenergic blockade has finally rendered thyroid ablation obsolete. Many other drugs are of value, but they act mainly as a sedative or even a placebo. Delayed-release glyceryl trinitrate tablets can be an effective prophylactic over a 6- to 8-hour period, but occasionally cause sustained headache and postural hypotension as a direct result of the nitrite action. "Long-acting nitrites" such as pentaerythritol tetranitrate on the other hand never achieve a pharmacologically sufficient level of nitrite in the blood. Drs. G. Sandler and G. A. Clayton, writing in the *B.M.J.* this week at page 268, have assessed an aerosol preparation of glyceryl trinitrate by an excellent double-blind trial but found it ineffective. Sustained-release tablets may be beneficial, and a few patients still prefer amyl nitrite inhalation. Monoamine oxidase inhibitors had a vogue, but their serious toxic effects and dangers preclude their use in angina, especially as any benefit they conferred was largely through their euphoriant action.

The physician has four lines of treatment in angina. The first two are general ones—to increase bodily efficiency and to try to prevent progression of the arterial disease. Obesity, hypotension, or diabetes is corrected.^{9,10} Restriction of dietary fat and the taking of clofibrate (Atromid S)¹¹ are advised only if the levels of serum cholesterol or triglycerides are abnormal. Smoking is to be condemned but alcohol allowed, and regular physical exercise is encouraged. A programme of graduated exercise is beneficial,¹² but whether through the psychology of group therapy, better general fitness, or an actual improvement in myocardial perfusion is not yet known. Whatever the explanation, there is no doubt that the patient with angina benefits greatly from this recently changed attitude towards exercise.

The mainstay of drug therapy is still glyceryl trinitrate supported by propranolol if further relief is needed. But, if angina remains recalcitrant, surgical revascularization should be considered. Before a decision can be made, coronary angiography is mandatory.¹³ It has now been shown that implantation of an internal mammary artery can in time revascularize an ischaemic but viable area of myocardium.¹⁴ These implants seem to "take" only in an area whose need for better perfusion can be demonstrated by finding delayed flow through a narrowed segment of artery or retrograde flow through collaterals from the opposite main vessel, and in which, preferably, new collateral vessels are already growing.

Reconstruction of the lumen of the left coronary artery or its main branches has been found to carry a high mortality, but the right coronary lumen has been successfully restored at low risk by reroofing it with a pericardial patch.¹⁵

In the last few years great progress has been made in the palliation although not in the prevention of coronary disease. Patients with angina tend to become emotional and introspective because their symptoms have so often been only temporarily alleviated by the hope of help from a new drug or a new physician. They need time, explanation, confidence, and a plan. These they can and should be given.

Computers in Medicine

The first electronic computer was produced in the United States in 1946. Immediately the speed of calculation was increased a thousandfold. Today the computer is a thousand times faster.

Computers as well as calculating can store and recall information, and unlike their human creators they do not forget. They can perform even more complex operations and can indeed operate any set of rules on any set of symbols. If the symbols are numbers and the rules are those of arithmetic the computer will calculate. If the symbols represent the words of two languages and the rules specify their grammar the computer will translate. The problem is to define the "grammar" to enable the computer to "translate." It is because the grammar of arithmetic is relatively straightforward that calculation by computer was quickly established. If the grammar for classifying electrocardiograms, electroencephalograms, or electromyograms was as simple the computer would be equally efficient in their interpretation. But its relative inefficiency at present is not the fault of the computer. The difficulty lies in preparing the programme for it. A diagnosis is more easily reached than explained, and the steps taken must be analysed before a programme can be prepared for a computer.

Even the most powerful computer can originate nothing. It can only carry out a sequence of operations and choose between alternative sequences when the need for this has been foreseen. Essentially it consists of a store, a control unit, an input unit, and an output unit. In the store are placed both the data to be worked on and the programme of instructions, specifying precisely what has to be done. Alphabetical and numerical data are stored electronically, so that on the mere press of a button in the control unit they can be processed by a programme of instructions also stored electronically. This function is called "automatic data processing." The output channel then reconverts the electrical impulses back into punched-paper tape, which is fed into a teleprinter-interpreter combination. This deciphers each digit in turn and types it out automatically on an electric typewriter. Both the teleprinter used for preparing input tapes and the teleprinter-interpreter combination are "off-line." This means they are not directly controlled by the computer and can therefore be hundreds of miles away. Devices such as the input reader and the output punch are directly controlled by the computer and are therefore "on-line" devices.

The enormous potential of computers in the medical and biological fields is only beginning to be appreciated. These

¹ Likoff, W., Kasparian, H., Lehman, J. S., and Segal, B. L., *Amer. J. Cardiol.*, 1964, 13, 7.

² Bernstein, L., Friesinger, G. C., Lichtlen, P. R., and Ross, R. S., *Circulation*, 1966, 33, 107.

³ Christensson, B., Karlefors, T., and Westling, H., *Brit. Heart J.*, 1965, 27, 511.

⁴ Gorlin, R., Bachfeld, N., Macleod, C., and Bopp, P., *Circulation*, 1959, 19, 705.

⁵ Sandler, G., Ilahi, M. A., and Lawson, C. W., *Lancet*, 1963, 1, 1130.

⁶ Epstein, S. E., and Braunwald, E., *New Engl. J. Med.*, 1966, 275, 1106 and 1175.

⁷ Feinberg, H., Katz, L. N., and Boyd, E., *Amer. J. Physiol.*, 1962, 202, 45.

⁸ Frieden, J., *Amer. Heart J.*, 1967, 74, 431.

⁹ Kannel, W. B., Dawber, T. R., Kagan, A., Revotskie, N., and Stokes, J., *Ann. intern. Med.*, 1961, 55, 33.

¹⁰ — LeBauer, E. J., Dawber, T. R., and McNamara, P. M., *Circulation*, 1967, 35, 734.

¹¹ Oliver, M. F., *ibid.*, 1967, 36, 337.

¹² MacAlpin, R. N., and Kattus, A. A., *ibid.*, 1966, 33, 183.

¹³ Sones, F. M., jun., and Shirley, E. K., *Mod. Conc. Cardiovasc. Dis.*, 1962, 31, 735.

¹⁴ Effler, D. B., Sones, F. M., jun., Groves, L. K., and Suarez, E., *J. thorac. cardiovasc. Surg.*, 1965, 50, 527.

¹⁵ — Groves, L. K., Suarez, E. L., and Favalaro, R. G., *ibid.*, 1967, 53, 93.

machines arrange vaccination and immunization programmes of some public health departments, and their vast possibilities in the field of biochemical laboratory measurements are becoming apparent. Autoanalytical methods are well developed for sampling blood plasma for electrolytes and are in use in most hospital laboratories. The results from these instruments are produced on automatic pen-recorded charts. Data from the charts can be inserted directly into the computer by a device that measures the height of the curves at intervals and converts each height into a coded row of holes on continuous paper tape. If a suitable programme is prepared the computer will then analyse and record the results. If previous biochemical records of the patient have been stored in the computer they can then be sought and retrieved from the store. With the number of hospital biochemical investigations doubling every five years such automation must obviously be exploited to the full.

Computers are playing a part in planning radiation treatment. The delivery of the optimum highest dosage to tumours while subjecting normal tissues to the minimum dose requires much work in the planning of individual treatments. An accurate assessment of differing absorption in fat, air, and bone demands much tedious and time-consuming work. By developing a computer programme using the knowledge of the most experienced physicist it is possible for less-informed junior staff to produce a plan of treatment.

The assistance of computers has, however, never been more essential in medical practice than in the investigation and diagnosis of cardiovascular disease. The assessment of its role in cardiovascular investigation by S. H. Taylor and his colleagues in a recent issue of the *British Heart Journal* is therefore timely.¹ The applications of computers include epidemiological studies, E.C.G. diagnosis, cardiovascular diagnostic investigations, and the continuous monitoring of patients with severe myocardial infarction. Indicator-dilution techniques for measuring cardiac outputs have been so automated that dilution curves can be produced by automatic injection and the sampling of arterial blood at any desired frequency and for any length of time. The information produced by these methods is overwhelming, for each hour spent in investigating provides more than 80 hours of work by skilled staff in assessing the results. This is not only time-consuming but intellectual imprisonment. Computer-assisted analysis offers an obvious solution. The curve from the automatic pen-recorded charts of cardiac output can be prepared for insertion into the computer in a similar way to biochemical autoanalytical data.

Taylor and his colleagues have been in the forefront of the application of computer programmes to cardiovascular problems. They have prepared computer programmes for cardiovascular investigations and have surmounted many of the problems presented by the computer's ineptitude at pattern recognition. They have assessed the precision with which three computers measure the cardiac output in man and have determined their usefulness in cases of abnormalities of cardiac rhythm and valvular disease. As well as showing how cardiac investigations may be advanced they have given an important lead in surmounting the many difficulties caused by artifacts in the tracings. Their work is a reminder that the potential of computers in the medical field is still largely untapped and it should stimulate the application of them to other branches of medicine.

Testing Drugs for Rheumatoid Arthritis

The medical treatment of rheumatoid arthritis is based on measures to reduce the pain, heat, redness, swelling, and inflammation. The pharmaceutical industry devotes vast resources to discovering new drugs for this purpose. Promising compounds are screened by animal tests. Those few which pass have still to be tested in man, since there is no guarantee that ability to check experimental inflammation in the rat implies ability to check rheumatoid inflammation in the human joint. But more effective anti-inflammatory drugs are needed, for the preparations at present available have many deficiencies, and there are always patients who fail to respond to one drug and yet respond to another. Any effective new preparation, even if not specially remarkable in itself, increases the pool of reserve drugs which can be brought into play.

Facilities for testing anti-inflammatory drugs in human disease are not easily found, nor are the doctors with both the will and the skill to do the task. Thus clinical testing is, to borrow the pharmacologists' jargon, the "rate-limiting factor" in the availability of new anti-inflammatory drugs. For this reason the paper by Drs. P. L. Boardman and F. Dudley Hart at page 264 of the *B.M.J.* this week is of practical importance in that it describes methods which are simple, reliable, and reproducible for assessing anti-inflammatory drugs in rheumatoid arthritis. These methods can be used in outpatient departments in any hospital or rheumatism clinic. They consist in a short-term, controlled trial, with alternate or random allocation of patients to an initial treatment group and then crossing-over to the other group. Measurements of heat and redness in rheumatoid arthritis being unreliable, Boardman and Hart concentrated their attention on measurements of swelling and function. They first used jewellers' rings to measure swelling in the finger 16 years ago.¹ But they have been able to show that a small instrument which measures the circumference of the joint directly is equally reliable and much more convenient for routine use. Strength of grip is another method long used for measuring hand function. A modified sphygmomanometer cuff of prescribed dimensions is inflated and connected to a mercury manometer. In practice strength of grip reflects both pain and structural dysfunction, but chiefly pain. Provided these methods are used at precisely the same time of day and the same time after giving the drug, they are now so reliable and reproducible that they deserve internationally agreed standardization.

Boardman and Hart found—as others have done—that placebos may apparently be followed both by "toxic" reactions and by apparent therapeutic benefit. Doctors untrained in mathematics used to boggle at the statistics involved in trials. Nowadays the path is eased by the technique of sequential analysis² and the now familiar "pair of trousers" charts,³ by which preferences between paired observations can be entered on the chart and the trial stopped as soon as a result unlikely to have happened by chance has been obtained. Using such methods, Boardman and Hart show that prednisolone has an undoubted anti-inflammatory action, that paracetamol has little, if any, anti-inflammatory action, and that salicylate in low dosage can relieve the pain of inflammation

¹ Taylor, S. H., MacDonald, H. R., Robinson, M. D., and Sapru, R. P., *Brit. Heart J.*, 1967, 29, 352.

² Hart, F. D., and Clark, C. J. M., *Lancet*, 1951, 1, 775.

³ Armitage, P., *Sequential Medical Trials*. 1960. London.

⁴ Bross, I., *Biometrics*, 1952, 8, 188.

but that high dosage is needed to affect the swelling. Their paper exemplifies methods which clinicians could use more widely for the clinical testing of potentially useful new anti-inflammatory drugs.

No Need for Change?

The Minister of Health in H.M. (67) 58 has told members of hospital boards and committees that he does not accept the need for fundamental changes in methods of training nurses proposed by the Royal College of Nursing in its publication *A Reform of Nursing Education*.^{1 2} The Minister believes that improvements can be produced by the provision of more tutors or better use of those available, by better selection of students and possibly the streaming of entrants, and by careful attention to the principles of student training.

Nurse administrators will read the form of self-examination suggested for their use somewhat glumly. Nothing is suggested that they have not often thought about before, but perhaps committees will listen with more attention to the Minister than they have to nurse advisers. In addition, hospitals will now be required to give returns of their student wastage, and, while this may be thought to amount to examining the stable door after the horse has bolted, the information ought to be available from all training schools.

The last section of the memorandum ends with suggestions for experimental schemes of nurse training. Hitherto, training schools have submitted such schemes to the General Nursing Council, which has sent those approved to the Ministry for ratification, and the Council has had many such schemes to consider. The Minister's list contains one new idea—that students might attend colleges of further education, presumably on a day-release basis, for "liberal studies."

At the same time as H.M. (67) 58 was published the General Nursing Council received from the students of a nurse-training school a letter which throws doubts on the validity of the Minister's belief that all is fundamentally well in nursing schools. Here is an extract:

"We wonder whether any of you know under what sort of conditions we are working here due to chronic shortage of staff. . . . This hospital seems to be staffed only by student nurses and a few sisters. The student nurses do not get any teaching experience on the ward due to the shortage of time and trained staff. One leaves a ward after three months' drudgery without ever being taught anything whatsoever. Does one attempt to do a procedure properly, we are very often told there is not time to do a sterile procedure. . . . Still exhausted from the previous day, we often find ourselves alone on the ward, dishing out breakfast for 28 patients, feeding many of them as well. . . . Night duty follows a very similar pattern. One is put alone in charge of a 28-patient ward without previous experience of night duty, giving out drugs, or general supervision of patients."

The full text was published in the *Nursing Times*³ recently and a copy was sent to the Minister. It reminds us that nobody and no organization concerned with nurse training can be satisfied with the present position.

¹ *A Reform of Nursing Education*. Royal College of Nursing, 1964. London.

² *Brit. med. J.*, 1964, 1, 1585.

³ *Nursing Times*, 22 September 1967.

Modernizing Hospital Medicine

One of the more depressing features of British medicine for those who believe in the N.H.S. is the antagonism between the profession and the Health Ministers. It is, therefore, all the more encouraging this week to find representatives of the two sides agreeing on the major faults in the organization of medical work in the hospital service. Just as welcome are their suggestions for reform, for these are both radical and realistic.

A joint working party of doctors and hospital administrators was set up by the Secretary of State for Scotland in 1965 with instructions to look for ways of improving efficiency in the hospital service. A little later a similar body was set up by the Ministry of Health and the Joint Consultants' Committee. Their first reports^{1 2} are summarized at page 291 of this week's *B.M.J.*

Fundamental to future planning for the hospital service is the knowledge that there are too few doctors and that there is no prospect of enough for at least ten years. So doctors must be used more efficiently, and their morale must be improved if they are not to emigrate. The Scottish report accepts that the discrepancy between the number of registrars and the number of potential consultant vacancies is responsible for much anxiety among junior staff, and recommends that numbers in the registrar grade should be reduced to the minimum which would allow for natural wastage and competition. The long-term solution to much of the discontent lies at this intermediate level of hospital work, where there is need for greater integration with general practice. The Scottish Working Party believes that much of the work could be done by family doctors if they could be brought into the hospitals as, say, part-time medical assistants. The report recognizes that expansion of the medical assistant grade has dangers, particularly the risk of consultant responsibility being carried by assistants—and it accepts that the present sessional rates of pay are not good enough to attract general practitioners. Such an appreciation of realities is welcome, as is the Working Party's conclusion that "these difficulties must be resolved however intractable they may seem."

Both reports agree that the tradition in hospitals of consultants having a fixed allocation of beds is inefficient and out of date. Both propose that hospitals should change over to a divisional system of staffing, similar to that widely used in North America. A division would consist of all the doctors working in one specialty—or in several specialties if they are linked in their functions. Chairmen of divisions would be appointed, and a committee formed of these chairmen or their representatives. Outside Scotland the chairman of this committee would hold a post roughly equivalent to the American chief of staff; in Scotland the position of medical superintendent would be retained.

These changes should lead to a greater exchange of ideas between medical staff, as well as promoting the more efficient use of beds, staff, and equipment. The danger is that a doctor's freedom to treat his patients as he thinks best may be eroded by pressures for the adoption of uniform regimens of management. Neither report even hints at the introduction of sanctions that could be used to force the nonconformist into obedience, though these do exist in certain American hospitals. The Scottish report states, "While we do not wish to depart from the principle that each

¹ *Organization of Medical Work in the Hospital Service in Scotland*, 1967. H.M.S.O. Price 6s. 3d.

² *First Report of the Joint Working Party on the Organization of Medical Work in Hospitals*, 1967. H.M.S.O. Price 2s. 9d.

consultant is personally responsible for his own patients, we see great value in the results of clinical work being examined on a group basis." Later in the report there are proposals for the introduction into Scotland of the "medical audit" and for alternatives to traditional systems for hospital care.

All these proposals will not easily find general acceptance. But if British medicine is to maintain its reputation internationally then modern methods of organization and assessment must be introduced. Clinicians must ensure that the new methods do not reduce their proper clinical freedom—the traditional duty of each doctor to treat his patients in the way he believes to be best.

Operation for Parkinsonism

At the beginning of this century Robert Clarke designed a machine, modifications of which have revolutionized the treatment of Parkinson's disease. Clarke's patent specification¹ clearly defined the principle of stereotaxis: "This invention relates to what may be termed stereotaxic surgical apparatus for use in performing operations within the cranium of living human beings . . . (it) is designed to enable a so-called probe . . . to reach, with absolute precision and by the shortest path, any predetermined point within the cranium through a comparatively small opening in the wall of the latter, the primary object being to obviate the necessity of extensively laying open or partially dissecting the head and removing considerable portions of the cranial contents in order to gain access to the exact spot whereat the actual operation is required to be carried out."

Clarke worked in association with Sir Victor Horsley, but they used the machine exclusively for work in animals. It was not until 1950 that E. A. Spiegel and H. T. Wycis reported the use of stereotaxis in man at a meeting of the American Neurological Association. Using a modified Clarke's stereotaxic apparatus,² they had succeeded in abolishing choreoathetotic movements by means of electro-coagulation of the globus pallidus of the side opposite to the involuntary movements. Spiegel and Wycis³ later found they could improve tremor and rigidity in Parkinson's disease by the same operation; but technical difficulties arose from the great variation in man between the external landmarks of the skull and the targets in the brain. J. Talairach and his colleagues⁴ overcame this problem by using ventriculography to relate cerebral structures to the target areas. Experience of many workers has shown that the nucleus ventrolateralis and the nucleus ventroposterior lateralis of the thalamus are better targets for the treatment of Parkinsonism than the globus pallidus.

Most patients with Parkinson's disease have a good chance of worthwhile relief of symptoms if certain conditions are fulfilled.⁵ There must be no mental deterioration and the Parkinsonism must not be so far advanced that the patient is entirely dependent on the help of others. The stereotaxic apparatus should be capable of finding the selected target accurately to within one millimetre. The passage of the electrode or cannula to the target should be made through a "silent" part of the cerebrum. Patients with bilateral manifestations of the disease can be successfully treated provided

that the smallest therapeutic lesion necessary to produce the desired effect is made on each side and that an interval of at least six months is allowed between treatment of the first and second sides. Individual variation in the position of the thalamic nuclei should be taken into account.

The most important factor other than technical considerations which affects the result of surgical treatment is the pattern of the disease. Patients with long-standing unilateral symptoms are almost certain to obtain complete relief, whereas patients who are completely incapacitated by the disease have little to gain. Between these two extremes are ambulant patients with bilateral symptoms, who can be offered substantial benefit from bilateral stereotaxic thalamotomy. Severe ataxia, dysarthria, and involuntary salivation are resistant to treatment.

Age alone does not appear to affect the result of operation—L. C. Oliver⁵ reported several patients over the age of 70 who had been treated successfully. A long history of slight or moderate disability is not necessarily an adverse factor; indeed it usually indicates slowly progressive disease and tends to favour a good and lasting result. This is true also of postencephalitic Parkinsonism, in which oculogyric crises are abolished or their frequency reduced in about a third of the patients. Finally, though nothing can be done at present to arrest the degenerative process underlying Parkinson's disease, follow-up of patients after operation seems to indicate that the development of further symptoms may be arrested by thalamotomy.

Complications of Vaccination

Vaccinia is much the commonest iatrogenic disease. Between 1951 and 1960 there were over 5 million cases in England and Wales,¹ though fortunately the great majority of them were mild and uncomplicated. Most of the patients, moreover, were immunologically better off after than before their illness. The argument is sometimes put forward that a person has little advantage in possessing antibodies against an infection he is unlikely to encounter, and it gains some support from the fact that, though there may be no harm in having a few reserve antibodies, in acquiring them some patients die, some pass through long, worrying illnesses, and some suffer enough discomfort to interfere with work and other pursuits. Vaccinia is a virus disease. If the infection were acquired naturally, virologists would be jostling for elbow room at their benches in their eagerness to isolate the virus and produce a vaccine against the disease. But with vaccinia the tables are turned, and it is the epidemiologists and the administrators who are left to control this troublesome infection.

The complications of vaccinia have been recently reviewed in Great Britain¹ and the U.S.A.² While there are several points of difference in the two studies, which might be related to such widely different factors as the strain of vaccine virus and the accuracy of reported figures, there are two important points of agreement. These are, firstly, that children under 1 year old suffer most complications, and, secondly, that many of the complications are preventable. In the British series¹ of over 5 million cases there were four deaths from eczema vaccinatum and seven from vaccinia gangrenosa, all in children under 1 year old; there were 22 deaths from postvaccinal encephalitis, 16 of them in children under 1 year old. In the American series of over 14 million cases the frequency of complications in children under 1 year was two or three times

¹ Clarke, R., Patent No. 22,455, 1912. London.

² Spiegel, E. A., Wycis, H. T., Marks, M., and Lee, A. J., *Science*, 1947, 106, 349.

³ ———, *Stereencephalotomy*, 1962, vol. 2. New York.

⁴ Talairach, J., de Ajuriaguerra, J., and David, M., *Presse méd.*, 1952, 60, 605.

⁵ Oliver, L. C., *Parkinson's Disease*, 1967. London.

higher than in any other age group, though it must be noted that no child under 1 died. There were 12 cases of post-vaccinial encephalitis, but only one in the first year of life, and all five children who died were aged between 1 and 14 years. There were two other deaths from eczema vaccinatum, both in children in the 1-4-years-old age group. The odd differences between the rates in the two series, especially for post-vaccinial encephalitis, cannot be explained, but such anomalies have been observed before. The figures collected by the Vaccination Committee of 1926 showed a preponderance of cases of postvaccinial encephalitis and of deaths in children of school age,³ whereas the figures reported to the Ministry of Health during 1951 to 1960 showed that both cases and deaths were much more frequent in the first year of life. Reporting of cases was probably incomplete in both periods and comparisons are therefore difficult, but the policy of recommending vaccination in the second rather than the first year of life is based on the more recent figures.

As to the prevention of complications, certain points are clear. Vaccinia is an infectious condition and infection can be readily transferred from the vaccination site to other parts of the body. This is the commonest cause of most cases diagnosed as generalized vaccinia. It is rarely a serious complication, but it should be preventable by careful hygiene. Transfer to another person is less common but may be more dangerous: 54 cases, including the two fatal cases, of eczema vaccinatum in the American series were caused in this way. A child with eczema must be protected rigorously against accidental vaccination from contact with a recently vaccinated person. Vaccination of a child with florid eczema is a hazardous operation and should be undertaken only on dangerous exposure to smallpox and under cover of hyper-immune vaccinia gamma globulin and possibly *N*-methylisatin beta-thiosemicarbazone. When the eczematous state is past or latent the risk is less, and such patients have often been vaccinated without trouble. This is true also of patients with asthma and other allergic disorders, but it is safer not to vaccinate such patients unless it is unavoidably necessary. Except during outbreaks, immigration authorities will usually accept a medical certificate stating the facts. Any immunological defect such as hypogammaglobulinaemia is another contraindication to vaccination,⁴ and a history of recurring infections during early infancy should lead the physician to obtain an analysis of blood globulins before he undertakes vaccination. Corticosteroids are known to affect immune responses, so that vaccination should be avoided for patients on long-term treatment with these substances, or, if it must be carried out, hyperimmune gamma globulin should be given beforehand. It is undesirable to vaccinate a patient with a skin infection. There is a very small risk of causing abortion by vaccinating women in the early months of pregnancy⁵ and of producing vaccinia in the foetus by doing it in the late months.⁶⁻⁸ Whatever the national policy about routine vaccination of a country, many of the complications can be avoided by excluding from the programme those patients in whom there is a contraindication to the treatment.

³ Conybeare, E. T., *Mth. Bull. Minist. Hlth Lab. Serv.*, 1964, 23, 126, 150, and 182.

⁴ Neff, J. M., Lane, J. M., Pert, J. H., Moore, R., Millar, J. D., and Henderson, D. A., *New Engl. J. Med.*, 1967, 276, 125.

⁵ *Report of Vaccination Committee*, Cmd. No. 3148, 1928. H.M.S.O.
⁶ Keidan, S. E., McCarthy, K., and Haworth, J. C., *Arch. Dis. Childh.*, 1953, 28, 110.

⁷ MacArthur, P., *Lancet*, 1952, 2, 1104.

⁸ Naidoo, P., and Hirsch, H., *ibid.*, 1963, 1, 196.

⁹ Entwistle, D. M., Bray, P. T., and Laurence, K. M., *Brit. med. J.*, 1962, 2, 238.

¹⁰ Tucker, S. M., and Sibson, D. E., *ibid.*, 1962, 2, 237.

Reform Needed

The absence of any successful appeal from a finding of the General Medical Council since the creation of the right of appeal to the Judicial Committee of the Privy Council in 1950 at first sight may appear to be a remarkable compliment to the G.M.C. But criticisms made by the Privy Council from time to time show the G.M.C. to be no less fallible or human than other judges. The lack of any successful appeal is really a reflection on the machinery provided for disciplinary proceedings by the Medical Act, 1956, and by statutory instrument. That machinery has been much criticized, and many of the criticisms have been forcefully stated recently by J. L. Taylor.¹

The results of the G.M.C.'s lack of jurisdiction to impose any sentence other than erasure from the *Medical Register* are far-reaching. To reduce the injustice that might result from a choice restricted to erasure or acquittal the device of postponing judgement or finding has been developed. This produces something like a sentence of being put on probation, but, as Taylor points out, the practitioner not only has to be of good behaviour during the period of probation but has to prove his good behaviour by providing references. It would be in the public interest, and merciful to the practitioner, if the G.M.C. had the power in appropriate cases to impose a fine or a period of suspension from practice. When the draughtsman of the Medical Act 1956 formulated the right of appeal in section 36 he accorded this right of appeal only to the practitioner whose name is ordered to be erased from the *Register*. In all other cases the practitioner either stands acquitted or he is told that no final judgement has been passed upon him. Though it is logically undesirable to grant a right of appeal from a decision which in form has not been made, postponement of judgement is in truth a finding of guilt, and justice demands that there should be an immediate right of appeal. The whole device of postponing judgement is a denial of justice which ought not to be tolerated. It is a basic requirement of justice that courts and tribunals should not only hear but also determine the issues before them as speedily as may be, and publish their determination forthwith.

In addition to a greater variety of punishments Taylor would like to see some machinery for imposing suspension without stigma when a practitioner's health (usually mental health) makes this desirable. Taylor also points out that in some circumstances a practitioner faces charges without being told the details of what is alleged against him. There is a good case for a requirement that a "circumstantial letter" be sent to every practitioner who is charged before the G.M.C.

It is not only in its machinery that the G.M.C. is hampered. The whole concept of "infamous conduct in any professional respect" requires deep examination. It is questionable whether it is desirable to try to separate the professional life of a professional man from his private conduct. A charge of "conduct unbecoming a medical practitioner" would enable the G.M.C. to make a more flexible approach to complaints against practitioners, though it may be that such flexibility would prove too severe upon practitioners. The esteem in which members of the G.M.C. are held contrasts markedly with criticisms of the procedure and rules of the disciplinary process of the profession. The whole subject is appropriate for examination by the Law Commissioners.

¹ Taylor, J. L., *Med.-leg. J. (Camb.)*, 1967, 35, 119.

Papers and Originals

Four Years of Respiratory Intensive Care

DONALD CAMPBELL,* M.B., CH.B., F.F.A.R.C.S., D.A.; J. M. REID,* M.B., CH.B., F.F.A.R.C.S., D.A.
A. B. M. TELFER,* M.B., CH.B., F.F.A.R.C.S.; W. FITCH,† M.B., CH.B., B.SC., D.OBST.R.C.O.G., F.F.A.R.C.S.

Brit. med. J., 1967, 4, 255-259

Each hospital community setting out to organize a system of progressive patient care, including an intensive care area, must attempt as a preliminary step to answer certain general questions. For example: How many beds out of the total available in the hospital will be required for intensive care of the most seriously ill patients? How long will these patients occupy the available beds? What will be the distribution of patients according to age? What mortality rate may be expected? In an attempt to answer these questions for the Glasgow Royal Infirmary a survey of patients in the hospital was carried out between July 1963 and January 1964. For the first three months the entire hospital population was assessed, and for the second three months the survey was confined to two general medical units and two general surgical units. This latter selective assessment made possible a closer scrutiny of the individual patients involved. In all, 280 patients were included, and the criteria for selection for the hypothetical intensive care area were taken to be: (a) if the patient required an individual nurse for any or all of the time, or (b) if any specific therapy requiring continual observation was necessary. The patients thus selected were arbitrarily classified according to whether the main problem was respiratory, cardiovascular, metabolic-biochemical, traumatic, etc.

Tables I and II give the results of the investigation in so far as age groups and bed occupancy were concerned. It was found that approximately 4% of the total bed complement

TABLE I.—Distribution of Intensive Care Patients by Age Groups

Report	Age Group (Years)								
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
Interim*	10	10	14	27	38	36	29	17	7
Final†	3	2	9	10	14	20	22	8	4

* Interim report represents a hospital-wide survey of three months' duration.
† Final report represents a three-months study of four selected units.

TABLE II.—Distribution of Patients by Number of Days of Intensive Care

Report	Duration of Intensive Care (Days)				
	1-2	3-5	6-10	11-20	Over 20
Interim	41	84	41	18	4
Final	19	42	19	9	3

of the hospital would be required for all intensive care purposes. For the Glasgow Royal Infirmary this would be about 40 beds.

The mortality in patients thought to require intensive care was found to be 19%. The overall hospital mortality during this six-month period was 4.2% for the first three months and 6.1% for the second three months.

* Consultant Anaesthetist, University Department of Anaesthetics, Royal Infirmary, Glasgow C.4.

† Registrar Anaesthetist, Royal Infirmary, Glasgow C.4.

Respiratory Intensive Care Unit

Against this background of general data acquired from the prospective study, it is of interest to examine in detail the actual experience in one of the intensive care units in the Glasgow Royal Infirmary—namely, the respiratory intensive care unit. In October 1962 a "pilot" four-bed unit for the treatment of acute respiratory emergencies, both surgical and medical in origin, was opened. This unit was converted from a six-bed side-ward, and despite the reduction in bed numbers was far from ideal so far as floor space was concerned, and too small to enable isolation cubicles to be constructed.

This paper comprises an analysis and discussion of 488 patients treated over a period of four years. Table III summarizes these results, classifying the patients under the headings indicating the primary cause of the respiratory problem. The number of patients requiring temporary tracheal intubation or tracheostomy and mechanical assistance to ventilation are shown. The average length of stay in the intensive care unit for each group is also given.

TABLE III.—Analysis of Patients Treated in the First Four Years in the Respiratory Intensive Care Unit

Condition	Cases		Requiring E.T.T. or Tracheostomy		Requiring I.P.P.V.		Average Stay in Unit (Days)
	No.	%	No.	%	No.	%	
Traumatic ..	195	39.95	108	55.4	52	26.6	10.3
Post-operative	202	41.4	130	63.3	49	24.2	4.1
Drug poisoning	42	8.6	40	95.2	28	66.6	3.1
Obstructive lung disease	16	3.3	11	71.4	7	42.9	8.3
Miscellaneous	33	6.76	24	72.7	21	63.6	9.8
Total 1962-6	488	100	313	64.1	157	32.1	7.1

E.T.T.=Tracheal intubation. I.P.P.V.=Intermittent positive-pressure ventilation.

Traumatic Respiratory Problems

In Table IV the traumatic group of respiratory problems is divided into those patients suffering from the "crushed chest" syndrome (75 patients), multiple injuries with a respiratory/metabolic upset (73 patients), and severe head injuries requiring special measures to maintain a clear airway and adequate alveolar ventilation (47 patients). The overall survival rate in these severely ill patients was 58.9, the lowest

TABLE IV.—Analysis of Traumatic Group of Respiratory Problems

	Cases	Survivals
Chest injuries ..	75	53 (70.6%)
Multiple ..	73	44 (60.3%)
Head ..	47	18 (38.3%)
Total ..	195	115 (58.9%)

survival rate being in the grave head injuries. Those patients who suffered severe injuries to the thoracic cage and lungs presented the greatest challenge to the staff of the intensive care unit. This type of injury has in the past always carried a high mortality. The method of treatment employed in the Glasgow Royal Infirmary has been reported elsewhere (Reid and Baird, 1965; Campbell, 1966).

Postoperative Respiratory Problems

Those patients who presented with significant postoperative respiratory difficulties, whether following elective or emergency surgery, were treated in the intensive care unit. As there was a shortage of 24-hour recovery facilities, inevitably a proportion of the patients in this group were admitted to the respiratory unit only for short-term postoperative observation and therapy. Nevertheless, the average length of stay was 4.1 days for a total of 202 patients. Of these, some two-thirds required tracheal intubation or tracheostomy and one-quarter mechanical assistance to ventilation.

It is our experience that "relaxant problems" commonly arise from unrecognized disturbances of metabolism or cardiovascular or respiratory function. The other groups were determined by assessment of the patient's history and clinical examination as well as radiographic and electrocardiographic findings. In this series there were instances where it was difficult to determine whether an upset in acid-base balance actually preceded rather than followed a period of cardiovascular depression or respiratory insufficiency.

It may be noted that difficulties involving the relaxant group of drugs alone were uncommon in both elective and emergency cases, and all such patients survived in this series, requiring merely prolonged assistance to ventilation. Only three cases of true suxamethonium apnoea were identified in this series. The high incidence of pre-existing lung disease, as diagnosed on clinical, biochemical, and radiological evidence, is not surprising in the City of Glasgow. The higher survival rate in the elective cases is taken as a reflection of the better pre-operative preparation of these patients and the ability to choose the optimal time during treatment for elective surgery.

Figs. 1 and 2 show the distribution of patients according to the site of operation, and indicate the comparative survival rates for the various procedures.

Two points arise with reference to the elective thoracic cases. Firstly, only a small percentage of the total number of admitted cases have had thoracic procedures, and these represent a minor fraction of the total performed in the hospital. Secondly, the higher survival rate compared with the elective upper abdominal procedures may reflect the fact that the thoracic cases are

usually more extensively assessed, and the operation if performed is done under optimal conditions.

Drug Poisonings

When respiratory failure complicates drug overdose, either accidental or self-administered, the patient is best treated in a respiratory intensive care unit working in close conjunction with a dialysis unit. Ideally, the two intensive care units should be adjacent, since more than one period of dialysis may be required, and this presents problems where the patient is still on intermittent positive-pressure ventilation. It is probably true to say that no patient need now die from the effects of barbiturate overdosage, since respiratory function can be supported almost indefinitely while forced diuresis or renal dialysis eliminates the drug. This view is supported by our experience of two remarkably high serum barbiturate levels successfully treated by this combined technique. One patient had an initial serum phenobarbitone level of 57 mg./100 ml. and the second had a serum butobarbitone level of 15 mg./100 ml. Both patients made a successful recovery (Kennedy *et al.*, 1967).

Nevertheless, only 37 patients out of 42 survived in this group, but those who died had already suffered prolonged severe hypoxia due to respiratory insufficiency before admission. Only two of these deaths were due to true barbiturate overdosage, the others being "mixed poisonings." Twenty-two of the patients were treated by forced diuresis and only three required artificial dialysis. No patient required a tracheostomy, endotracheal intubation with a cuffed tube being the method of choice at that time when an artificial airway was necessary (40 out of 42). The tracheal tube was not left in situ for longer than 72 hours in this group of patients, and their average stay in the unit was 3.1 days. Intermittent positive-pressure ventilation was necessary in 28 of the 42 patients.

Miscellaneous Cases of Respiratory Failure

Though this group of patients requiring respiratory intensive care is small in number, it comprises many of the most interesting and challenging types of respiratory disturbance. Table V details the individual conditions, and it can be seen that there is a variety of comparatively uncommon conditions represented here. The overall survival rate of 33.3% is low, but it must be remembered that only the most gravely ill patients with these conditions were admitted.

This miscellaneous group of patients averaged 9.8 days of treatment in the intensive care unit. A large proportion required tracheostomy (72.7%) and intermittent positive-

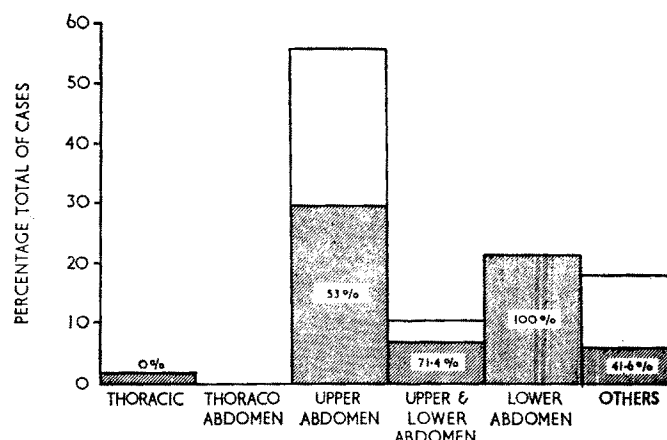
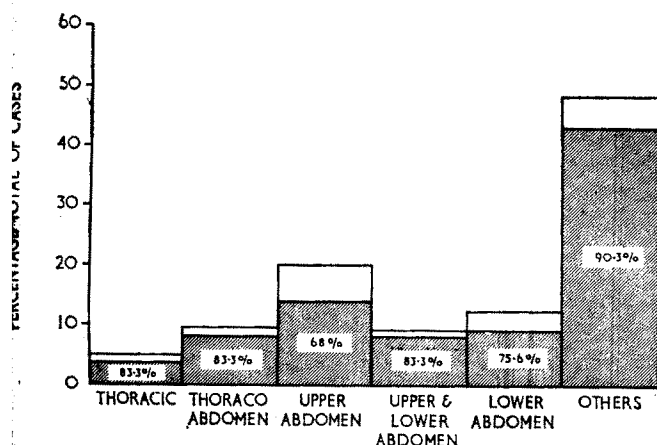


FIG. 1.—Analysis, according to site of operation, of 131 elective patients who developed postoperative respiratory insufficiency. The cross-hatched areas represent the percentage survival for each procedure. FIG. 2.—Analysis, according to the site of operation, of 71 emergency patients who developed postoperative respiratory insufficiency. The cross-hatched areas represent the percentage survival for each procedure.

pressure ventilation (63.6%). Tracheostomy was commoner than endotracheal intubation (20 out of 24 cases) mainly owing to the length of time required for treatment.

TABLE V.—Variety of Conditions in Which Acute Respiratory Insufficiency Required Energetic Treatment. All Required Active Measures to Support Respiration In Addition to Specific Therapy

Condition	No.
Accidental hypothermia	2
Cerebrovascular accident	7
Drowning	1
Myasthenia gravis	2
Myocardial infarctions with cardiac arrest	3
Myxoedema coma	2
Neurological and polyneuritis	7
Status eclampticus	1
Status epilepticus	4
Tetanus	2
Upper airway obstruction	2
	33

Obstructive Lung Disease

In the initial stages of the pilot respiratory intensive care unit those suffering from an acute exacerbation of chronic obstructive lung disease were admitted. Sixteen patients were treated during this period, 11 requiring intubation or tracheostomy and seven intermittent positive-pressure ventilation. These patients are now largely taken care of in a separate unit within the hospital, and this is highly desirable, since they tend to be an important source of infection and present a real hazard to the "clean" cases, particularly those in the traumatic group. If such patients are to be managed along with uninfected cases, there is no doubt that they should be isolated and if possible barrier nursed.

The standard treatment for this group of patients was controlled low oxygen therapy with the Edinburgh mask (Flenley *et al.*, 1963). Tracheal intubation was used rather than bronchoscopy to facilitate frequent and thorough aspiration of secretions. Tracheostomy was reserved as a last resort. Intensive physiotherapy is an essential part of treatment here, as indeed in all the patients treated in the intensive care unit, and this is combined with measures to stimulate coughing along with the appropriate antibiotic therapy.

Special Problems in Respiratory Intensive Care

Whatever the underlying cause leading to the episode of respiratory failure in an individual patient, certain common problems require consideration, and certain techniques have been evolved which are applicable to the treatment of all cases.

Cross-infection

Without doubt a major problem in a respiratory intensive care unit is the control of infection and the segregation of known infected cases. In the small four-bed unit the infection rate was high, and all tracheostomies became technically infected as judged by serial culture of tracheal swabs, though this did not necessarily result in intrapulmonary infection. In addition, a large number of these patients required indwelling urinary catheters, and, despite aseptic precautions, bladder infections were inevitable in most long-stay cases. The close juxtapositioning of the four beds, approximately 5 ft. (1.5 m.) apart side to side and 6 ft. (1.8 m.) apart end to end, defeated the most stringent aseptic precautions in the handling of tracheostomies. Again there was no provision for ventilation of the ward with filtered air, and the mechanical ventilators were not able to be adequately sterilized for the first two years. The main infecting organism was the resistant *Staphylococcus aureus*, but when this was eliminated by use of the newer potent antibiotics a secondary invasion with *Escherichia coli*, *Proteus mirabilis*, or *Pseudomonas pyocyanea* was common. The lack of cubicles prevented barrier nursing of known

infected cases, and resulted in a further increase in the infection rate. On those occasions when the infection rate reached epidemic proportions the unit was closed for thorough cleansing, including washing of walls from floor to ceiling.

Since early 1966 a new respiratory intensive care unit has been in use which represents a great advance, particularly from the point of view of control of infection. Fig. 3 shows the plan of this eight-bed unit, which is a conversion from a 26-bed Nightingale ward. Two large cubicles (dimensions 15 by 12 ft.; 4.6 by 3.7 m.) are available for the barrier nursing of selected cases, both patients known to be infected and those potentially infected—for example, those with superficial burns. In addition, the whole unit is ventilated with filtered warmed air by a plenum system with extractor fans at each bed station. Humidity of the air is also controlled. One cubicle can be separated from the plenum system and the atmosphere independently controlled by means of a standard office-type air-conditioning unit. The main advantage, however, in this new unit is that the beds are widely set apart in individual bays. Each bed station has its own trolley with all its own instruments—for example, Wright's respirometer and laryngoscope. No equipment or instrument is permitted to be transferred from one bed station to another. Entry to the unit is controlled by means of an interchange area, and all persons visiting the unit are required to wear gown, mask, and overboots. Such cases of known infection as have been admitted

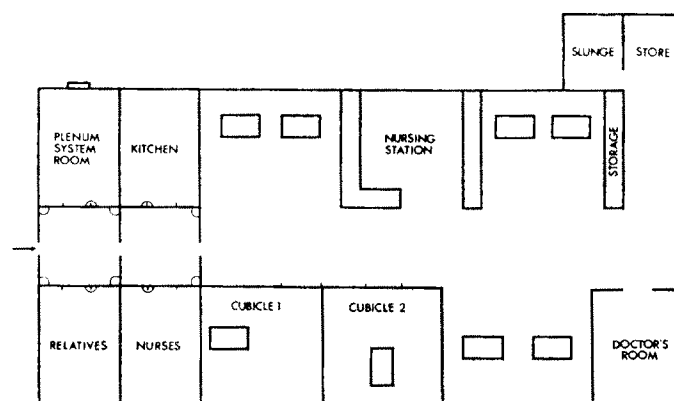


FIG. 3.—Plan of respiratory intensive care unit. The interchange areas lie between the inner doors opposite the kitchen and nurses' staff-room. The laboratory, which is adjacent to but outside the unit, is not shown.

of necessity have been nursed in the cubicles without any evidence of cross-infection. The practice is for every patient to be swabbed (nasopharynx or trachea and skin) and a urine culture done at the time of admission. This latter test is repeated, if the patient is catheterized, at least twice weekly throughout the patient's stay. All staff have regular nasopharyngeal swabs taken.

A further advance in the control of infection has been in the sterilizing of the ventilators. These are now sterilized with ethylene oxide, after thorough cleansing, before being reused (Bishop *et al.*, 1962). In long-term cases these machines should be changed every three to four days. Currently an investigation is being carried out into the advantages of bacterial filters on the ventilators. A record is kept of the bacteriological history of each machine and its associated parts—for example, spirometer and humidifier—in order to facilitate tracing the source of any outbreak of pulmonary infection.

Oxygen Therapy

Controlled oxygen therapy is an important part of treatment in these patients. Control implies measurement, and this consists of regular oximetry to monitor the inspired oxygen concentration by means of the Beckman instrument. In addition, blood gases are measured at frequent intervals in all

acutely ill patients as a guide to the efficiency of treatment. This demands a "bedside" service, and the medical staff in the unit are all trained in the use of the appropriate apparatus to measure haemoglobin oxygen saturation, arterial oxygen tension, arterial carbon dioxide tension, acid-base state, and haemoglobin in the laboratory adjacent to the unit.

In addition to its function as originally described for administering controlled low-oxygen concentrations, the Edinburgh mask is also used, with the modification described by Campbell (1967), to administer inspired concentrations up to approximately 80%. The advantage of this system is that one basic disposable mask can be used for all types of oxygen therapy.

Metabolic Care and Nutrition

Intensive care demands a great deal of assistance from the biochemist. The measurement and restoration to normal of blood volume, hydration, and electrolyte levels are well understood.

One feature of patient care which often suffers neglect is the provision of an adequate nutritional regimen. This aspect of the care of the surgical patient is well described by Moore (1959). It applies to all patients, particularly those in an intensive care unit (Peaston, 1967).

The importance of adequate nutrition cannot be overstressed, since many of these patients suffer a severe catabolic response after injury or surgery, and this may be aggravated by concomitant infection when the calorific requirement may reach 4,000 calories a day. If muscle wasting is allowed to develop then "weaning" from the ventilator may be prolonged, despite a return to normal pulmonary function, since the patient is unable to perform the required work of respiration. The condition of such a patient can resemble that of a severe myasthenic.

Central Venous Pressure

The measurement of central venous pressure in the surgical patient (Sykes, 1963) is of value where there has been severe blood loss. A catheter can be introduced into the superior vena cava via the external jugular or an antecubital vein, but if this is impracticable a saphenous cut-down at the groin enables a wide-bore catheter to be introduced into the inferior vena cava. The presence of a caval cannula also enables parenteral feeding to be instituted at an early stage in treatment without the complications of peripheral venous thrombosis.

Monitoring of Vital Functions

It has been found invaluable to make use of a central monitoring system whereby E.C.G., heart rate, temperature, and respiratory rate can be observed continuously in every patient. The recording of these functions can be carried out even by a nursing-aide, thus enabling the more skilled nursing staff to carry out the heavy demands of patient care. Blood pressure is, in our experience, still best measured by the mercury sphygmomanometer at the bedside and only in special cases via an indwelling arterial cannula. Respiratory measurements carried out by the nurse include minute volume, airway pressure, and respiratory frequency when on intermittent positive-pressure ventilation, and respiratory frequency and minute volume when breathing spontaneously. Regular auscultation of both lung fields is also carried out by the nursing staff to detect any gross changes in air entry.

Intelligent use of modern technological aids can to some extent mitigate the shortage of skilled nursing personnel, though it must be remembered that monitoring devices are only an

extension of the nurse's own senses and not in any way a substitute for acute observation and constant attention at the bedside.

Organization and Staffing

The Glasgow Royal Infirmary respiratory intensive care unit not only serves the parent hospital but also provides a group service for the associated hospitals. Some 5% of cases, a figure which is increasing, come from other hospitals throughout the Western Region, and a small number are referred from hospitals outside this region. This intensive care unit is associated with other intensive care areas within the hospital—namely, the renal dialysis, cardiovascular-surgical, acute coronary, and medical respiratory units.

Medical Staff

The unit is administered by the department of anaesthetics. Three consultant anaesthetists share the senior duties on a sessional basis. Two anaesthetic registrars are in training at any one time, each for a period of two months, with no other duties. An anaesthetist is always on duty in the unit, where simple sleeping accommodation is provided. The medical staff are also responsible for the anaesthetic side of the hospital emergency resuscitation and cardiac arrest service, which is on a "crash call" basis. This ensures that experienced anaesthetic assistance is immediately available in appropriate cases. The importance of the integration of such an emergency service within the organization of the intensive care unit has been mentioned by Campbell (1965).

Ward rounds, at least four in a 24-hour period, are conducted by the consultant anaesthetist on duty. That is, apart from a primary concern with the patient's respiratory problem, the consultant is responsible for overall care. Administrative responsibility for the running of the unit cannot readily be separated from a clinical responsibility to the patients. Joint bedside examination and discussion of each case, if necessary several times throughout the 24 hours, is essential to full co-operation between the various specialists involved in the treatment of an individual patient. As a consequence, treatment is under continual review, continuity of care progressing from the intensive care unit to the general ward. This co-operative effort has been a most successful and rewarding feature of this work, and the advantages of the system have been stressed by Kennedy *et al.* (1963).

Nursing and Ancillary Staff

While the ideal number of trained nursing staff per patient has been variously estimated at from one to two per patient per shift (Nolan, 1965), the following staffing has been found adequate for most of the time in this respiratory unit: four sisters, two full-time and three part-time staff nurses, and two trained nurses assigned to the unit while on postgraduate intensive care training course; two student nurses; three full-time and two part-time State-enrolled nurses; two male orderly-technicians and one female orderly; one housekeeper; and one domestic.

An eight-hour shift system is not possible with these numbers and a "partial" shift system is operated. The working day is from 8 a.m. until 9 p.m., and night from 9 p.m. to 8 a.m., and this arrangement has not led to any lack of continuity in care. There is no doubt that, taking into consideration the demanding nature of the work, a two-day rest period a week is essential. Great use is made of ancillary nursing staff, who can all be employed in such a way that trained staff are relieved of the simpler but necessary non-nursing duties.

The contribution made by the physiotherapy staff deserves special mention. Their services have proved invaluable, and they are required throughout the 24 hours. Indeed, all

supporting services, laboratory and diagnostic, must be on a 24-hour seven-day week basis.

Despite the physically and mentally exhausting nature of the work morale is high. This is thought to be largely attributable to the fact that medical and nursing staff have been to some extent self-selective. In addition, there is the fullest discussion of all problems, theoretical and practical, between medical, nursing, and ancillary staff. This is carried out both at the bedside and in the form of lecture-tutorials. Finally, despite the high mortality rate, the successes have been such that no member of the staff requires any further demonstration of the value of the concept of intensive care for patients with acute respiratory difficulties.

Summary

It is suggested that an essential preliminary to the setting up of a new intensive care unit is the conducting of a preliminary survey of the hospital population to determine the likely number of patients requiring this degree of care. Such a prospective study, carried out in the Glasgow Royal Infirmary, to assess the total requirements for intensive care is described. The next step, which may be carried out simultaneously, is to set up a small "pilot" unit in which actual experience may be gained of the problems of organization and care of patients. The final phase, if indicated, is the establishing of a definitive unit for the intensive care of one or other group of patients—for example, respiratory problems, acute coronary cases, renal problems, etc.

The results of the intensive care of 488 patients with acute respiratory problems are presented. Certain aspects of organization and patient care involved in the treatment of these cases are discussed.

We should like to pay tribute to our colleagues of the medical and nursing staff of the Glasgow Royal Infirmary, whose co-operation, interest, and hard work have made the success of the respiratory intensive care unit possible. In particular we are deeply indebted to the staff of the Department of Physiotherapy for their invaluable contribution to patient care. We are grateful to the members of the committee who carried out the original prospective study on intensive care needs in the hospital, and the Board of Management of Glasgow Royal Infirmary for permission to publish the results given in Tables I and II.

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Visuo-motor Disability in Schoolchildren

MAY WOOLF BRENNER,* PH.D.; SELMA GILLMAN,* PH.D.; O. L. ZANGWILL,* M.A.
 MARGARET FARRELL,† M.A.

Brit. med. J., 1967, **4**, 259–262

In a recent study the visuo-motor abilities of 810 schoolchildren (427 boys and 383 girls) aged 8–9 years were sampled by means of a new group test-battery. This comprised 11 tests designed to explore various aspects of visuo-motor capacity and to provide norms for the assessment of disability. The tests used could be classified under three general headings: (1) dexterity—for example, use of scissors and simple pencil control within guiding lines; (2) perceptual analysis—for example, the capacity to discriminate overlapping designs or to isolate figures "embedded" in more complex designs; and (3) constructional skill, as evidenced in block design, drawing, and other simple constructional tasks. Full details of the tasks and the principal findings are available elsewhere (Brenner and Gillman, 1966). In addition, verbal intelligence was measured with the standard National Foundation for Educational Research Verbal Test I. All testing was carried out by two of us (M. W. B. and S. G.).

A high correlation was found between scores on the visuo-motor test-battery and verbal I.Q. However, the inquiry brought to light 54 children (6.7%) with I.Q. above 90 whose scores on the visuo-motor test-battery deviated more than 1 S.D. from the means established for their I.Q. groups. The performance of these 54 children, who were equally divided between boys and girls, was so poor as to suggest a specific developmental disability. Despite the fact that verbal intelli-

gence was in no case below 90 (and not infrequently above 110), school performance was in general found to be poor, especially in regard to spelling, writing, and arithmetic—though reading was as a rule adequate. The characteristic most frequently remarked on in these children was *clumsiness* in gait, in movement, or in fine motor control. Untidy, careless, and slovenly school work was constantly reported.

In the 31 most seriously affected children the visuo-motor test scores deviated 2 S.D. or more from the mean. Fourteen children in this group who were still resident in the area and who remained available for continued follow-up study over a three-year period form the subject of the present report. Each of these children was matched for age, sex, handedness, verbal I.Q., and home and school background with a child drawn from the same sample who had shown no appreciable discrepancy between verbal I.Q. and the score on the visuo-motor test-battery. The children in both groups, which are termed the experimental and control groups, were retested one year after the initial examination, and their progress at school was followed for two further years. Information regarding previous history was obtained from parents, supplemented in some cases by reports from general practitioners. In interviews with parents and teachers, semi-standard forms of questionnaire were used, and no information was given on whether a particular child had been assigned to the experimental or the control group. All test data were scored by at least two of us independently.

* Psychological Laboratory, University of Cambridge.

† Child Psychiatric Clinic, Cambridge.

Intelligence Test Scores

The children in both groups were tested on the Wechsler Intelligence Scale for Children one year after completion of initial survey. In the experimental group the mean verbal I.Q. was 108.5 and the mean performance I.Q. 94.1. In the control group the mean verbal I.Q. was 110.1 and the mean performance I.Q. 115.6. Thus the discrepancy between verbal and performance I.Q. was 14.4 (V 7 P) in the experimental group and 5.5 (P 7 V) in the control group. This difference is significant at the 1% level (*t* test for small samples).

The marked inferiority of children in the experimental group on non-verbal tasks was shown also on a number of other standard tests which call for the exercise of spatial judgement and manipulative skill. These comprised the draw-a-man test (Goodenough, 1926); the Bender-Gestalt test (Bender, 1938),

both the Pascal and Suttell (1951) and the Koppitz (1964) scoring methods being used; the Stanford-Binet "plan-of-search" subtest (Terman and Merrill, 1937, Form L); a peg-board design test adapted from the Goldenberg Marble Board (Strauss and Kephart, 1955) and including an additional immediate memory test; and a right-left discrimination test (Benton, 1959). The results are shown in Table I. It will be seen that, with the sole exception of the right-left discrimination test, the differences in mean scores between the two groups (Goodenough, 1926; the Bender-Gestalt test (Bender, 1938), are all significant at the 1% level. In the case of the Bender-Koppitz, the scoring system measures number of errors; hence the lower the score the better the performance.

Birth and Medical Histories

The main findings relevant to birth history, previous illnesses, and present condition of the children in the two groups are presented in Table II. It would appear from this information that the children in the experimental group include a considerable number with indications of exposure to a variety of perinatal hazards. There are also definite indications of hyperkinesia, clumsiness, speech defects, or poor motor co-ordination in a high proportion of these children. In the control group, on the other hand, indications of prenatal or perinatal hazard, clumsiness, hyperkinesia, or poor co-ordination are virtually absent.

TABLE I.—Mean Scores and Standard Deviations on Seven Visuo-spatial Tests

Test	Maximum Score	Experimental Group		Control Group		Difference
		Mean	S.D.	Mean	S.D.	
Draw-a-man	25	7.39	3.30	16.25	3.08	8.86*
Bender-Gestalt	30	14.07	3.10	27.79	1.57	13.72*
Bender-Koppitz	25	6.40	2.52	1.50	1.45	-4.90*
Plan-of-search	9	0.79	0.77	2.50	0.82	1.71*
Peg-board design	9	6.21	2.37	8.86	0.11	2.65*
Immediate memory	9	4.08	1.61	8.38	1.33	4.30*
Right-left discrimination	6	4.69	1.54	5.50	0.73	0.81†

* Significant at 1% level. † Not significant.

TABLE II.—Birth and Medical Histories

Subject	Birth History			Medical History	Present Condition
	Maternal		Infant		
	Pregnancy	Labour and Delivery	Neonatal Condition		
Experimental Group					
E 1	Normal	Normal	Restless	No illness	Speech defect. Defective vision. Hyperactive
E 2	"	"	"	Occasional eczema. Whooping-cough (3 yrs). Measles. Mumps. German measles. Chicken-pox	Normal
E 3	"	Breech delivery	Under 5 lb. (2,270 g.)	German measles. Chicken-pox. Mumps. Perforated ear-drum	Slight hearing loss. Hyperactive
E 4	Diabetes	Caesarean section	Restless	Hospital examination for slow development (21 mth). Speech defect	Normal. Slight clumsiness
E 5	Normal	Normal	Rh-negative	Infantile eczema. German measles. Mumps. Chicken-pox	Clumsy
E 6	Previous miscarriage. Toxaemia	"	Restless	Infantile eczema. Severe catarrh	Overweight, grossly clumsy
E 7	Normal	Labour 36 hours	Slightly jaundiced	Mumps. Chicken-pox. German measles. Severe measles (7 yrs)	Slight fine motor incoordination
E 8	"	Induced labour, forceps delivery	Normal	Asthma. Severe measles (4 yrs). Tonsillectomy (5 yrs). Appendicectomy. Pneumonia (6 yrs)	Clumsy, slightly overweight. Emotionally disturbed. Asthmatic
E 9	"	Normal	Restless	Chronic bronchitis. Tonsillectomy (4 yrs). Pneumonia x 3. Antrum surgery (6 yrs)	Peculiar shuffling gait. Defective vision
E 10	"	Premature birth	Under 5 lb. (2,270 g.). Very restless	Infantile asthma. Measles. Mumps. Chicken-pox	Speech defect. Underweight. Undersized
E 11	"	1 month premature	Over 5 lb. (2,270 g.)	Severe infantile bronchitis. Measles. Chicken-pox	Emotionally disturbed
E 12	Unknown	Unknown	14th child, poor home conditions	Unknown (mother deceased)	Normal
E 13	Previous miscarriages	Normal	Rh-negative	Severe measles (4 yrs)	Emotionally disturbed. Clumsy
E 14	Psychological distress	Premature birth. Twins	Elder of twins. Wt. 4 lb. (1,815 g.). Incubator 2 weeks. Frequent vomiting	Fit with high temperature (3 yrs). Severe measles. Mumps. Tonsillectomy (7 yrs)	Undersized. Underweight. Poor motor co-ordination
Control Group					
C 1	Psychological stress. Previous miscarriage	Episiotomy	Normal	No illness	Normal
C 2	Normal	Normal	"	Severe measles (1 yr). German measles. Mumps. Chicken-pox	"
C 3	"	"	"	Bad fall down stairs (15 mths). Measles. Mumps. Chicken-pox	"
C 4	High B.P.	"	"	Cardiac surgery, arterial stricture (5 yrs). Chicken-pox. German measles. Scarlet fever	"
C 5	Normal	"	"	Migraine	"
C 6	"	"	"	Measles. Tonsillectomy (5 yrs). Chicken-pox	"
C 7	"	"	"	Measles. German measles. Mumps	"
C 8	"	"	"	Measles. Mumps. Chicken-pox	"
C 9	High B.P. (chronic)	"	Restless; colicky	Catarrh. Severe measles (2½ yrs)	"
C 10	Normal	"	Normal	Measles. Chicken-pox. Mild whooping-cough. Temporary enuresis due to emotional upset (10 yrs)	"
C 11	"	"	Restless	Measles. Chicken-pox. Mumps	"
C 12	"	"	Normal	Measles. German measles. Chicken-pox. Scarlet fever	"
C 13	"	"	"	Measles. Mumps. Chicken-pox	Emotionally disturbed following death of father
C 14	"	"	"	Pneumonia x 3 (5-6 yrs)	Normal

In their developmental history there was a definite suggestion that the children in the experimental group had been slower in attaining their "milestones" than the control children. Eleven mothers of children in the former group volunteered the information that they thought their children were clumsy or had particularly poor fine motor co-ordination. (Typical comments were: "He'd fall over a match-stick"; "She's absolutely useless with her hands"; "It took him twice as long as it should to learn to ride a bicycle.") Several of these mothers also confessed that their children had been very slow to learn to dress themselves, their greatest difficulty having been in learning to tie shoe-laces or fasten buttons.

Educational Status

Information from school records and interviews with teachers disclosed that only two of the children in the experimental group were thought to have made satisfactory progress at school. In the control group, on the other hand, only two children were thought to have had any difficulties at school.

The school subjects which presented the greatest obstacles to the children with visuo-motor handicap were spelling and arithmetic. In the case of arithmetic, difficulty lay less in connexion with basic principles than with the layout of written work. Handwriting was almost always poor, and two children were backward in reading.

Despite the fact that the two groups were so closely matched for verbal intelligence, only one child with visuo-motor handicap passed the eleven-plus examination, as compared with five children in the control group. Among the failures in the experimental group were a boy with a verbal I.Q. of 137; another, with an I.Q. of 128, refused even to sit the examination because of his anxiety about arithmetic.

As might be expected, the children in the two groups differed greatly with regard to interests and hobbies. In the control group 11 children enjoyed model-making, carpentry, jigsaws, or, in the case of girls, knitting or sewing; in the experimental group, on the other hand, not a single child enjoyed any of these activities. Only one child in the experimental group, as compared with eight children in the control group, was reported to be at all proficient at games.

Ratings by teachers of a number of personality traits revealed marked differences between the two groups. Whereas there was little difference in the case of traits such as concentration or persistence, most children in the experimental group were regarded as clumsy, awkward, untidy, and inept on the sports field. Two were rated as overactive. Most of these children tended to be described by teachers as particularly irritating, difficult, lacking in self-confidence, and unpopular with their peers.

Emotional Adjustment

According to their parents, six children in the experimental group and 12 in the control group were normal or well-adjusted. Seven in the experimental group and two in the control group were said to have shown some behaviour disorder. This was described as severe in three cases, two of which were in the experimental group. At the same time it is noteworthy that only two children, one in each group, had on any occasion been referred to a child-guidance clinic.

Discussion

It is significant that the children with visuo-motor handicap described in this paper were identified not by referral from clinics or hospitals but by screening a supposedly normal school population. Indeed, only one child had ever been referred to a child psychiatric clinic, and then on account of emotional rather than perceptual-motor disability or difficulty in learning.

Yet most of these children had for years been regarded by their parents as abnormally awkward or clumsy, and by their teachers as untidy, difficult, and irritating. In spite of mounting problems at school, none had been referred to the educational psychologist or the child-guidance services.

Somewhat similar cases have been described by Walton, Ellis, and Court (1962) and Gubbay, Ellis, Walton, and Court (1965). Our findings bear out the contention of Gubbay *et al.* that developmental agnosic-apraxic syndromes are a great deal more common than is generally supposed. We can also confirm their allegation that when these disorders are present without obvious neurological signs the children affected seldom receive the understanding and sympathy which might be thought their due. As these authors point out, such children are often accused of laziness or misbehaviour, or suspected of being mentally dull. "The natural outcome is a feeling of frustration, often leading in turn to a behaviour disorder which aggravates the child's problems of learning and performance" (Gubbay *et al.*, 1965).

Though the similarity between developmental and acquired agnosic-apraxic defects should not be overstressed, the resemblance between the visuo-motor difficulties displayed by these children and those of neurological patients with posterior cerebral hemisphere lesions (Critchley, 1953) is too striking to be ignored. Though the element of unilateral neglect is lacking, the failures in spatial judgement and the difficulties in carrying out simple assembly and constructional tasks are almost identical with those displayed by patients exhibiting visuo-spatial agnosia or constructional apraxia. It is also noteworthy that constructional apraxia in adults is often associated with defects in spelling and calculation, which were also noted in our children with visuo-motor handicap. Similar findings in some children with developmental dyslexic syndromes have been described by Kinsbourne and Warrington (1963).

The aetiology of visuo-motor and kindred defects in otherwise healthy children has been discussed by Gubbay *et al.* (1965), who call attention to the not infrequent incidence of minimal signs of pyramidal or cerebellar dysfunction, to mild grades of E.E.G. abnormality (as a rule diffuse though occasionally focal), and to a high incidence of perinatal abnormality. These findings led them to the conclusion that underlying brain damage is responsible in a majority of cases. Though no formal neurological examination could be undertaken in the present inquiry, there was evidence of clumsiness or poor motor co-ordination in 11 children in our group with visuo-motor handicap and of hyperkinesia in two. There was also evidence of perinatal abnormality in at least six cases. It is probable, therefore, that a minimal grade of organic cerebral dysfunction underlies visuo-motor impairment.

It may be urged that a need exists for the early detection and proper management of children who present agnosic-apraxic disabilities of the type described in this paper, irrespective of whether or not they are associated with obvious neurological signs or with educationally more prominent defects such as developmental dyslexia. From an educational point of view, visuo-motor handicap has important implications for academic progress, secondary-school selection, and choice of career; and its relatively high incidence in a "normal" school population should be appreciated by teachers and educational authorities generally. From a psychiatric point of view, early detection and recognition of agnosic-apraxic disorder would do much to allay parental anxiety and to reduce the incidence of consequent psychiatric disturbances. It should be added that research into the degree to which the disability may be overcome, or compensated, by appropriate remedial training is urgently needed.

Summary

A survey of visuo-motor ability in a sample of 810 healthy schoolchildren brought to light 54 cases (6.7%) in which

performance was so deficient as to suggest a specific developmental failure. Fourteen of these children were matched for age, sex, handedness, verbal I.Q., and home and school background with an equal number of children drawn from the same sample who had shown no evidence of selective visuo-motor impairment. Both groups were followed up for a three-year period.

The children with visuo-motor defect were found to be significantly inferior to the controls on a series of tests of spatial judgement and manual skill, to present a variety of educational problems, especially in regard to spelling and arithmetic, and to give evidence of a relatively high incidence of maladjustment. There was also evidence of a relatively high incidence of perinatal abnormality in this group, raising the possibility of minimal early brain damage.

This study supports the contention that agnosic-apraxic disabilities in otherwise normal children are by no means rare and warrant wider recognition.

This work is supported by a grant from the Spastics Society. We wish to express our thanks to the Cambridgeshire County

Education Department and to the many head teachers and others who helped us in the work, not least the children themselves and their parents. Mrs. P. Koskinen gave assistance in testing and Dr. J. L. Gedye helpful advice on the preparation of this paper.

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Effect of Salicylates in Urticaria

MIRIAM MOORE-ROBINSON,* M.D., M.R.C.P.; ROBERT P. WARIN,* M.D., F.R.C.P.

Brit. med. J., 1967, 4, 262-264

The ingestion of aspirin often seems to be responsible for attacks of urticaria and it has been assumed that there is an immunological basis for this effect. However, in the past few years it has been realized that in some patients with chronic urticaria which is apparently unrelated to food or drug allergy an exacerbation may be caused by taking aspirin (Calnan, 1957; Warin, 1960). The purpose of this investigation was to determine the incidence of this phenomenon and whether there are any clinical differences between patients with chronic urticaria who react in this way to aspirin and those who do not. In addition, we wished to discover which part of the aspirin molecule was responsible and whether the effect extends to the physical urticarias and weals induced by intradermal injections of histamine.

Subjects and Methods Used

Patients included in the study were drawn from those routinely seen in the outpatient department at the Bristol General Hospital. Others were referred to us by colleagues and in answer to a circular sent to general practitioners in the area. For the purpose of this study we have defined chronic urticaria as urticaria without an obvious cause which had been present for at least six weeks. All the patients had dermal weals, most of them also had attacks of angioedema. A few who presented with angioedema had had at some time a phase of dermal wealing. A total of 228 patients have been studied. The proportion of males to females was 1:1.7, and ages ranged from 3 to 71 years.

As part of a detailed interview patients were questioned regarding the ingestion of aspirin or aspirin-containing compounds, and any association with an increase in weals. If there was any possibility of exacerbations from this cause an aspirin test was carried out. This was done on a patient-blind basis, and consisted of control inert tablets identical in size, colour, and taste to aspirin labelled "A" and aspirin

tablets labelled "B." The inert tablet was always taken first, as it was felt that if the patients were given the aspirin first and reacted badly to it they would be reluctant to take the second tablet and so invalidate the test. A and B tablets were taken on consecutive days, the dose varying according to the history. Thus if the history were suggestive of an aspirin reaction the initial dose was 300 mg., whereas if the history were less certain it was 600 mg. of aspirin. Any change in the skin and the timing of such a change was noted by the patient. In eight patients the provocation tests were repeated with increasing doses of aspirin. In 21 of the patients who reacted to the test doses these were repeated with sodium salicylate (18 patients) and phenyl salicylate (3 patients) in equivalent molecular doses.

In order to assess the effect on physical urticaria 10 patients with dermographism, five with cholinergic urticaria, and three with cold urticaria were studied. Measurements in all cases were carried out four hours after administration of an inert tablet and later aspirin (300 or 600 mg.). In the dermographic patients a standard method of measurement of the wealing tendency was evolved. A spring-loaded blunt-ended projection which could give known pressure effects of 60, 120, 180, and 240 g. was applied to the volar surface of the forearms in a 3-4 cm. line through a piece of thin metal, cut to admit the projecting point. The width of the weals was measured direct after seven minutes and a graded response to the different pressures obtained. Patients with cholinergic urticaria were exercised for 10 minutes and the amount of wealing was assessed clinically by the patient and the observer. In cold urticaria the size of the weal produced by contact with ice for 10 minutes was difficult to measure and was again assessed clinically. Four patients with urticaria pigmentosa were also studied and weals measured with the same method as used in the dermographic patients before and after aspirin.

In a group of 14 patients comprising four who had reacted to the aspirin test and 10 who had not, the effect of aspirin on induced histamine wealing was decided by measuring the weals produced by intradermal injections of

* The United Bristol Hospitals.

0.05 ml. of 0.0001%, 0.001%, and 0.01% histamine acid phosphate solution on two separate occasions—the first four hours after the control tablets and the second four hours after 600 mg. of aspirin. Weals were measured by first taking a tracing of the weal and then transferring this to millimetre graph paper. An accurate measurement of surface area could be calculated by counting the squares in the outline of the weal.

Results

Out of the 228 patients with chronic urticaria, from the history, there appeared to be a possibility of an exacerbation caused by taking an aspirin-containing compound in 112, and in these the provocative test was carried out. There was no response in any case to the inert tablet, but 50 patients reacted to aspirin. This was usually felt within four hours. Pruritus, often of the lips and eyes, was the first symptom, and was followed by the development of widespread weals, and in many cases swelling of the lips and eyelids. The attack settled in a time varying from a few hours up to four to five days, but a few patients noted that the worsening from one dose of aspirin lasted for several weeks. It was thus shown that aspirin had an exacerbating effect in at least 22% of all the patients with chronic urticaria.

Of the eight patients tested with increasing doses of aspirin, four failed to react at all to 300 mg. of aspirin and had successively worse reactions with 600 and 1,200 mg. In four others the reaction worsened so markedly between 300 and 600 mg. of aspirin that a third dose was not given.

Furthermore, this quantitative effect was supported by clinical observations in other patients who commonly reported that they had taken a single aspirin without effect, but on occasion had ingested a larger dose over a short period—for example, two tablets (600 mg.) four times a day for two days—with the result that their urticaria became worse.

Of the 21 aspirin reactors on whom provocative tests were performed with compounds chemically related to aspirin, 13 out of 18 suffered worsening of their urticaria after sodium salicylate and two out of three after phenyl salicylate.

In the 10 patients with dermatographism the measurement of the weal width was in no case greater after aspirin than after the inert tablets. The weal size in the four cases of cold urticaria did not appear to be larger after aspirin. The five patients with cholinergic urticaria also showed the same degree of wealing after exercise with both the aspirin and inert tablets. Thus no effect of aspirin on these physical urticarias was demonstrated. The four cases of urticaria pigmentosa showed no increase in the width of weal after aspirin as compared with the inert tablets, and none had any general reaction to it.

The 14 patients in whom the effect of aspirin on induced histamine wealing was assessed can be divided into two groups; the first comprising 10 who had not reacted to the test dose of aspirin and in whom the histamine weal size was not different before and after aspirin, and the second com-

prising four who had reacted to aspirin, in whom the histamine weals were significantly larger after aspirin (Tables I and II). Table I shows the weal size in both groups four hours after ingestion of inert tablets. There is no statistical difference between the two sets of figures. Table II shows the same measurement four hours after taking 600 mg. of aspirin. The weal surface area in the four patients who had reacted to aspirin is obviously much greater—($P=0.001$). The reaction to 0.05 ml. of 0.0001% histamine acid phosphate solution was such in all four patients that intradermal tests with higher concentrations of histamine were not attempted.

TABLE II.—Weal Surface Area Measured Four Hours After Ingestion of 600 mg. of Aspirin

0.05 ml. Histamine Acid Phosphate Solution Intradermally	Non-reactors (10 Patients)		Reactors (4 Patients)	
	Actual Areas (sq. mm.)	Mean (S.E.)	Actual Areas (sq. mm.)	Mean (S.E.)
0.0001%	67, 69, 70, 73, 75, 76, 77, 79, 80	74 (± 1.4)	275, 281, 288, 296	285 (± 4.5)
0.001%	173, 177, 181, 184, 186, 186, 187, 189, 193, 194	185 (± 2.1)		
0.01%	285, 286, 288, 292, 295, 301, 305, 306, 306, 306	297 (± 2.8)		

Further clinical observations of the series of patients revealed points of interest. Firstly, there would appear to be no clinical difference or variation in the pattern of urticaria between those patients who react to aspirin and those who do not. There was evidence that the effect of aspirin becomes apparent in a susceptible individual only when several factors are acting at the same time. Patients often mentioned that a head cold, sore throat, gastrointestinal upset, period of anxiety, plus taking a large dose of aspirin exacerbated their urticaria.

The urticarial tendency in patients with chronic urticaria fluctuates in degree, and the severity of an aspirin-induced exacerbation is greater when the wealing tendency is pronounced. Thus patients who have shown a reaction with 300 mg. of aspirin, at a later stage when the wealing tendency was less have had little or no reaction with 600 mg., and in some patients tested when the urticaria had cleared an aspirin effect has been obtained only when doses up to 2,400 mg. of aspirin have been given.

Another interesting clinical association was that of the 50 patients who developed an exacerbation after aspirin four also had exacerbations after both penicillin and antitetanus serum on different occasions.

The series include four families in which successive generations have suffered from chronic urticaria and exacerbations due to aspirin. In one, the mother, who had suffered from chronic urticaria for 17 years, was shown to react to aspirin and sodium salicylate. One of her sons has had urticaria for nine years and is also an aspirin reactor. In one of our youngest patients, aged 4, who has had urticaria since the age of 18 months, wealing is increased after aspirin and also penicillin; her mother and one maternal aunt suffer from chronic urticaria which is severely increased after taking aspirin.

Discussion

It is difficult to understand the mechanism of this weal-exacerbating effect of aspirin in 22% of patients with chronic urticaria. A nonspecific histamine-liberating effect has been suggested, and Hamrin (1957) described a case of a patient with urticaria pigmentosa who developed flushing, vomiting, and collapse after aspirin, and it was considered that this result was due to histamine release. However, we have been unable to repeat these observations in the four patients with urticaria

TABLE I.—Weal Surface Area Measured Four Hours After Ingestion of Inert Tablets

0.05 ml. Histamine Acid Phosphate Solution Intradermally	Non-reactors (10 Patients)		Reactors (4 Patients)	
	Actual Areas (sq. mm.)	Mean (S.E.)	Actual Areas (sq. mm.)	Mean (S.E.)
0.0001%	59, 62, 65, 68, 70, 70, 71, 71, 71, 71	68 (± 1.5)	68, 69, 72, 75	71 (± 1.6)
0.001%	185, 188, 189, 192, 195, 198, 200, 200, 201, 202	195 (± 1.9)	195, 199, 201, 209	201 (± 2.9)
0.01%	274, 276, 278, 280, 281, 283, 285, 288, 292, 293	284 (± 2.0)	284, 289, 296, 307	294 (± 5.0)

pigmentosa, and, moreover, on pharmacological grounds it would be unlikely for aspirin, an acid substance, to have such an action, as most recognized histamine liberators are bases.

Another possibility would be that aspirin was acting as a hapten, forming an antigen when combined with serum proteins. We have no clear evidence against this, but we would have to assume that at least one in five patients who suffered from chronic urticaria would also have such an allergy to aspirin.

That aspirin in some way renders the skin in these patients more sensitive to histamine is suggested by the present report that intradermal histamine weals were larger after aspirin in these patients. In this connexion it is interesting that Juhlin and Rune (1962) have reported that the threshold to 48/80, a known histamine liberator, is lowered in acute urticaria.

It has been stated in the past that aspirin sensitivity is specific to acetylsalicylic acid and does not extend to related compounds. In the present investigations similar reactions were obtained in most patients from sodium salicylate and phenyl salicylate, and it would seem likely that it is the salicylic acid radical which is responsible for aspirin reactivity.

Whatever the underlying cause, it is now established that a point of great practical importance in the management of patients with urticaria is to avoid any administration of salicylates.

The investigation of a patient with chronic urticaria, aspirin reactivity, and jaundice revealed abnormal liver histology described as atypical portal cirrhosis. This finding prompted the investigation of all patients who reacted to aspirin. To date, two other similar cases have been found. It is intended to report later the details of these three cases with the triad of chronic urticaria, aspirin reactivity, and liver disease.

Summary

Aspirin-containing drugs will cause exacerbation in some patients with chronic urticaria. In 112 out of 228 patients with chronic urticaria such a reaction could not be excluded

from the history, and provocative test doses of aspirin were given; 50 patients (22%) developed a well-marked increase in the urticaria. No clinical differences could be observed between the patients who reacted in this way and those who did not.

This action of aspirin is probably due to the salicylic acid radical, as most patients tested have had similar reactions with doses of sodium salicylate and phenyl salicylate.

It has been shown in eight patients that the increase in wealing is proportional to the dose of aspirin administered. In four patients who did not react at all to 300 mg. of aspirin there were successively more severe reactions to 600 and 1,200 mg. In four others the reaction increased so much between 300 and 600 mg. that a larger dose was not given. The quantitative effect is further supported by the clinical observation that some patients have developed exacerbations when large doses of aspirin have been taken and have shown no reaction to isolated small doses.

With appropriate measurements, before and after aspirin, it has been shown that there was no effect on the physical urticarias, including 10 patients with dermatographism, five with exertion urticaria (cholinergic), and three with cold urticaria. Similarly, no effect was demonstrated in the wealing in four patients with urticaria pigmentosa.

It has been demonstrated that induced intradermal histamine weals measured four hours after 600 mg. of aspirin were larger in a group of patients who had reacted to aspirin than in a control group. It is suggested that the mode of action of aspirin in chronic urticaria is by enhancing the effect of histamine in the skin.

This work was carried out with the help of an M.R.C. grant, and we should like to express our thanks for this. We also wish to thank Dr. C. D. Evans, Dr. R. R. M. Harman, and other colleagues who have so kindly referred cases to us. We are grateful to Mr. F. Wellington, Chief Pharmacist, Bristol General Hospital, who gave us invaluable help.

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Clinical Measurement of the Anti-inflammatory Effects of Salicylates in Rheumatoid Arthritis

P. L. BOARDMAN,* M.D., M.R.C.P.; F. DUDLEY HART,* M.D., F.R.C.P.

Brit. med. J., 1967, 4, 264-268

Salicylates in relatively low dosage modify certain components of the inflammatory reaction in animal experiments (Adams and Cobb, 1963). Theoretically they may be used in rheumatoid arthritis to promote the relief of pain or for their anti-inflammatory effect. It is important to determine whether there is a different dose-response relationship for each of these characteristics.

The cardinal signs of inflammation—pain, heat, redness, and swelling—are the indices available for the direct clinical assessment of inflammatory activity in rheumatoid arthritis. Pain is subjective and difficult to quantitate. Joint heat was studied by Smyth and Clark (1957) and by Vaughn, Howell, and Kiem (1959); it was found to be of little value. The latter authors also found redness an unsatisfactory index for assessment. Hart and Clark (1951) introduced the method of standard

jewellers' rings for the measurement of joint size, by which accurate serial recordings could be made.

Fremont-Smith and Bayles (1965) investigated the effect of high dosage of salicylate in 11 patients in hospital with rheumatoid arthritis. Aspirin was given orally in increasing quantity over a five-day period until the largest tolerated dose was reached—on average, 5.2 g./24 hours. In most cases dosage increase was stopped because of tinnitus or deafness. Potent analgesics without anti-inflammatory action were then abruptly substituted. An increase in joint size, measured by standard jewellers' rings, and deterioration of grip strength, symptoms, and other indices followed rapidly the withdrawal of aspirin. They concluded that all patients with active rheumatoid arthritis, whether it was mild or severe, should receive salicylates regularly in the largest tolerated dosage in the absence of obvious contraindications. Because of side-effects "blind" techniques and quantitation of the changes were not attempted.

* Westminster, Hospital, London S.W.1.

A further point requiring critical consideration is whether the rebound deterioration following cessation of treatment is the direct consequence of the withdrawal of an anti-inflammatory agent or whether more complex mechanisms are of significance (Bywaters, 1963).

The aim of this study was to establish a quantitative method for measuring joint size by a technique based on the use of standard jewellers' rings under double-blind controlled conditions, and to differentiate reduction of swelling, an index of anti-inflammatory activity, from pain relief or analgesic effect with various doses of salicylates.

The results of the following four trials are reported: (1) comparison of prednisone with placebo to determine the effect of a known anti-inflammatory agent; (2) comparison of paracetamol with placebo to determine the effect of a known analgesic agent; (3) comparison of high dosage of salicylate with low dosage; and (4) comparison of low dosage of salicylate with placebo.

Material and Methods

Each trial was in the form of a double-blind cross-over comparison. The results were expressed sequentially, preference being based on alteration of joint size during the two periods.

All patients had classical or definite rheumatoid arthritis (American Rheumatism Association, 1959) of at least one year's duration. They were selected from consecutive attenders at the rheumatism clinic provided that they had synovitis of the small joints of the hands and that there was no history of intolerance to the relevant drugs. Only those patients were included in whom it was possible to stop all treatment for 14 days before the trial.

In trial 1 prednisone 7.5 mg. daily was compared with placebo, both being administered as a single evening dose. In trial 2 paracetamol 6 g. daily was compared with placebo; each was administered as three tablets four times daily. In trial 3 high dosage of salicylate was given at 5.3 g. (80 gr.) daily in four equal doses and low dosage at 2.6 g. (40 gr.) daily. In trial 4 low dosage of salicylate, 2.6 g. daily, was compared with placebo.

Each drug was given for seven consecutive days, each trial lasting 14 days. All tablets were taken after food. Salicylate was given in its glycinated form as a single tablet containing 660 mg. (10 gr.). After each treatment period the bottles were collected and the number of tablets remaining was checked.

Patients were interviewed a minimum of four times at weekly intervals in each trial. At the first visit joint size and grip strength were measured. These indices were measured again at the second visit. If the difference in joint size was less than 4 mm. and the overall change of grip strength less than 50 mm. Hg they were regarded as having a stable baseline and the trial was started. In those with greater changes further baseline assessment was made until the indices became stable. At the third visit—the end of the first seven-day trial period—the indices were measured and side-effects recorded, direct questions being avoided. The same programme was followed at the fourth visit, which marked the end of the trial, and the individual preference for either of the treatment periods was noted.

Joint size was measured as the circumference of the proximal interphalangeal joints of the four fingers of each hand, and the distal interphalangeal joint of each thumb—that is, the sum of the circumference measurements of the 10 digits. It was measured by a gauge (Fig. 1), the actual readings being recorded to the nearest millimetre. This gauge was used instead of standard rings, as it is quicker, the result is less likely to be influenced by the frictional state of the skin, and the tension at which it is applied is probably more consistent, particularly

over a tender joint. It is also preferred by the patient. The possibility of error developing at the extreme ranges of the scale because of variation in tension of the plastic spring was considered, but comparison against the rigid standard rings excluded significant inaccuracy. In Fig. 2 the results of 100 pairs of measurements of joint size with the two instruments are plotted. There is good correlation throughout the whole range.

Grip strength was measured for each hand with the cuff inflated to 30 mm. Hg, the result of a single sustained squeeze being recorded.

Joint size was measured before grip strength, or preference was assessed to avoid bias from knowledge of the other indices. The measurements were recorded without knowledge of those obtained at the previous visit.

One observer (P. L. B.) carried out all assessments. Variation between observers may be responsible for differences greater than significant changes in joint size. Table I gives the results obtained by observers in practice and those without previous experience of the method. Each of three observers with previous practice measured the joint size of 10 patients with rheumatoid

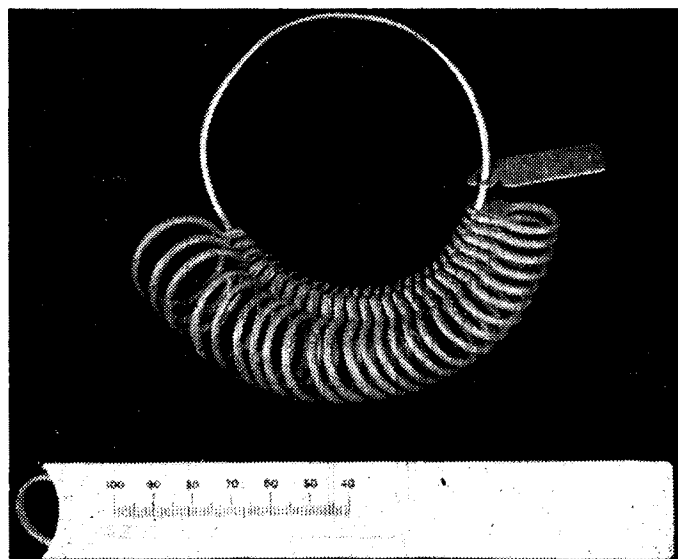


FIG. 1.—Photograph of gauge for measuring joint size in millimetres; standard jeweller's rings are also shown.

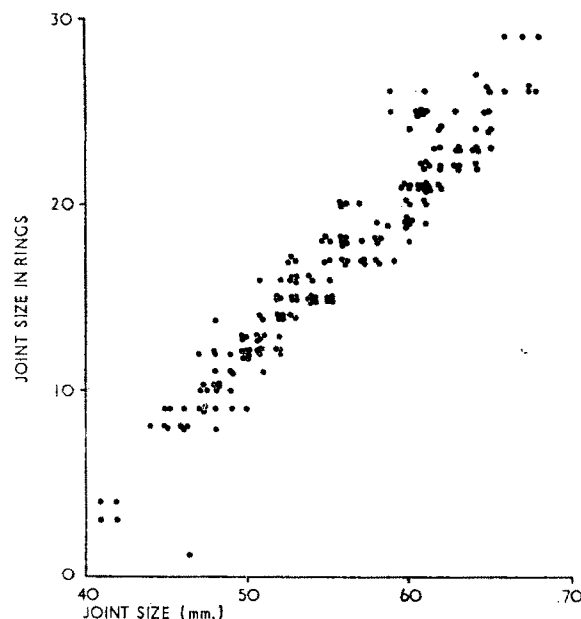


FIG. 2.—Comparison of 100 measurements of joint size made on the gauge with those obtained with standard rings. Coefficient correlation 0.948.

arthritis twice at an interval of an hour. The average difference between the two readings was 3.0 mm. For three observers without previous experience of the method, under similar conditions, the mean difference was 4.5 mm.

All patients were seen at the same time of day. In a group of eight patients in hospital with active rheumatoid arthritis there was an apparent decrease of joint size throughout the day (Fig. 3). The grip strength was greater in the evening than in the morning, the usual diurnal pattern (Wright, 1959), but the difference was not statistically significant.

TABLE I.—Observer Variation. Comparison of Results Obtained by Three Observers with Previous Experience of the Method with Similar Readings made by Three Without Prior Practice

Observer	Difference between Measurements (mm.)	
	With Practice	Without Practice
1	3.0	3.8
2	2.9	5.1
3	3.2	4.6
Mean	3.0	4.5

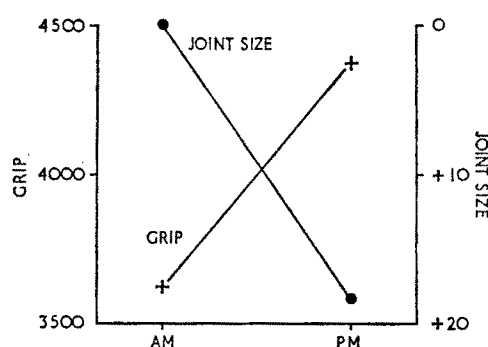


FIG. 3.—Diurnal variation of joint size and grip strength in eight patients with rheumatoid arthritis. Joint size is measured in millimetres (+ indicates improvement). Grip strength is measured in mm. mercury, the sum for each time being plotted.

To express the results sequentially it is necessary to define a significant difference of joint size. In 50 outpatients with rheumatoid arthritis joint size was measured twice at an interval of seven days (Table II). The readings at the beginning and end of the week differed by 3 mm. or less in 42 (84%) of the patients. The mean difference was 2.12 mm. (S.D. 1.4). In eight patients (16%) the difference was 4 mm. or greater. A difference of 4 mm. was therefore arbitrarily assumed to be significant over a seven-day period.

TABLE II.—Significant Difference in Joint Size

Difference in joint size (mm.)	0	1	2	3	4	5
No. of patients	5	15	11	11	6	2

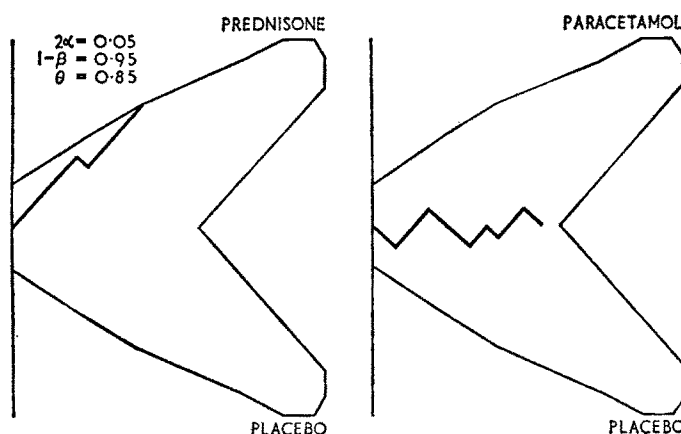


FIG. 4

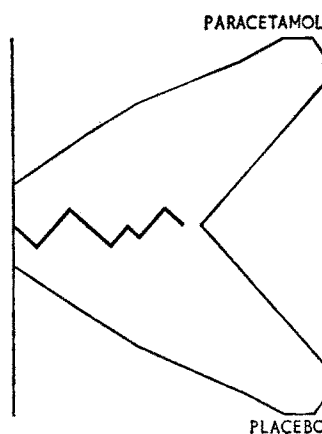


FIG. 5

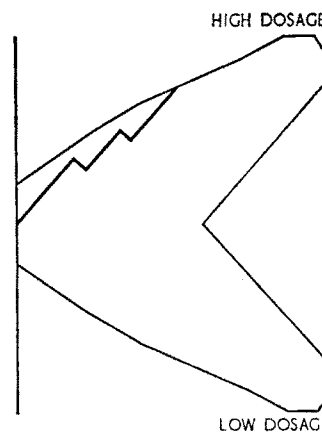


FIG. 6

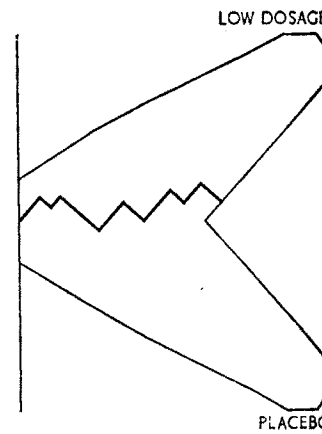


FIG. 7

FIG. 4.—Comparison of joint size on prednisone with placebo. FIG. 5.—Comparison of joint size on paracetamol with placebo. FIG. 6.—Comparison of high dosage of salicylate with low dosage. FIG. 7.—Comparison of low dosage of salicylate with placebo.

Results

Trial 1: Prednisone v. Placebo.—A significant decrease of joint size on prednisone compared with placebo was reached after plotting 11 results (Fig. 4). As there was a difference of less than 4 mm. of joint size in two patients, the total number involved in the trial was 13. There was a significant increase in grip strength on prednisone compared with placebo in those patients in whom there was reduction of swelling. The mean grip strength on prednisone was 379 mm. Hg and on placebo 292 mm. Hg ($t=2.3$; $n=20$; $0.05>P>0.02$). The preference was for prednisone in 8 of the 11 patients, 1 preferred placebo, and 2 found no difference.

Trial 2: Paracetamol v. Placebo.—There was no significant difference of joint size in patients on paracetamol compared with placebo (Fig. 5). Of the 14 fulfilling the criteria for inclusion in the sequential analysis seven had less swelling on paracetamol and seven on placebo. Four patients were excluded from this trial because they had inadequate alteration of joint size. The 14 patients included in the trial had a mean improvement of grip strength from 303 mm. Hg on placebo to 326 mm. Hg on paracetamol. This difference is not significant ($t=0.57$; $n=26$; $P>0.05$). The preference was for paracetamol in six and for placebo in three patients, five finding them to be equally effective.

Trial 3: High Dosage of Salicylate v. Low Dosage.—There was a significant decrease of joint size on high dosage of salicylate compared with low dosage after 14 results were plotted (Fig. 6). In four patients joint size did not change sufficiently for inclusion in the analysis. The mean grip strength was 322 mm. Hg on high dosage compared with 309 mm. Hg on low dosage. This difference is not significant ($t=0.3$; $n=26$; $P>0.05$). The high-dosage regimen was preferred by 11 patients and the low dosage by one, two noting no difference.

Trial 4: Low Dosage of Salicylate v. Placebo.—There was no significant difference in joint size on low dosage compared with placebo (Fig. 7) after 15 results were plotted. In nine patients joint size did not change significantly on either preparation: these were discarded from the analysis. The mean grip strength on low dosage of salicylate was 312 mm. Hg compared with 348 mm. Hg on placebo. In five patients the preference was for low dosage and in three for placebo, seven finding no difference.

Side-effects

In trial 1 two out of 13 patients had subjective reactions on prednisone.

In trial 2 side-effects occurred in 10 out of 18 on paracetamol—generally dyspepsia and drowsiness—compared with three on placebo, all of which were dyspepsia.

High dosage of salicylate (trial 3) was associated with side-effects in six out of 18 patients, the complaint being tinnitus in four and nausea in two. On low dosage giddiness and abdominal distension were each noted once.

In trial 4 four out of 15 had complaints on low dosage of salicylate. These were frequency of micturition (1), giddiness (1), and dyspepsia (2). Placebo was associated with side-effects in three patients, two complaining of depression and one of a hot feeling.

Discussion

Trial 1 illustrates the effect of a known anti-inflammatory agent. Significant reduction of joint swelling is associated with improvement of grip strength and preference for prednisone.

Trial 2 defines the pattern that is obtained from a known analgesic agent without anti-inflammatory action: There is no difference of joint size on paracetamol compared with placebo. Both grip strength and preference suggest that there is some benefit from paracetamol compared with placebo, though neither alters to a statistically significant extent.

These findings suggest that under certain conditions alteration of joint size may be related specifically to reduction of inflammation. Grip strength and preference are less specific indices in that they may also improve after the administration of analgesic agents.

In trial 3 high dosage of salicylate is associated with reduction of joint size when compared with low dosage. The preference is strongly in favour of high dosage. The mean grip strength is better on high dosage, though the change does not reach significant levels.

There is no difference of joint size on low dosage of salicylate compared with placebo, a point shown in trial 4. There is no difference of preference: the grip strength is better on placebo but not to a significant extent.

A possible disadvantage of sequential analysis is the introduction of selection, because experiments in which there is no significant difference are discarded. In our study this is accepted deliberately to exclude the patient who lacks reversible soft-tissue inflammatory swelling. The alteration of joint size that follows the administration of an anti-inflammatory agent is relatively small. It is impossible to determine beforehand which patients possess only irreversible joint swelling. The results obtained from comparative studies of groups are diluted by the presence of patients without reversible inflammatory swelling. Although trends may be demonstrated, this factor may prevent the attainment of statistically significant differences.

It is probable that selection is not of importance in trials such as those reported in this study, in which each patient serves as his own control. The only trial in which a relatively large number were excluded from analysis was the comparison of low dosage of salicylate with placebo, trial 4. The mean age of the 15 patients included was 42 years: 12 were females and three males. The mean age of those excluded was 46 years: six were females and three males.

The trial consisted of two periods, each of seven days. This short duration was chosen to minimize variation due to the natural history of the disease. It was thought preferable to keep the administration of prednisone to a minimum. It was noted in patients studied in hospital that changes in joint size after the administration of rapidly acting anti-inflammatory agents are rapid, often occurring maximally within 48 hours (Hart and Boardman, 1963). In the presence of a limited amount of inflammatory swelling it is possible that any factor promoting improvement is associated with reduction of joint size, provided the period of administration is long enough. In these circumstances differences may be demonstrated more clearly by comparing the rate of change during a limited period.

The use of a cross-over trial may be criticized, because subjects starting on an active agent may have less chance of responding

in the second trial period. Rebound exacerbation after corticosteroid withdrawal may also affect the findings. The results obtained suggest that this is relatively unimportant under these defined conditions. It is unlikely that the order of administration affected the objective measurement of joint size in the three trials involving placebo. In the comparison of high and low dosage of salicylate analysis revealed no pattern of response that might depend on the order of the drugs. In the first week on high dosage improvement of joint size occurred in five out of seven, and in the second week in 7 out of 11. In the first week on low dosage 1 out of 11 improved, and in the second week 1 out of 7. The mean improvement in joint size on high dosage of salicylate in the first period was +5 mm.; in the second period it was +4 mm.

Clinically, joint size may consist of irreversible swelling and potentially reversible disease, the latter including inflammatory oedema, stasis oedema, and vascular dilatation. Irreversible swelling is excluded by the sequential method of analysis. Vascular dilatation is relatively unimportant, as the mean increase of joint size in a group of eight patients with rheumatoid arthritis and in three healthy control subjects after exercise and heat was about 1 mm. for the 10 joints of the hands. The changes in joint size were not the result of the elimination of stasis oedema after increased activity from satisfactory analgesia, because paracetamol alone was not associated with alteration of joint size. The apparent diurnal variation of joint size may be related to immobility during the night. In a further attempt to avoid this factor patients were assessed in the afternoon. The changes of joint size are therefore most likely to reflect alteration in inflammatory swelling.

Side-effects were no problem. It is of interest that drowsiness or dyspepsia occurred in over 50% of those receiving paracetamol. Tinnitus was the main complaint on high dosage of salicylate.

These findings confirm the importance of administering high dosage of salicylates in rheumatoid arthritis, irrespective of symptoms and their severity, if the aim of treatment is the promotion of nonspecific anti-inflammatory action. Relief of pain by low dosage of salicylate appears to be strictly limited and anti-inflammatory activity nonexistent under the conditions defined.

The measurement of joint swelling is accurate under controlled conditions. The response is so small that factors such as observer variation and differences in the time of the day may introduce error greater than the actual response.

In comparative drug trials the unrestricted use of salicylates, to be taken by the patient whenever necessary for supplementary analgesia, affects the results obtained, particularly at high dosage. If the number of tablets ingested by each group is different there may be selective alteration of the criteria of inflammatory activity. The number of tablets ingested in each period is therefore not a satisfactory index of progress. Low dosage of salicylate should be avoided, as it is probable that in combination it affects the response to other agents of indices such as joint size. Jick, Pinals, Ullian, Slone, and Muench (1965), using sequential analysis, showed that the addition of aspirin in small doses (1.5 g. daily) increased the therapeutic efficiency of dexamethasone 0.75 mg. daily to the level of 1.5 mg. daily.

It is suggested that for the assessment of anti-inflammatory effect of rapid onset in patients measurement of joint size under controlled conditions may be used, the results being interpreted by sequential analysis.

Conclusions

Joint size may be measured serially with reasonable accuracy under controlled conditions for the clinical assessment of inflammation in rheumatoid arthritis.

The patient's preference and grip strength indicate improvement on drugs which are anti-inflammatory or analgesic agents; under defined conditions joint size is an index of specific anti-inflammatory effect.

The reduction of joint size by prednisone, an anti-inflammatory agent, is contrasted with the absence of change in paracetamol.

High dosage of salicylate, unlike low dosage, is associated with reduction in joint size.

There is no detectable difference between low dosage of salicylate and placebo in their effect on joint size.

It is suggested that high dosage of salicylate, unlike low dosage, has a clinically measurable anti-inflammatory effect. Suppression of inflammation is desirable in rheumatoid arthritis high dosage of salicylate is indicated independently of symptoms.

Unlimited use of high dosage of salicylate in trials may affect the findings. Low dosage modifies the response if given in combination. Salicylate intake should be eliminated from comparative trials of anti-inflammatory agents.

It is suggested that the plan of this trial provides a simple method for the clinical assessment of the anti-inflammatory properties of a rapidly acting drug.

We wish to thank Dr. Peter Fowler for providing the millimetre gauge for the measurement of joint size; Dr. E. Lewis-Fanning for statistical advice; and Mr. J. A. Baker, chief pharmacist at the hospital, for organizing the provision of tablets suitable for the trials. Our thanks are also due to many members of the unit and to students for assisting in the assessment of error, in particular for the work illustrated in Fig. 2.

The above work formed the basis of a paper read to the Heberden Society in June 1967.

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Glyceryl Trinitrate in Angina Pectoris: Tablet or Aerosol?

G. SANDLER,* M.D., M.R.C.P.; G. A. CLAYTON,† M.B., CH.B.

Brit. med. J., 1967, 4, 268–270

Though many drugs have been used in the symptomatic treatment of angina pectoris almost the only one which has been consistently shown to be of benefit in relieving the myocardial ischaemia is glyceryl trinitrate. In a previous study it was shown to be of considerable value when used prophylactically, but no better than a placebo when given after an attack of anginal pain had developed (Sandler *et al.*, 1963). It has been suggested that this lack of effect of glyceryl trinitrate in relieving established anginal pain might be due to the time it took to dissolve in the mouth (Evans, 1963), so that by then the angina had improved spontaneously. In relation to this possibility the development of an aerosol preparation of glyceryl trinitrate seemed of considerable interest, since such a preparation would be rapidly absorbed in the lungs with more rapid arrival in the myocardium. Preliminary observations (G. G. Gensini, unpublished; A. Black, unpublished) suggested that glyceryl trinitrate aerosol was of value in treating angina, and it was therefore decided to undertake an objective evaluation of the aerosol preparation (Cardamist) in treating angina pectoris and to compare it with the standard tablet trinitrate preparation.

Patients and Methods

Twenty-three patients with well-authenticated and typical attacks of angina pectoris were studied. These subjects, aged from 39 to 69 years, comprised 20 men and 3 women. In all of them the angina had settled down to a stable pattern, and the duration ranged from 3 to 72 months, with attacks occurring from 3 to 40 times weekly. The presumptive cause of the angina was coronary artery disease in all 23, but only four had evidence of previous myocardial infarction.

All the patients were admitted to hospital for a period of six days for the trial, and a daily exercise tolerance was carried out in each of them. The type of test has been described in detail in an earlier publication (Sandler, 1961), and is based on a modification of the Master two-step test, the patient exercising over two steps, each 9 in. (23 cm.) high, until he develops angina or completes 100 circuits over the steps; the test is stopped immediately if significant ischaemic change appears in the electrocardiogram during exercise. In addition to conventional electrocardiography, recording chest lead V5 before and after exercise, the patient is monitored continuously during exercise by means of a radiocardiograph. By this means ischaemic change can be detected immediately, even if unaccompanied by anginal pain, and the exercise terminated (Sandler, 1967). Depression of the ST segment of plane or sagging contour lasting at least 0.08 second, in either the radiocardiogram or the V5, was taken as evidence of myocardial ischaemia (Lloyd-Thomas, 1961; Master and Rosenfeld, 1961; Bellet *et al.*, 1962). Junctional depression, when it occurred, was accepted as significant of ischaemia only when the QX/QT ratio exceeded 50% (Master and Rosenfeld, 1961).

The preparations studied were glyceryl trinitrate aerosol delivering 0.13 mg. of the drug per inhalation—the dose investigated being 0.26 mg. (two inhalations)—an identical placebo aerosol, and standard tablets of 0.5 mg. of glyceryl trinitrate. Study of the aerosol preparations was made on a double-blind basis, and the distribution of active and placebo preparations in each pair of aerosols was randomized. It was not thought necessary to include a placebo tablet with the glyceryl trinitrate tablet, since a previous double-blind study had confirmed the effectiveness of the latter in this type of trial (Sandler *et al.*, 1963). Each of the three preparations—glyceryl trinitrate aerosol, placebo aerosol, and glyceryl trinitrate tablet—was assessed when given both before exercise was

*Consultant Physician, St. Helen Hospital, Barnsley.
†Medical Registrar, St. Helen Hospital, Barnsley.

undertaken and after, so that altogether six exercise-tolerance tests were carried out in each patient, each acting as his own control. Each exercise test was made at the same time in the morning, in the same environment, and with the same medical and technical staff present. To minimize the effects of progressive rest in hospital on the performance of the exercise-tolerance tests, the three preparations were varied in their order of administration in successive patients as they came under trial; this scheme is shown more clearly in Table I. All patients were fully ambulant between the exercise tests.

TABLE I.—Varying Order of Administration of Aerosol Preparations and Glyceryl Trinitrate Tablets to Successive Patients

Patient	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
1	A.1 B/E	A.1 A/E	A.2 B/E	A.2 A/E	Tab B/E	Tab A/E
2	A.1 B/E	A.1 A/E	Tab B/E	Tab A/E	A.2 B/E	A.2 A/E
3	Tab B/E	Tab A/E	A.1 B/E	A.1 A/E	A.2 B/E	A.2 A/E
4	A.1 B/E	A.1 A/E	A.2 B/E	A.2 A/E	Tab B/E	Tab A/E
5	A.1 B/E	A.1 A/E	Tab B/E	Tab A/E	A.2 B/E	A.2 A/E
6	Tab B/E	Tab A/E	A.1 B/E	A.1 A/E	A.2 B/E	A.2 A/E

A.1 = First aerosol
A.2 = Second aerosol
Tab = Glyceryl trinitrate tablet. B/E = Before exercise. A/E = After exercise.

In addition to the inpatient assessment all patients were asked to use the aerosols as outpatients after discharge from hospital, again on a double-blind basis, and were subsequently questioned on several aspects of their use—which of the two aerosols was found more effective, whether the aerosol was better than the glyceryl trinitrate tablets previously used in relieving anginal pain, whether there was any difficulty in using the aerosol in public, and, finally, if any side-effects had been encountered with the aerosols.

Results

Table II shows the mean number of circuits undertaken by the patients with the three preparations. The control observations in this and subsequent tables are those recorded when the drugs were given after exercise had been completed, so that no medication had been taken before the exercise. In addition to calculation of the mean values for the whole group, the differences in individual patients resulting from each of the three preparations have been analysed statistically, so that variation between different subjects was eliminated and any changes produced by the drugs would have become more apparent. In Table II there were no significant differences, either in the mean number of circuits or in the mean change in the number of circuits, between any of the three preparations when given before exercise.

Table III shows the influence of the three preparations given before exercise on the number of patients developing angina, the time taken for the angina to develop, and the duration of

TABLE II.—Mean Number of Circuits and Mean Change with Administration of Active Aerosol, Placebo Aerosol, and Glyceryl Trinitrate Tablets Before Exercise (23 Patients)

	Glyceryl Trinitrate Tablets	Active Aerosol	Placebo Aerosol
Control No. of circuits	80.0	81.5	80.9
Mean No. of circuits with drug	80.9	83.5	83.0
Mean change in No. of circuits	+0.6	+2.0	+2.1

TABLE III.—Incidence, Exercise Time, and Duration of Angina (Mean Values)

	Glyceryl Trinitrate Tablets	Active Aerosol	Placebo Aerosol
No. of patients with angina	8	8	7
Exercise time before angina (sec.)	332.7	350.3	280.9
Duration of angine (sec.)	371.3	339.1	404.0
Change in exercise time	+68.2	+14.5	+64.9
Change in duration of angine	158.9	158.9	218.0

the angina (no control value was available for the duration of angina, since the control observations are those recorded when drugs are given after exercise). No significant differences were apparent between the three preparations in the number of patients developing angina, the time taken for angina to occur, or in the duration of the angina.

Table IV compares the degree of ST depression occurring during exercise in the radiocardiogram and after exercise in both radiocardiogram and V5; it shows the mean values for the different groups and the mean of the changes produced in individual patients by all three different preparations administered before exercise was undertaken. Considering first the changes in the radiocardiogram during exercise, the least ST depression occurred when a tablet of glyceryl trinitrate was given before exercise, and when compared with the mean ST depression after placebo administration before exercise the difference was seen to only just exceed the 5% probability level. Though the mean ST depression following glyceryl trinitrate aerosol before exercise was also less than that with the placebo, the difference was not significant ($0.15 < P < 0.2$). The mean change in ST depression during exercise did not differ significantly between the three preparations. When the changes in the radiocardiogram after exercise are considered there was significantly less depression in the ST segment with glyceryl trinitrate tablets than with the placebo ($P < 0.05$), and again there was no significant difference between the active and placebo aerosols. The changes in V5 after exercise did not show any significant differences between the three preparations.

TABLE IV.—Comparison of Degree of ST Depression in Radiocardiogram and V5

	Glyceryl Trinitrate Tabs		Active Aerosol		Placebo Aerosol	
	No. with Changes	Mean ST Depression (mm.)	No. with Changes	Mean ST Depression (mm.)	No. with Changes	Mean ST Depression (mm.)
Mean ST Depression						
R.C.G. { D/E	11	0.91	12	1.12	11	1.32
V5 { A/E	11	0.59	15	0.87	11	1.08
	8	0.75	14	0.71	13	0.79
Mean of Changes in ST Depression						
	No. of Patients	Mean Change in ST Depression (mm.)	No. of Patients	Mean Change in ST Depression (mm.)	No. of Patients	Mean Change in ST Depression (mm.)
R.C.G. { D/E	19	0	22	+0.02	22	+0.34
V5 { A/E	19	-0.24	23	-0.07	22	+0.18
	22	0	23	+0.05	22	+0.07

D/E = During exercise.

The duration of ST depression in the radiocardiogram and V5 is shown in Table V. When the three drugs were given before exercise no significant differences in the duration of ST depression were apparent between the glyceryl trinitrate either in tablet or in aerosol form, and the placebo. Similarly when the three preparations were given at the end of the exercise neither of the two active preparations significantly influenced the duration of the ST depression compared with the placebo.

Outpatient assessment showed that 10 patients regarded the active aerosol as more effective in relieving anginal pain, 11

TABLE V.—Duration of ST Depression in Radiocardiogram and V5 With Drug Administration Before and After Exercise

	Glyceryl Trinitrate Tablet		Active Aerosol		Placebo Aerosol	
	No. with Changes	Mean Duration ST Depression (sec.)	No. with Changes	Mean Duration ST Depression (sec.)	No. with Changes	Mean Duration ST Depression (sec.)
Drugs { R.C.G.	10	384	15	306	11	344
B/E { V5	8	405	15	490	13	308
Drugs { R.C.G.	11	368	16	317	10	369
A/E { V5	12	365	15	350	13	288

chose the placebo aerosol, while two regarded active and placebo aerosols as equally effective. When asked to compare the aerosol preparation with glyceryl trinitrate tablets five patients thought the active aerosol more effective than the tablets, and seven thought the placebo aerosol the more effective. Only two patients thought that tablets were better than aerosol. The only side-effect encountered with the active aerosols was headache, which occurred in six patients. Only one patient, a woman, thought that use of an aerosol preparation in public was embarrassing.

Discussion

The effectiveness of glyceryl trinitrate in the management of angina pectoris depends primarily on its route of administration. The sublingual route has been found to be most useful clinically (Riseman *et al.*, 1958); for when the drug is swallowed, even in greatly increased doses, it is much less effective and the onset of activity is considerably delayed (Russek *et al.*, 1953; Russek, 1956). The introduction of aerosol administration of glyceryl trinitrate theoretically offers more rapid absorption through the alveolo-capillary membrane, and enables more rapid access to the myocardium and coronary vessels by eliminating the mouth-to-lung circulation time, usually 10 to 12 seconds. In addition, more consistent and concentrated absorption is possible, since sublingual administration may be modified by local oral factors. In a comparative trial of the aerosol and sublingual routes of glyceryl trinitrate administration in 31 anginal patients, A. Black and M. Black (unpublished observations) found that the aerosol gave more rapid relief of angina than the tablets in 27 patients, but assessment was made solely on subjective criteria.

In the present objective study the aerosol preparation given before exercise was no more effective than the placebo aerosol in influencing the amount of exercise possible, the incidence and duration of angina, or the degree and duration of the ischaemic ST depression induced by exercise. On the other hand, sublingual glyceryl trinitrate given before exercise did significantly improve the amount of ST depression occurring both during and after exercise. Though the doses of the aerosol and tablet preparations were not similar, the dose of 0.26 mg. of glyceryl trinitrate in the aerosol form was regarded as a potentially effective dose, since an earlier study had shown that a 0.25-mg. tablet of glyceryl trinitrate favourably influenced exercise-tolerance tests in anginal patients (Sandler *et al.*, 1963). The lack of effect of the aerosol preparation in this study is unlikely to have been associated with defects in absorption from the lungs, since care was taken to exclude any patient with clinical or radiological evidence of pulmonary disease, and the development of headache in six patients using the active aerosol indicates that adequate absorption has occurred, at least in these subjects.

The mode of action of glyceryl trinitrate in angina still remains controversial. Though coronary vasodilatation occurs in normal subjects, doubt has been expressed on whether it develops in atherosclerotic subjects (Gorlin *et al.*, 1959). However, more recent work with radioactive flow techniques and cineangiography has confirmed that coronary vasodilatation can occur in anginal patients (Johnson and Sevelius, 1960; Sones and Shirey, 1962). It is likely, however, that production of coronary vasodilatation by glyceryl trinitrate is beneficial only when the drug is used before exercise, since maximal coronary vasodilatation has probably already occurred when angina has developed owing to release of powerful local vasodilator meta-

bolites by the hypoxic myocardium (Wiggers, 1954; Friedberg, 1966). Gorlin *et al.* (1959) believe that the main benefit of glyceryl trinitrate in angina is due to peripheral pooling in the venocapillary system, leading to a diminished venous return and consequent reduction of cardiac work. The earliest concept of the mechanism of action of glyceryl trinitrate is reduction of cardiac work owing to systemic hypotension (Brunton, 1897), but assessment of blood-pressure changes after glyceryl trinitrate administration, both in the present study and in a previous one (Sandler *et al.*, 1963), has shown that this is an inconstant and very variable factor. It is likely that the beneficial effects of this drug are due to a combination of its two main actions—coronary vasodilatation and reduction of external cardiac work.

Summary

A controlled double-blind objective evaluation of the use of an aerosol preparation of glyceryl trinitrate was made in 23 patients with typical angina pectoris, and the results are compared with a standard 0.5-mg. tablet of glyceryl trinitrate administered sublingually. Assessment was made by exercise-tolerance tests with continuous radiocardiographic monitoring during and after exercise, as well as a conventional pre- and post-exercise electrocardiogram. The dose of aerosol studied was 0.26 mg. delivered in two inhalations, and both aerosol and tablet preparations were assessed before and after exercise.

The active aerosol was no more effective than the placebo aerosol in favourably influencing the amount of exercise performed, the incidence and duration of angina, or the degree and duration of the ischaemic change in the electrocardiogram; these results applied to administration both before and after exercise. On the other hand, glyceryl trinitrate tablets significantly improved ischaemic changes in the electrocardiogram when given before exercise, but not when given after it.

It is concluded that the aerosol preparation of glycerol trinitrate used in the present trial is ineffective, and prophylactic sublingual administration of glyceryl trinitrate tablets still remains the treatment of choice.

We are indebted to Miss A. Swingler and to Mr. B. Bamford for their technical assistance in the electrocardiography. Dr. W. S. Ogden, of Nicholas Laboratories Ltd., kindly supplied the active and placebo aerosols.

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Intravascular Coagulation in a Case of *Clostridium perfringens* Septicaemia: Treatment by Exchange Transfusion and Heparin

M. L. RUBENBERG,* M.D.; L. R. I. BAKER,† M.B., M.R.C.P.; J. A. McBRIDE,‡ M.B., M.R.C.P.
L. H. SEVITT,§ M.B., M.R.C.P.; M. C. BRAIN,|| D.M., M.R.C.P.

Brit. med. J., 1968, 4, 271-274

Clostridium perfringens (*Cl. welchii*) infection following an abortion has always been associated with a very high mortality, often as great as 80% (Toombs and Michaelson, 1928; Hill, 1936; Russell and Roach, 1939; Butler, 1945). Although the use of antibiotics in addition to antitoxin might have been expected to reduce the death rate, the fatality rate recorded by Mahn and Dantuono (1955) differed little from that of previous reports. Immediate hysterectomy (Decker and Hall, 1966), hyperbaric oxygen (Brummelkamp *et al.*, 1963; McAllister *et al.*, 1963; Brummelkamp, 1965), and exchange transfusion (Bessis, 1949; Funck-Brentano *et al.*, 1965) have also been used in treatment. The relative merits of these newer forms of treatment have not yet been clearly established.

The case we report presented with massive intravascular haemolysis and anuria, complicating *Cl. perfringens* septicaemia. It was thought likely that a state of intravascular coagulation was present and that this was being maintained by the release of thromboplastin from toxin-damaged red cells. Therefore, in addition to treatment with antibiotics and antitoxin, an immediate exchange transfusion was performed to remove as many of the damaged red cells as possible, and treatment with heparin was begun so as to stop the intravascular coagulation.

The effect of these measures on intravascular haemolysis, the level of coagulation factors, platelet survival, fibrinogen catabolism, and the level of fibrin degradation products in the serum are presented.

Methods

Routine haematological procedures were carried out as described by Dacie and Lewis (1963). Platelets were counted by the method of Brecher and Cronkite (1950). Platelet survival was measured by using ⁵¹Cr-labelled platelets prepared by the method of Morrison and Baldini (1967). Fibrinogen was estimated by the method of Ratnoff and Menzie (1951). Fibrinogen catabolism was measured, using fibrinogen prepared by the method of Regoeczi and Walton (1967) and iodinated by the ¹³¹I monochloride method of McFarlane (1963). The fractional catabolic rates of fibrinogen and the relative partition of the protein between the intravascular and the extravascular compartments were calculated by the method of Matthews (1957).

Fibrin split products were assayed in the serum by agar-gel immunodiffusion (Ouchterlony, 1958) and by the tanned-red-cell haemagglutination inhibition assay, using rabbit anti-human fibrinogen antiserum (Merskey *et al.*, 1966).

Fibrinolysis was assessed by measurement of plasminogen (Alkjaersig *et al.*, 1959), lysis of fibrin plates (Alkjaersig *et al.*, 1959), and euglobulin lysis time (Nilsson and Olow, 1962).

* Special Fellow, USPHS (NIAMD). Present address: Department of Haematology, Maimonides Hospital of Brooklyn, 4802 10th Avenue, Brooklyn, New York 11219, U.S.A.

† Registrar in Haematology and Medicine.

‡ Senior Registrar in Haematology. In receipt of a grant from Glaxo Ltd.

§ Registrar in Medicine.

|| Lecturer in Haematology; Consultant Physician.

M.R.C. Group for the Study of Haemolytic Mechanisms, Departments of Haematology and Medicine, Royal Postgraduate Medical School, London W.12.

Case Report

A 32-year-old woman was admitted to hospital two days after an attempt to procure an abortion, after 12 weeks of amenorrhoea, by using a solution of Dettol (chloroxylenol sol. 5%) and water. On the day of admission to another hospital, 1 December 1966, she complained of pain in the lower abdomen and back, developed a foul vaginal discharge, and became oliguric. Her temperature was 100.4° F. (38° C.).

Examination of a peripheral blood film and a high vaginal swab stained by Gram's method revealed large Gram-positive encapsulated bacilli, and a heavy growth of *Cl. perfringens* was cultured from both blood and vaginal swab. She was treated immediately with cephaloridine 1 g. six-hourly, as there was a history of penicillin allergy, and gas-gangrene antitoxin 20,000 units intravenously. The next day, 2 December (Day 1), she was pale, jaundiced, and cyanosed, and because of complete anuria was transferred to Hammersmith Hospital.

Clinical Findings.—She was conscious, euphoric, and confused. She was febrile (101° F.; 38.3° C.) and hyperpnoeic (respiratory rate 40). The skin was a striking mahogany colour and the sclerae were yellow. Her nose and fingers were cold and blue, and diffuse magenta-coloured bruises were present on the left side of the neck and at venepuncture sites. The respiratory system was normal on percussion and on auscultation. The pulse was regular (120 per minute), and the jugular venous pressure was not raised. No cardiac murmurs were heard. Blood pressure was 105/55. There was marked lower abdominal tenderness with guarding. Bowel sounds were present. The vagina contained blood and necrotic material. The size of the uterus was felt to be consistent with a 12-week pregnancy. The optic fundi and cranial nerves were normal. Tendon reflexes were present and equal.

Laboratory Investigations.—Haemoglobin 7.2 g./100 ml.; P.C.V. 26%; M.C.H.C. 27%; reticulocytes 1.0%; white cell count 50,000/cu. mm. (segmented neutrophils 57%, non-segmented neutrophils 23%, metamyelocytes 9%, myelocytes 1%, lymphocytes 7%, eosinophils 1%, monocytes 2%); nucleated red blood cells 2 per 100 white cells; platelets 88,000/cu. mm. The peripheral blood film showed striking spherocytosis and microspherocytosis of the red cells, fewer than 20% being normal in appearance (Fig. 1).

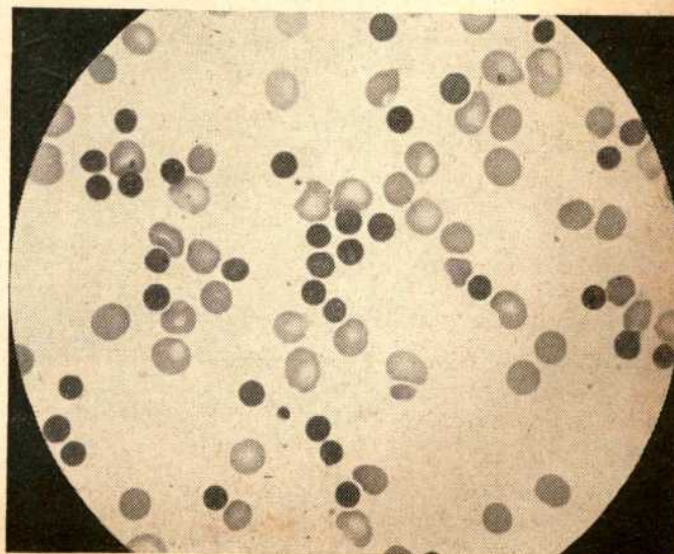


FIG. 1.—Peripheral blood film on admission. (×610.)

Occasional Howell-Jolly bodies were present in red cells. No Gram-positive bacilli were seen. The whole blood clotting-time was 14 minutes. Clot retraction was normal. The plasma fibrinogen was 140 mg./100 ml. The level of factor VIII was 8% of normal. The patient's plasma had antithrombin activity when assayed by serial dilutions of thrombin, and prolonged the thrombin time of normal plasma, indicating the presence of a circulating anticoagulant. No increased fibrinolysis was observed in either whole blood clot or euglobulin clot within five hours, or on a fibrin plate within 18 hours. Plasminogen and activator were present in normal amounts as estimated by use of heated and unheated fibrin plates. Plasminogen was also normal when measured by casein lysis. Fibrin split products were detected in the serum both by immunodiffusion and by the haemagglutination inhibition assay (see Fig. 3). The plasma haemoglobin was 2,200 mg./100 ml. Serum electrolytes: sodium 124, potassium 6.4, chloride 89, and bicarbonate 13 mEq/L; blood urea 122 mg./100 ml.

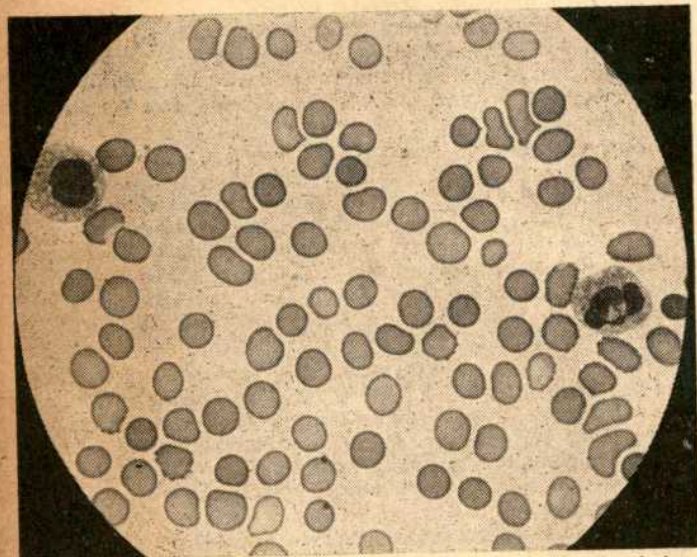


FIG. 2.—Peripheral blood film 10 hours after exchange transfusion. ($\times 610$.)

Progress

Four hours after admission a Scribner shunt was placed between the right radial artery and vein and an exchange transfusion carried out. Nine litres of 18-hour-old bank blood was exchanged within 65 minutes; 2,000 units of heparin, 150 mg. of calcium chloride, and 100 mg. of hydrocortisone were added to each 500 ml. of blood. The central venous pressure and electrocardiogram remained within normal limits, and the blood pressure did not fall below 95/50 during the exchange transfusion.

There was marked improvement in the patient's condition; the mahogany discoloration of the skin was reduced and the nose and fingers became warmer. This was accompanied by a fall in plasma haemoglobin to 320 mg./100 ml., and a reduction in the level of fibrin split products (Fig. 3).

Next morning, 10 hours after the exchange transfusion, the peripheral blood film was nearly normal, with only occasional spherocytes (Fig. 2). The level of factor VIII had risen to 58% of normal, and the level of fibrinogen was 165 mg./100 ml.

Treatment was continued with heparin in a dose of 20,000 units subcutaneously every six hours, erythromycin 300 mg. intramuscularly every six hours, cephaloridine 1 g. intravenously every 12 hours, and gas-gangrene antitoxin 30,000 units intravenously every six hours. Oral fluid and dietary protein were restricted.

Fever subsided within 24 hours of admission. On Day 3 bleeding at injection sites and leakage of blood from the arteriovenous fistula occurred. This was attributed to heparin, and the morning dose was halved and the next dose omitted. Protamine sulphate 100 mg. was given at noon and a second dose of 85 mg. three hours later.

The following morning, 24 hours after stopping heparin and despite giving protamine, the bleeding tendency persisted. The level of fibrin split products had risen again (Fig. 3) and there was a slight fall in fibrinogen concentration. The whole blood clotting-time was 14 minutes and the prothrombin time 14 seconds.

Fibrinogen 7.5 g. was infused and heparin treatment restarted, 20,000 units being given daily by continuous intravenous infusion for the next 10 days. The bleeding lessened, and ceased within three days. The level of fibrin split products fell and the fibrinogen concentration and platelet count rose progressively, to reach peak values at 720 mg./100 ml. on the 10th day and greater than 700,000/cu. mm. on the 28th day respectively (Fig. 4). Haemoglobin levels remained normal and the white cell count returned to normal values within two weeks.

Complete anuria persisted during her first two weeks in hospital. The blood urea was maintained at approximately 100 mg./100 ml. by continuous peritoneal dialysis from Day 3 onwards. During the third week she began to pass small amounts of urine, which increased in volume over the next month to reach a daily output of 350 ml. The blood urea was kept at about 100 mg./100 ml. by peritoneal dialysis at night only.

During the seventh week of her admission she developed signs of consolidation of the lower lobe of the left lung. A heavy growth of *Pseudomonas pyocyanea* was cultured from the sputum. In spite of treatment with gentamicin 20 mg. intramuscularly eight-hourly her condition deteriorated and she died on the 48th day of her admission.

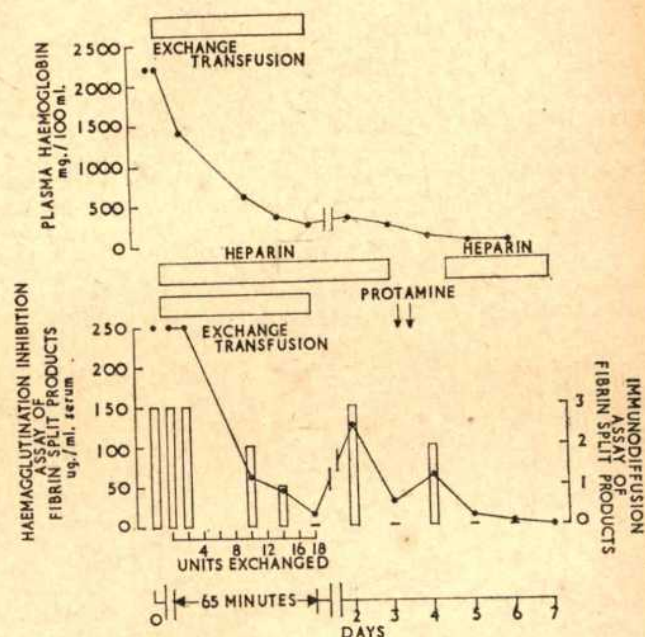


FIG. 3.—Effect of exchange transfusion and heparin treatment on level of plasma haemoglobin and fibrin split products ($\mu\text{g./ml.}$ of immunological reactive fibrinogen).

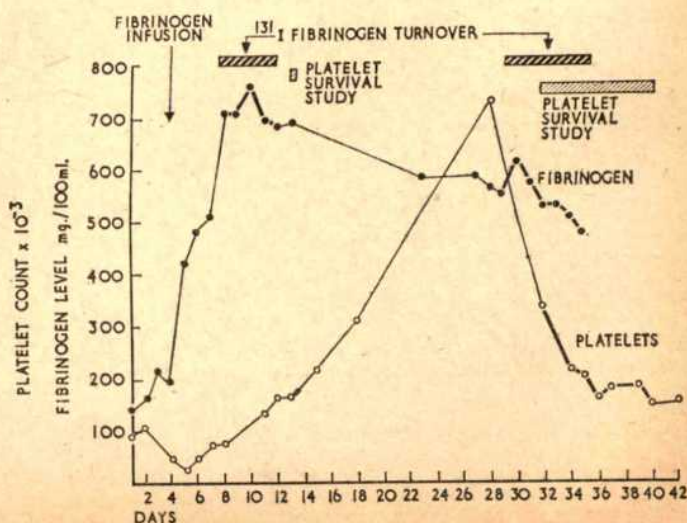


FIG. 4.—Level of plasma fibrinogen and of platelet count during patient's illness. The ^{131}I -fibrinogen and ^{51}Cr -platelet studies are indicated by heavy lines.

Post-mortem Examination

This was performed by the coroner's pathologist, Dr. D. A. Pocock, three days after death. There was a large purulent effusion in the left pleural cavity and pus could be expressed from the consolidated lower lobe of the left lung. There was no evidence of pulmonary infarction. The heart was normal except for minimal hypertrophy of the wall of the right ventricle. The peritoneal cavity showed no abnormality. The liver weighed 400 g. and on microscopical examination revealed fatty infiltration and occasional small areas of recent necrosis. The kidneys weighed 235 and 250 g. Microscopical examination showed severe tubular necrosis with numerous pigmented casts. The tubular epithelium showed signs of regeneration and there was no evidence of cortical necrosis. The uterus and adnexae were normal in size and appearance. Minimal signs of inflammation were found on microscopy. There was no evidence of thrombosis of the veins of the pelvis or lower limbs.

Special Haematological Studies

Fibrinogen Catabolism (Table and Fig. 5).—On Day 4 ^{125} I-labelled fibrinogen from a normal donor was injected. The level of radioactivity fell exponentially during the first four days, despite the rising level of plasma fibrinogen (Fig. 4). The catabolism of fibrinogen has been calculated between Day 8 and 12, when the plasma fibrinogen level was between 695 and 760 mg./100 ml. The half-life was 49.5 hours, and the fractional catabolic rate (the total amount of body fibrinogen catabolized daily expressed as a percentage of intravascular pool) was 46.8%. This represents a catabolic rate of 172 mg. of fibrinogen per kg. body weight per day. No significant amounts of radioactivity could be recovered in a trichloroacetic acid precipitate of peritoneal dialysate. A sample of the same batch of ^{125} I-fibrinogen injected into a normal control subject had a half-life of 114.5 hours and a normal catabolic rate. On Day 29 the ^{125} I-fibrinogen turnover was re-measured with the use of fibrinogen prepared from the patient's own plasma: the half-life was 65 hours and the fractional catabolic rate normal (27.3% per day).

Platelet Survival.—A survival study, using ^{51} Cr-labelled platelets obtained from a normal donor, was carried out on Day 13, when the platelet count was 165,000/cu. mm. All the radioactivity disappeared from the blood within one hour and none was detectable

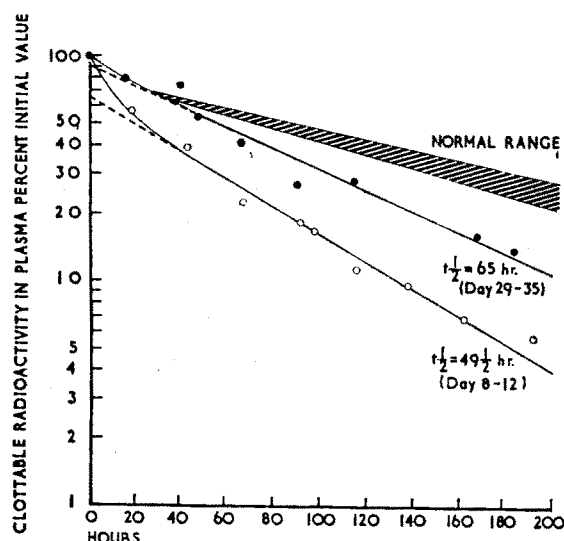


FIG. 5.—Level of ^{125} I-fibrinogen in plasma during the two turnover studies.

^{125} I-fibrinogen Catabolism Calculated by the Method of Matthews (1957). For the First Study (Day 8–12) Fibrinogen was prepared from Plasma Obtained from the Control Subject. For the Second Study (Day 29–35) Fibrinogen was Prepared from Patient's Own Plasma

	Body Weight (Kg.)	Plasma Volume		Plasma Fibrinogen				Catabolic Rate		
				Pool		Half-life (Hr.)	I.V. fraction (%)	% / day	g. / day	mg. / kg. / day
		ml.	ml. / kg.	g.	mg. / kg.					
Patient { Day 8–12	57	3,170	55.6	22.6	396.5	49.5	78.5	46.8	9.8	172
Day 29–35	57	3,258	57.1	18.1	318	65	93.2	27.3	4.9	87
Control	70.6	2,693	38.2	6.6	93	114.5	87	17.0	1.1	16

in the circulation during the next four days. The survival re-estimated by using autologous platelets on Day 32, when patient's platelet count was 350,000/cu. mm. On this occasion mean platelet life-span was 134 hours (normal 192–240 hours).

Discussion

The patient had the classical features of severe clostridial septicaemia: anaemia, haemoglobinaemia, thrombocytopenia, generalized bleeding, and anuria (Isham and Finch, 1956; Muller, 1964; Decker and Hall, 1966).

Haemolytic Effect of Clostridial Alpha Toxin

The haemoglobinaemia was very severe and was associated with marked microspherocytosis of the red cells, probably due to the direct effect of the alpha toxin (lecithinase C) (Macfarlane *et al.*, 1941). Lecithinase C hydrolyses lecithin, a phospholipid component of the red cell membrane. The progressive loss of membrane phospholipid leads to the formation of spherocytes and microspherocytes (Jacob, 1966), possibly by a process of "fragmentation" (Weed and Reed, 1966). Such spherocytes are extremely sensitive to osmotic lysis. Loss of haemoglobin from red cells may also result from holes produced in the red cell membrane by some preparations of *Cl. perfringens* (Dourmashkin and Rosse, 1966). Lecithinase C also causes hydrolysis of platelet phospholipid, producing lysis, without aggregation, and the release of thromboplastin (platelet factor 3) and thrombocytopenia (Furr *et al.*, 1952). Intravascular coagulation will result from the release into the circulation of thromboplastins derived from both the platelets and the damaged red cells (Quick *et al.*, 1954; McKellar and Dacie, 1958; Bradlow, 1961; Rodriguez-Erdmann, 1965).

Evidence for Intravascular Coagulation

The low level of factor VIII and fibrinogen and the low platelet count present on admission indicated the consumption of coagulation factors. Further evidence of the occurrence of intravascular coagulation was the presence in the serum of fibrin split products, formed presumably as the result of fibrinolysis of microthrombi. These fibrin split products were probably also responsible for the antithrombin activity in the plasma (Fletcher *et al.*, 1962). The presence of fibrin split products implies activity of fibrinolysis, but the normal whole blood and euglobulin lysis times and the presence of normal levels of activator and plasminogen suggest that the fibrinolysis was restricted to sites where fibrin had been deposited in blood vessels (Pechet, 1965).

Yet further support for the continuance of a state of intravascular coagulation came from the findings of increased fibrinogen catabolism and shortened platelet life-span. The most striking finding in the ^{125} I-fibrinogen studies was the greatly increased fractional catabolic rate of 46.8% per day in the first study (Day 8–12). This contrasts with our finding of a fractional catabolic rate of $23 \pm 7\%$ per day in 10 control subjects (Baker *et al.*, 1967). In previous reports of fibrinogen catabolism in patients with elevated levels of fibrinogen and in normal control subjects the fractional catabolic rate has been found to be relatively constant, in keeping with the view that fibrinogen is catabolized as a first-order reaction, the amount

catabolized being directly proportional to the size of the fibrinogen pool (McFarlane *et al.*, 1964; Regöeczi *et al.*, 1964). Increases in fractional catabolic rate have been observed, however, in five other patients suspected of having intravascular coagulation (Baker *et al.*, 1967). In the second study (Day 29) an increase in the total amount of fibrinogen catabolized was associated with a normal fractional catabolic rate.

The first ^{51}Cr -platelet survival with use of normal donor platelets on Day 13, when the platelet count was 165,000/cu. mm., was highly unusual in that no circulating ^{51}Cr was detected one hour after injection. We believe this to be a valid observation, since the only previous occasion on which such a rapid rate of removal of platelets has been observed by us was in another patient with intravascular coagulation and only moderate thrombocytopenia (Brain *et al.*, 1967). The second platelet survival study on Day 32 with use of the patient's own platelets gave a nearly normal survival.

Effect of Exchange Transfusion and Heparin

The exchange transfusion resulted in a dramatic fall in the levels both of plasma haemoglobin and of fibrin split products; however, 10 hours later the levels of both had risen substantially. This might have been due to a redistribution of free haemoglobin and fibrin split products between the extravascular and intravascular compartments. Alternatively, the reabsorption into the circulation of tissue-bound alpha toxin might have continued to cause red cell damage despite treatment with antitoxin (Furr *et al.*, 1952). The rise in the level of fibrin split products might have been due to the continuing lysis of capillary microthrombi initially present or continuing to be formed.

A further rise in the level of fibrin split products, but not of plasma haemoglobin, occurred when heparin was stopped and protamine was given to neutralize the circulating heparin. These measures did not correct the bleeding state, and in fact resulted in a prolongation of the Quick one-stage prothrombin time and the whole blood clotting-time, and in the reappearance of a circulating antithrombin. These changes suggest that intravascular coagulation was accelerated when heparin was withdrawn. Reintroduction of heparin on Day 4 resulted in the complete disappearance of fibrin split products within 72 hours. A similar rise in the level of fibrin split products has been reported by Merskey *et al.* (1964), following the withdrawal of heparin given to a patient with disseminated intravascular coagulation. This observation, too, was interpreted as indicating a recurrence or continuance of intravascular coagulation.

The studies in this patient emphasize the importance of recognizing and treating the intravascular coagulation that may accompany clostridial septicaemia, a complication which would not be influenced by treatment with antibiotics and antitoxin. Though the continuing intravascular coagulation may be controlled with heparin, the presence of large numbers of damaged red cells, which would continue to undergo haemolysis and release thromboplastin, suggests that exchange transfusion may play an important part in the management of the initial stages of this serious condition.

Summary

A patient who had *Clostridium perfringens* (*Cl. welchii*) septicaemia following a self-induced abortion developed massive intravascular haemolysis, bleeding, and anuria. Approximately 80% of the red blood cells were spherocytes or microspherocytes. The finding of reduced levels of coagulation factors in the plasma, a low platelet count, and the detection of the products of fibrinolysis (fibrin split products) in the serum indicated the occurrence of disseminated intravascular coagulation. It was thought that this coagulation state

would be maintained by the continued release of thromboplastin from the toxin-damaged red cells.

The patient was therefore given an immediate exchange blood transfusion and heparin in addition to conventional management with antitoxin and antibiotics. The exchange transfusion was shown to remove spherocytic red blood cells, free haemoglobin, and fibrin split products from the circulation; it was followed by dramatic clinical improvement.

Subsequent measurements of serum level of fibrin split products, the turnover of ^{125}I -fibrinogen, and ^{51}Cr -platelet survival suggested that heparin therapy controlled but did not completely prevent the continuation of intravascular coagulation. These studies were repeated during the fourth week, three weeks after heparin had been stopped, and were now normal or nearly so.

The level of blood urea was controlled by peritoneal dialysis, and urine began to be passed in increasing amounts from the third week. The patient, however, developed pneumonia, and, despite treatment with antibiotics, died 48 days after admission.

Exchange transfusion and heparin may play an important part in the management of the initial stages of severe *Cl. perfringens* infections.

We are grateful to Dr. Oliver Wrong for allowing us to study the patient under his care, to Dr. Sheila Worledge for her assistance in obtaining the blood for the emergency exchange transfusion, and to Dr. D. A. Pocock for post-mortem specimens. We are indebted to Professor J. V. Dacie for help in the preparation of this paper, and to Misses Marion Scales and Gillian Bolton for their skilled assistance.

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Comparison of Betamethasone 17-Valerate Ointment with Fluocortolone and Fluocortolone Caproate Ointment

DOWLING D. MUNRO,* M.B., M.R.C.P.; H. T. H. WILSON,† M.D., F.R.C.P.

ELLEN L. RHODES,‡ M.R.C.P., D.C.H.

Brit. med. J., 1967, 4, 275-276

Topical corticosteroids have revolutionized the therapy of many dermatoses. The value to the dermatologist of commercially available preparations reflects many factors, including the cost, potency, therapeutic efficiency, and cosmetic acceptability of the medicaments. Furthermore, since the pharmacology of most corticosteroids is similar, and the newer fluorinated compounds are of high potency, it becomes increasingly difficult for the clinician to assess the value of different preparations on the market.

Clinical impressions resulting from uncontrolled observations can be misleading, but properly conducted double-blind trials avoid the errors arising from bias on the part of the physician or patient. The present investigation compares the value of betamethasone 17-valerate ointment (Betnovate), with fluocortolone and fluocortolone caproate ointment (Ultralanum Plain). It is not intended as a comparison of the value of the constituent steroids or their bases, but as a clinical comparison of the two preparations as marketed in the United Kingdom.

Methods and Materials

Double-blind trial packs were prepared in pairs marked left and right. Betnovate ointment—that is, 0.1% betamethasone 17-valerate—and Ultralanum Plain ointment—that is, a mixture of 0.25% fluocortolone and 0.25% fluocortolone caproate—were randomly allocated to the left and right sides: each tube contained 30 g. of the relevant ointment. Each paired pack was numbered and the code given to the clinicians in sealed envelopes, which remained closed throughout the trial.

Three dermatologists from different centres co-operated in the trial. The same dermatologist saw the patient before and after treatment, and recorded details of the cases on a standard form.

Individuals admitted to the trial were suffering from either eczema or psoriasis and were treated as outpatients. Only those having approximately symmetrical involvement of right and left sides were studied, and there was random selection in so far as all suitable patients referred to the clinics were consecutively included in the trial. Patients were instructed to apply the test ointments twice daily; some, where it was felt to be necessary, were told to occlude affected areas with polyethylene film. Mild sedatives or antihistamines were administered if indicated.

Detailed records of individual patients included name, age, sex, diagnosis, and sites and extent of the disease, together with the history and duration of previous therapy. In the trial the dermatologist's assessment ("objective") and the patient's views ("subjective") of the relative improvement between sides were compared and separately recorded as "healed," "improved,"

"static," or "worse." The dermatologist assessed improvement by observing reduction in erythema, scaling, induration, and oedema of the diseased skin. The patient assessed the changes in itching or other symptoms. The two sides were simply compared, no attempt at quantitative assessment being made. The patients were normally reviewed after seven days, though some were seen more frequently, and a few at slightly longer intervals.

When the investigation on each patient was concluded, the completed form was returned to a co-ordinating secretary, who decoded the results and plotted them consecutively on previously constructed restricted sequential analysis graphs (Armitage, 1960) having a design designated by the factors

$$2\alpha = 0.05, 1 - \beta = 0.95, \theta_1 = 0.85.$$

A total of 109 patients were included in the trial. Of these, 66 had eczema and 43 had psoriasis. Their ages ranged from 6 months to 76 years and the sex ratio was 48 males to 61 females. These two groups were subdivided into those occluded with polyethylene, and those treated without polyethylene. Two patients who were initially included in the trial failed to carry out the instructions given by the clinicians and were therefore excluded from the investigation.

The total numbers treated are shown in the Table. Statistical investigations, by means of restricted sequential analysis, of the results in the first two groups are shown in Fig. 1 (eczema) and Fig. 2 (psoriasis). This method of statistical evaluation excludes patients in whom both sides responded equally ("tied pairs"), but these are shown in the Table.

Comparison of Betamethasone 17-Valerate Ointment with Fluocortolone Caproate Ointment in Treatment of 66 Patients with Eczema and 43 Patients with Psoriasis

	Eczema				Psoriasis			
	Non-occl.		Occluded		Non-occl.		Occluded	
	Phys	Pat	Phys	Pat	Phys	Pat	Phys	Pat
Betamethasone 17-val. superior ..	23	21	14	14	11	10	14	15
Fluocortolone comp. superior ..	5	5	10	7	3	4	3	3
Equally good ..	9	11	5	8	9	9	3	2

Phys = Physician's opinion. Pat = Patient's opinion.

In the eczema group (Table and Fig. 1) betamethasone 17-valerate was shown to be statistically superior at the 5% level in patients treated without occlusion, and the boundary was reached after 30 patients. In patients treated with plastic occlusive dressings the "no significant difference" boundary was reached after 25 patients had been investigated.

In the psoriasis group (Table and Fig. 2) patients treated either with or without polyethylene occlusion responded better to betamethasone 17-valerate ointment than to the fluocortolone compound ointment. The statistically significant boundary at the 5% level was reached after 20 cases were treated with occlusion and 17 cases without occlusion.

The patient's own opinions, also included in the Table, show a remarkable correlation between them and their physicians in

* Research Fellow, St. Mary's Hospital, London W.2; Consultant Dermatologist, Mount Vernon Hospital, Northwood, Middlesex, and Edgware General Hospital, Edgware, Middlesex.

† Consultant Dermatologist, Central Middlesex Hospital, London N.W.10, and Royal Northern Hospital, London N.7.

‡ Consultant Dermatologist, St. Helier and Kingston Group Hospitals, Surrey.

the assessment of response. On the whole, when they differed in their views on which side was most improved, the variation between sides was slight.

Discussion

Under the conditions of the trial betamethasone 17-valerate ointment was impressively better than the fluocortolone preparation in the treatment of psoriasis, whether occluded or not, and in eczema when used without occlusion. In other independent trials—mainly psoriasis treated with occlusion—fluocortolone alone, and also with fluocortolone caproate and clemizole-hexachlorophane, has similarly been shown to be less effective than betamethasone 17-valerate (Sneddon, 1966, 1967). The use of occlusive dressings increases humidity and the temperature of the skin, resulting in increased percutaneous absorption. This tends to mask differences in efficiency of steroid

were not too subtle for the patients to be conscious of them. A multicentred trial such as the present one has the advantage that minor centre-by-centre differences in the objective assessments tend to be corrected. In one centre, investigation of the eczema non-occluded group of cases was continued after the main trial was completed, and showed a similar pattern of significance for betamethasone 17-valerate ointment after 20 cases had been studied.

There are difficulties in assessing statistically the biological response to two drugs, and sequential analysis has disadvantages if the number of "tied pairs" of equal response is large. Variation in the pattern of the graph can occur, depending on the order in which results are plotted. In this investigation the results were plotted strictly according to the date of reaching a conclusion for a particular patient in the trial. If two cases were completed on the same date, then the lower number of the paired packs was plotted first. The advantages of sequential

analysis are that, by prior determination of the limits of the trial, a statistically acceptable assessment is achieved with the minimum number of patients, and that such data can be easily presented.

It should be emphasized that this trial does not compare the active constituents of the two ointments but was specifically designed to compare two commercially available products. The total strengths of the steroid constituents differed as did the bases, the betamethasone 17-valerate preparation being in a soft paraffin and hydrogenated lanolin base, while the fluocortolone preparation was in a soft paraffin aqueous emulsion containing 30% water. One preparation (betamethasone 17-valerate ointment), was superior to the other (fluocortolone

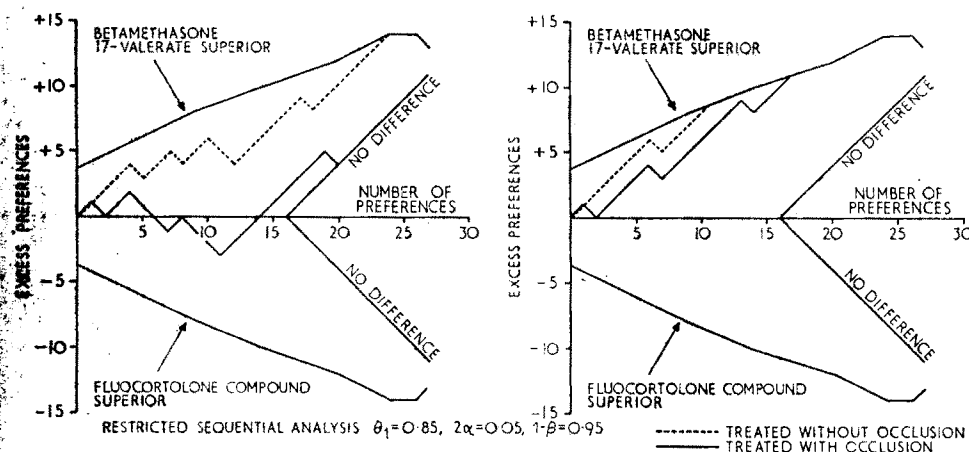


FIG. 1.—Statistical investigation of patients with eczema. FIG. 2.—Statistical investigation of patients with psoriasis.

preparations of different potency (Thomsen, 1966), and was demonstrated in the present trial by the group of patients suffering from eczema and treated with occlusion, in whom the two preparations gave a similar response. Topical corticosteroids when applied in large amounts under occlusive dressings may depress the hypothalamic-pituitary-adrenal axis (Scoggins, 1962; Strange and Hjorth, 1965; Munro *et al.*, 1967). In small quantities, such as were used in this investigation, systemic effects would be minimal.

Psoriasis is more resistant than eczema to treatment with corticosteroids, and even hydrocortisone, which gives little benefit in psoriasis, usually produces considerable improvement in eczema. It would appear, therefore, that response in psoriasis is a more stringent test of the efficacy of a corticosteroid than response in eczema. The superiority of betamethasone 17-valerate ointment in this context is noteworthy. The mechanism of action of corticosteroids on psoriasis is unknown but probably relates to the prolongation of epidermal cell turnover times which has been shown to occur in normal skin treated with a corticosteroid (Munro, 1967). However, from a clinical viewpoint corticosteroids, while useful in some psoriatic cases, are not the treatment of choice in many cases owing to their tendency to relapse when therapy is discontinued—presumably as the result of epidermal cell proliferation returning to the psoriatic pattern.

Differences in the response to the two preparations were slight in many patients, and it had been noted previously that experienced observers tended to record differences which were not obvious to clinicians less accustomed to observing dermatological disease. However, the correlation between objective and subjective findings was good, thus emphasizing that differences

caproate ointment) in three out of the four groups studied, but this does not mean there is no place in the market for the compound that appeared in this short-term trial to be less effective. Individuals respond differently, and some steroid compounds seem to become less effective as treatment continues. The dermatologist is often looking for different potent compounds to use while the natural tendency for the skin to heal is occurring. Both the ointments tested contain powerful corticosteroids and, as such, have their use.

Summary

In a double-blind trial 0.1% betamethasone 17-valerate ointment (Betnovate) has been compared with 0.25% fluocortolone and 0.25% fluocortolone caproate compound ointment (Ultralanum Plain) in the treatment of eczema and psoriasis, with and without polyethylene occlusion. The betamethasone 17-valerate ointment was significantly better than the fluocortolone ointment in patients with eczema treated without occlusion, and in psoriasis, with or without occlusion. No significant difference was demonstrated in cases of eczema treated with the ointments and occluded with polyethylene.

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Medical Memoranda

Unusual Cause of Charcot Joints in Early Adolescence (Riley-Day Syndrome)

Brit. med. J., 1967, 4, 277-278

Familial dysautonomia, a disease almost completely confined to Ashkenazic Jews, was first described by Riley *et al.* (1949). Recently interest has been renewed in searches for the basic defect of this puzzling clinical picture, which as yet remains unknown (Dancis and Smith, 1966; Riley and Moore, 1966). It is known to be transmitted as an autosomal recessive trait, which suggests a single enzyme defect as a possible cause (McKusick *et al.*, 1967).

The characteristic manifestations are not confined to the autonomic nervous system, as the name might imply. Common clinical features are defective lacrimation, which, coupled with corneal hypalgesia, may lead to ulceration of the cornea; relative insensitivity to pain (some children have had fractures set without anaesthesia); defective taste sensation coupled with absence of the fungiform papillae of the tongue (the latter being probably pathognomonic); orthostatic hypotension and paroxysmal hypertension; bouts of unexplained pyrexia; kyphoscoliosis; incoordination and dysarthria; areflexia; emotional lability; defective swallowing; and characteristic responses to certain drugs (Dancis and Smith, 1966). Though the condition is often manifest in the first days of life, the late effects in adolescence may bring the patient to doctors in various specialties. While diminution in pain sensitivity is a well-established phenomenon in this disease, neuropathic joints have not hitherto been described.

CASE HISTORY

The patient, a girl aged 12 years at the time of study, first developed swelling of the left knee at the age of 9 years. She was

born of Jewish parentage (both of Eastern European origin but without known consanguinity), the pregnancy and delivery being uneventful. There is one normal older sib. Feeding difficulties occurred from birth and recurrent fever and respiratory infection were common in the early years of life. The diagnosis of familial dysautonomia was confirmed at 12 months. A moderate degree of incoordination, diminished sensitivity to painful stimuli, and corneal ulceration were all noted.

At the age of 9 years she quite suddenly developed painless swelling of the left knee (due to effusion), which was attributed to trauma, though there was no clear history of this. The knee seemed to be "dislocated," and in subsequent months "gave way on her" repeatedly. The swelling never completely subsided and the knee has remained disorganized and unstable but at all times pain-free. At age 11 years, two years after the initial onset, the right knee became swollen and deformed. Bilateral brace supports were required. A fairly severe degree of kyphoscoliosis had also developed over this period.

Examination of the knees showed bilateral swelling and deformity (Fig. 1) with knock-knee stance (and unsteady gait). There was considerable effusion into the right knee and some degree of lateral mobility with marked instability of the joint and audible crepitus. The left knee was somewhat less swollen but was grossly disorganized,



FIG. 1.—The knees at age 12.



FIG. 2.—X-ray films of right knee at age 11.



FIG. 3

FIG. 4

Figs. 3 and 4.—X-ray films of right knee at age 12.

with hypertrophic changes on the medial aspect of the joint and with shift of the patella laterally.

Neurological examination revealed hypotonia and absent deep tendon reflexes. Cerebellar function appeared intact. Light touch and position sense were normal, but vibration sense was somewhat diminished and pain sensation greatly reduced. Temperature sensation also appeared to be diminished.

Figs. 2-4 show the right knee, the radiological changes in the left knee being similar but less severe. At age 11, soon after the initial symptoms in the right knee, there was considerable destructive change involving principally the lateral aspect of the epiphysis (Fig. 2). A year later (Figs. 3 and 4) soft-tissue calcification and ossification were visible. There was subluxation and irregularity of the femoral condyles. The ossification was compatible with Pelligrini-Stieda fracture, indicating recurrent trauma to the joint.

COMMENT

In attempting near complete ascertainment of cases in the North American continent we (McKusick *et al.*, 1967) have obtained first-hand information on 164 families (200 patients). Among the 60 children examined in detail we have found two further young adults with similar joints—one with a painless, acutely swollen, disorganized knee joint and the other with a painless arthropathy of the shoulder.

Charcot joints occurring before closure of the epiphyses are rather uncommon and present different radiographic findings

from the more usual adult picture. Though most reports of familial dysautonomia have appeared in the American literature, there are three reports in British journals (McKendrick, 1958; Hutchison and Hamilton, 1962; Keith, 1965) and one in Australia (Burke, 1966), and other cases in the United Kingdom are known.

My thanks are due to Professor Victor A. McKusick for his kind encouragement and permission to publish this case.

PETER W. BRUNT,* M.B., M.R.C.P.,
Division of Medical Genetics, Department of Medicine,
Johns Hopkins University, Baltimore, Maryland,
U.S.A.

* In receipt of a Wellcome Trust travel grant.

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Spinal Subarachnoid Haemorrhage in Patient with Coarctation of Aorta

Brit. med. J., 1967, 4, 278-279

Patients with coarctation of the aorta are liable to develop cerebrovascular complications (Woltman and Shelden, 1927; Tyler and Clark, 1958). Intracranial haemorrhage with or without a demonstrable aneurysm occurs in some 12% of untreated cases (Reifenstein *et al.*, 1947). Spinal complications are much rarer (Weenink and Smilde, 1964). They are believed to be due to ischaemia resulting from reduced blood flow to the lower portion of the cord, and from vascular abnormalities associated with the collateral circulation. This paper describes the occurrence of paraplegia after spinal subarachnoid haemorrhage in a patient with coarctation.

CASE REPORT

A 44-year-old woman was admitted to Sydney Hospital in May 1964 with confusion, severe pain between the shoulder blades, and loss of power in the legs.

At the age of 7 she had been known to have a heart murmur, and at 12 had been diagnosed as having "rheumatic carditis," the illness consisting of slight fever, chest pain, occasional involuntary writhing movements, and sore joints. At 14 she had a systolic blood pressure of 180 mm. Hg, for which she was not treated. During her second pregnancy, at the age of 25, she had an episode of loss of consciousness while in hospital for an antepartum haemorrhage. On regaining consciousness she had no neck stiffness or headache and no residual neurological symptoms. She was told that she had had a "cerebral haemorrhage," and caesarean section was carried out with delivery of a normal infant.

At the age of 42 a chest x-ray film taken during a mass survey showed rib notching and an enlarged heart. Clinical examination revealed a blood pressure of 220/90, with femoral pulses greatly diminished in intensity and delayed in comparison with the radial pulses. The second heart sound was increased in intensity, and

a soft systolic murmur was heard at the apex, left sternal border, and between the scapulae. Conservative treatment with guanethidine 50 mg., rauwolfia 4 mg., and bendrofluazide 5 mg. daily was decided on, and she remained well until admission.

On the day of admission she was on the toilet when she felt a strange sensation in the back "as if something were shooting up her spine," and she was unable to get up. She was carried to her bed, and there lost consciousness for several minutes. On arrival at hospital one hour later she was confused and complained of severe pain between the shoulder blades, frontal headache, and inability to move her legs, but had no neck stiffness. On examination the blood pressure was 220/90, with other findings in the cardiovascular system essentially unchanged. There were coarse crepitations at the base of both lungs. Cranial nerves and fundi were normal. Motor power and pain and temperature sensation were lost below the level of T8. Vibration, light touch, and position sense were unimpaired. Knee and ankle jerks were absent bilaterally, as were the plantar reflexes. There was tenderness over T5 and 6. Spine and neck rigidity developed a few hours after admission.

The C.S.F. was grossly blood-stained, with a pressure of 160 mm. of water, a protein content of 154 mg./100 ml., and a glucose content of 35 mg./100 ml. The blood urea nitrogen was 15 mg./100 ml., and the haemoglobin concentration 16.6 g./100 ml. A blood film showed neutrophilia with a white cell count of 26,000/cu. mm. Plain x-ray examination of the abdomen showed no evidence of dissection. Apart from some pulmonary oedema the chest x-ray picture was unchanged. A left carotid angiogram was inconclusive, due to spasm of the anterior cerebral artery, and a right carotid angiogram was normal. A myelogram showed the dye to flow freely to the base of the skull, but in the lower cervical, upper thoracic, and mid-thoracic regions there were numerous filling defects suggestive of grossly dilated vascular structures. The lumbar puncture was repeated three days after admission, the Queckenstedt test showing no transmission of impulses. The C.S.F. was blood-stained with xanthochromia.

Leg power and sensation improved over the next few days, and full voluntary control of the bladder was present. Two weeks after admission the patient had an episode of loss of consciousness lasting five minutes, with masseter spasms and incontinence of urine and faeces. When she regained consciousness she complained of severe back pain; her physical signs were essentially unchanged. The next day a laminectomy performed at levels of T7 to T10 showed

blood-clot filling the subarachnoid space with no abnormality of the cord. One abnormal dilated vessel was found and tied off, and there was no further active haemorrhage.

Postoperatively the pain in the back disappeared, but she could move only her toes and regained no other active movement in the legs. When last seen in 1966 her blood pressure was over 300/120, and there were signs of inadequate blood supply to the legs. She was otherwise well, using a wheel-chair for ambulation.

COMMENT

The aneurysmal dilatations of collateral vessels in coarctation of the aorta are well documented in the literature (Boyd and Werblow, 1937; Cleland *et al.*, 1956). Histologically the walls of these dilated vessels are deficient in muscle and elastic tissue, and in some places they are composed solely of intima and adventitia (Cleland *et al.*, 1956). These changes may affect the spinal arteries as well as other collaterals. Wyburn-Mason (1943) recorded a total of seven cases in which enlarged tortuous spinal arteries with or without local aneurysm formation were found in cases of coarctation. Weenink and Smilde (1964) found a dilated anterior spinal artery at necropsy in a patient who presented with paraplegia of sudden onset.

The combination of spinal subarachnoid haemorrhage and coarctation of the aorta has, to my knowledge, been reported only once before (Wyburn-Mason, 1943). This patient had temporary weakness of one leg after the haemorrhage. Henson and Croft (1956), in their review of spinal subarachnoid haemorrhage, found permanent paraplegia directly due to the haemorrhage to be a rare occurrence.

Paraplegia with loss of pain and temperature and retention of touch and joint position sense is characteristic of the anterior spinal artery syndrome (Peterman *et al.*, 1958; Henneaux, 1960). The mechanism of its production in the above case must remain in doubt. The anterior spinal artery may have been compressed by clot. There may have been arterial spasm (Paulson, 1963), or, most likely, a portion of the cord previously supplied by the ruptured vessel became ischaemic.

My thanks are due to Associate Professor Solomon Posen and Mr. C. R. Letham for allowing me to see the patient and for their continuing interest.

A. B. WATSON, M.B., B.S.,
Resident Medical Officer, Royal Newcastle Hospital,
Newcastle, New South Wales, Australia.

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True Heartburn

Brit. med. J., 1967, **4**, 279-280

Heartburn, while sounding like a pathological description, is a descriptive term common in dyspeptic symptomatology—a symptom that most people experience and one that is not normally regarded with any great apprehension, nor does it carry a connotation of cardiac pathology. However, exceptions occur and the following case is one of them.

CASE REPORT

The patient, a bachelor aged 45 living with his mother, for many years had been a seaman, but during the previous two years had been working as a coffee roaster. On 7 January 1967 while sitting at home with his mother and feeling depressed as a result of delusions of persecution, he placed a poker in the fire and watched it heating until it was red. When he thought that the maximum heat had been generated on the tip of the poker he placed it over his heart and pushed hard. With little or no sensation of pain he observed that the poker passed quite easily into his chest; he felt faint and fell on the floor. His mother summoned the neighbours for assistance, and, as it was seen that, though pale, he was still alive, the ambulance was summoned. He was admitted to the Western Infirmary in the early hours of 8 January.

Observation from a distance showed that the handle of the poker was projecting from the fourth left interspace, about 8 cm. from the midline (Fig. 1). Oscillation of the poker indicated that the heart was beating and the pulse rate was 120 per minute. His blood pressure was 80/50 mm. Hg and he was pale, perspiring, but not in any respiratory embarrassment. On closer observation it was seen that there was a ring of charring around the entrance wound, and that there was little or no haemorrhage. A lateral x-ray film taken with a portable machine confirmed what was already obvious, that the larger portion of the poker was in the left thoracic cavity.

Intravenous infusion was immediately begun and plasma administered, which produced a rise in systolic pressure to 100 mm. Hg. At this point it seemed prudent to explore the left thorax to determine the exact nature of the tissue damage. The chest was opened by an anterolateral incision through the fifth interspace. The lung was found to be collapsed and there was 200-300 ml. of blood in the thoracic cavity.

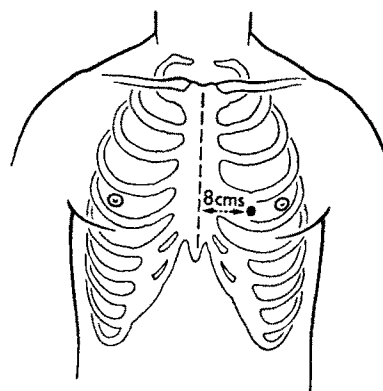


Fig. 1.—Entry wound in fourth left interspace.

Fig. 2 shows how the poker had passed through the pericardial cavity, the tip of the poker resting about 2 cm. from the posterior thoracic wall. There was no evidence of injury to the lung, but both entrance and exit wounds in the pericardium showed evidence of charring, and when the bridge of pericardium was divided it was seen that an area of the left ventricle, 2 by 4 cm., was whitened and clearly had been burnt as the hot poker passed over it. There was no active bleeding, and the poker was withdrawn without causing any further damage. Cardiac action seemed normal, and, as the patient's blood pressure had risen to normal levels after the transfusion of 2 pints (1,140 ml.) of blood, it was decided that no further action should be taken about the burning of the myocardium. As

a result of loss of tissue, the pericardium could not be sutured. A drain was inserted into the thoracic cavity and the thoracotomy wound was closed.

The first two days of his convalescence were marked by persistent hypotension, but tissue perfusion always seemed adequate and urinary secretion was established normally. There was some diminished air entry on the left side, and some evidence of collapse of the left lung. After these two days his convalescence progressed fairly satisfactorily. The main surgical complication of the con-

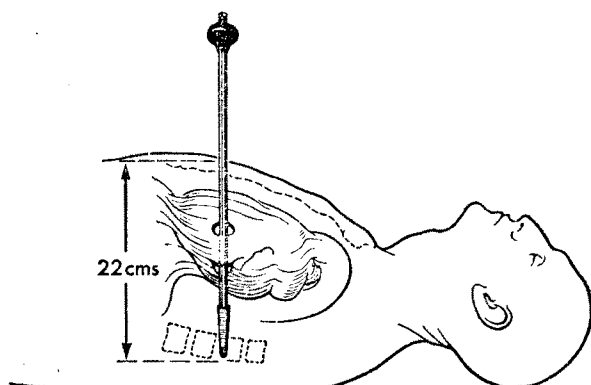


FIG. 2.—Position of poker in left hemithorax.

valescent period was a continued discharge from the front end of the thoracotomy wound, which was due to the establishment of an abscess cavity involving pericardial and thoracic cavities. With drainage this gradually closed, and, though one sinogram showed evidence of a bronchopleural fistula, the cavity closed without further complication.

The electrocardiographic changes were particularly interesting. The first tracings after operation were consistent with a recent anterior myocardial infarction (Fig. 3). Widespread ST elevation was consistent with some degree of pericarditis. The most recent tracings (2 June) showed that ST elevation in anterolateral leads persisted. The absence of Q waves seemed to exclude the possibility of a ventricular aneurysm and screening of the chest also showed no evidence of an aneurysm. His clinical condition was excellent: he had no residual cardiac or respiratory symptoms; the anterior end of his wound had healed; and he had returned to his former occupation. His psychiatric state was investigated and the opinion was that he was suffering from a paranoid psychosis, though his suicidal act had apparently produced a remission in his mental symptoms. During his stay in the ward he was a model patient, and a casual observer would have found no abnormality in his mental attitude. He continued to attend as an outpatient for further psychiatric supervision. He had lost his delusions and acquired a myocardial scar.

COMMENT

There appear to be no references to similar cases in the literature. Rivkin (1963) and Tedeschi and White (1954) both reported on burning injuries to canine hearts in the course of studies designed to find out the damage caused to cardiac musculature by electric defibrillation. The lesions produced are similar to those that could be produced by myocardial infarction, but there seems to be no study determining the long-term behaviour of burnt areas of myocardium. In the present case the assumption is that the patient will behave as one who has had an anterior myocardial infarction. The prog-

nosis should be good, as there is no occlusion of the main coronary vessels and it is likely that the anastomotic circulation is good. E.C.G. tracings do not suggest that the area of necrosis penetrated the full thickness of the myocardium, so it is not likely that he will develop an aneurysm. In a discussion with the patient it was not possible to find out why he chose this particular method of committing suicide except that the

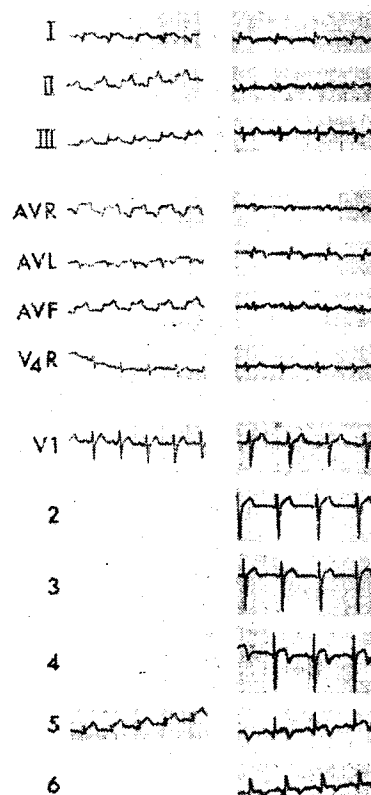


FIG. 3.—Electrocardiographic tracings; left, a day after injury (January 1967); right, six months later (June 1967).

poker was handy; the actual idea of suicide did not occur until the poker was already heated and glowing red.

This case is recorded as the first reported true case of acute heartburn, and also as an example of an avoidable cause of myocardial infarction.

My thanks are due to Dr. Ian Short and Dr. Gerald Timbury for their advice on the medical and psychiatric care of this case, and to the Department of Medical Illustration, Western Infirmary, for the illustrations.

A. D. ROY, M.B., CH.B., F.R.C.S.

Department of Surgery,
Western Infirmary, Glasgow W.1.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Duodenal Ulcer—I

IAIN E. GILLESPIE,* M.D., F.R.C.S.

It is the purpose of this paper to discuss duodenal ulcer under three headings: diagnosis, medical management, and indications for elective operation. The treatment of emergency complications such as perforation and haemorrhage will not be considered.

Diagnosis

Duodenal ulcer continues to be a common disorder in Britain. It still shows a predominance in males, though there is a suggestion that the difference in incidence between the two sexes may not be as great as it was 20 years ago. Reliable data on the overall incidence of peptic ulceration is understandably difficult to acquire in view of the very variable severity and natural course of the disease. If the incidence of perforation is one factor capable of fairly precise measurement, there is evidence¹ that at least in one part of the country there has been a real decrease in the number of such complications in the last ten years. Although several interpretations of this finding are possible, it may be that it reflects a recent change in the incidence of duodenal ulcer, just as there is evidence that the pattern of gastric ulcer, at least in Australia, may also be changing.²

The diagnosis of duodenal ulcer is usually strongly suspected from the clinical history alone. The chief and often sole complaint is of epigastric or right hypochondriac pain or discomfort most frequently experienced when the patient is hungry, and by the time he seeks medical advice he has generally noted that eating a meal affords substantial relief for an hour or two. There may also be recurrence of the upper abdominal pain during the night, and if this causes interruption of sleep the patient often has noticed that drinking a glass of milk or taking a small snack will let him return to his sleep. Vomiting is not as common an occurrence in patients with duodenal ulcer as it is with gastric ulcer, but in a minority of duodenal ulcer patients even without pyloric stenosis some vomiting does from time to time occur. Usually this is of partly digested food or clear gastric juice, and the act of vomiting often brings relief of abdominal discomfort. A few patients may deliberately induce vomiting to obtain such relief. Repeated attacks of copious vomiting, particularly of retained gastric contents, do of course suggest the occurrence of pyloric stenosis.

By the time the patient seeks medical help he has usually experienced several episodes of his pain or discomfort with remissions of variable length intervening. Since a large variety of antacid and other "indigestion" preparations are widely advertised, and readily available, most patients will have tried one or several of such preparations. Most will have experienced at least partial relief from this self-selected medication, and a good proportion will claim that a dose of bicarbonate of soda is as good as anything to ease the pain.

Radiation of the pain through to the back usually occurs only in the most severe relapses of ulcer pain, and this feature is

generally taken to indicate a posterior ulcer irritating or penetrating into the retroperitoneal tissues.

There does not seem to be any particular group of food substances which are regularly blamed for the onset of ulcer dyspepsia. Many patients complain, however, that spicy or greasy foods do bring on their symptoms, though intolerance of such foods seems to be a non-specific feature of most disorders of the upper digestive tract. An individual patient with a duodenal ulcer may relate the somewhat abrupt onset of his symptoms with the ingestion of a particular food substance and therefore believe that it was responsible for the symptoms. However, the variety of foods blamed in this way is so large that no set pattern emerges.

Barium-meal examination will confirm the diagnosis in the majority of cases, and it is reasonable to expect a diagnostic accuracy of over 90%. The largest ulcers will usually be clearly shown directly, and for the remainder the indirect signs of deformity of the duodenal cap, abnormalities of the mucosal pattern, or difficulty in satisfactory filling of the duodenal cap will give the diagnostic indications. It is not an uncommon experience for those clinicians and radiologists who regularly jointly review ulcer patients to find quite gross disparity between the x-ray findings and the severity of the clinical history at the time of the examination. Quite minimal deformity of the duodenal cap may be seen in a patient having severe pain almost incapable of relief by medical measures, while by contrast a large ulcer crater with gross scarring of the duodenal cap is found in a patient having minimal dyspepsia. Because of this variable relation between clinical history and radiological findings, when a patient has convincing symptoms of a duodenal ulcer but an apparently normal barium meal it is reasonable to repeat the examination after an interval of a few months should the symptoms persist. Even with repeated expert radiological examination a few duodenal ulcers may escape x-ray detection and come to light only at a subsequent laparotomy. This is unusual, and is more likely when the ulcer is abnormally situated.

Who Do the Barium Meal?

It might be argued that if the symptoms are quite typical and clear-cut there is no necessity to perform the barium meal. This argument is not valid. It is important to have the x-ray results in all suspect cases for several reasons. Firstly, it is virtually impossible on symptomatology alone to differentiate with any confidence between duodenal and gastric ulcer, and since there are some important differences in the management of the two types of disorder it is essential to know the location of the ulcer. Secondly, the concurrent presence of both duodenal and gastric ulcers is being recognized increasingly frequently, and it is important to detect this. Thirdly, other abnormalities of the upper alimentary tract such as hiatus hernia, congenital abnormalities, or diverticula may be present and have a bearing on treatment.

* Senior Lecturer in Surgery, University of Glasgow.

In most patients the diagnosis is adequately established by barium-meal examination, but a number of further diagnostic aids may be valuable in special circumstances.

Gastroscopy.—Inspection of the gastric lumen by the flexible fibroscope or the direct-viewing gastro-camera is indicated in patients with a strong dyspeptic history and a normal barium-meal examination. The gastroscopic examination may reveal a small undetected gastric ulcer or other gastric lesions but will of course not normally permit direct inspection of the duodenum itself.

Acid Secretion Measurements.—The diagnostic application of these tests is quite limited. Assessment of the maximal acid response to either histamine³ or more recently the synthetic gastrin-like pentapeptide pentagastrin⁴ has replaced other tests of acid secretion. Though the maximal acid response of duodenal ulcer patients is twice that of normal controls there is a very large range of individual values in each group and considerable overlap between the two groups. Thus a high value for the maximal acid response in an individual patient will not clearly establish the diagnosis of duodenal ulcer, but will only make the diagnosis more likely. In return for the high order of close supervision, thoroughness, and time-consuming care which must be expended to obtain reasonably accurate secretory measurements the diagnostic usefulness of these tests is disappointingly small.

Where the clinical history may raise the suspicion of the very rare Zollinger-Ellison syndrome (unusually severe ulcer dyspepsia, multiple ulcers on radiological examination, and/or severe watery diarrhoea), comparison of the unstimulated gastric acid secretion with that obtained after maximal stimulation with histamine or pentagastrin may add considerable support to the diagnosis. In this condition it is characteristic, though not invariable, to find a very large output of acid in the unstimulated phase as a result of the continuously large production of the gastrin-like secretagogue from the pancreatic tumour, and the additional administration of a "maximal" dose of histamine or pentagastrin does not bring about much further increase in the gastric acid secretion.

There has been much interest in the relationship between peptic ulceration and blood group distribution. The present position, recently reviewed by Langman,⁵ may be briefly summarized as follows. Both duodenal and gastric ulcers are more likely to occur in persons belonging to blood group O, particularly if they are incapable of secreting the blood group substances in their mucus secretion. The increased risk of these group O non-secretors, though statistically significant, is relatively slight, and a knowledge of the blood group and secretor status of an individual patient with duodenal ulcer does not at present help in establishing the diagnosis or in planning the clinical management.

Medical Management

Most duodenal ulcer patients are treated in the first instance by conservative measures: advice regarding diet, drugs for symptomatic relief—such as alkalis, anticholinergic drugs, and sedatives, and some advice regarding the general pattern of daily life, work routine, and social activities.

Diet

Traditionally patients have been advised to restrict their dietary intake to "bland" constituents with a predominance of milk, milk-containing foods, and carbohydrates. In the past quite detailed restrictions have been advocated, such as milk and fish for prolonged periods. There is no good evidence that such strict limitation of diet is of any real value in achieving symptomatic relief or in preventing further relapses. Detailed advice should not be given on foods to be preferred or avoided. Many patients find it difficult if not impossible to stick to a grossly limited diet during a normal day. The patient should

be told simply to avoid any particular items which have regularly caused a bout of dyspepsia. Foods which are highly seasoned should probably be avoided, as many spices are known to have a local irritant action on the gastric mucosa, unless the patient is inordinately fond of them and has found that he can eat them without any discomfort.

Since nearly every duodenal ulcer patient finds that a drink of milk will give prompt relief of the ulcer pain, an increased intake of milk or milk-containing drinks spaced frequently throughout the day is often recommended. However, there is no real evidence that milk is better than other substances in neutralizing gastric acid or in any other way. The patient with a duodenal ulcer may be advised to take extra milk if he likes it, with and between meals, but there seems no justification in insisting that those patients who strongly dislike milk should take it.

Timing of Meals

The timing of meals is probably much more important than the actual food. Lennard-Jones and Babouris⁶ have shown that there is much less fluctuation in intragastric pH when a diet of the patient's own selection is fed at two-hourly intervals as compared with four-hourly. Translated into practical terms this means that the patient should be urged to have a mid-morning and mid-afternoon snack in addition to the three main meals, and that he should also have something to eat in the middle of the evening and last thing at night before retiring to bed. Sometimes the patient's occupation makes this regimen difficult, but it is generally possible to persuade him to carry some packaged food with him and to take this at the appropriate times.

For how long should such a diet pattern be followed? There is unfortunately no clear-cut guide on this question, but it is probably unnecessary to prolong it beyond a few weeks after complete remission has occurred. A gradual return could then be made to normal spacing. The patient should be told that it is unwise for him to miss a meal or go for much longer than three to four hours without something to eat.

This advice is likely to lead to an increase in weight, and on occasions to gross obesity. Fortunately patients with duodenal ulcer on average tend to be a bit underweight, and the weight gained as a result of the dietary measures may not always pose too much of a problem.

What advice should be given about the taking of alcohol? Alcohol is known to stimulate the gastric secretion of acid, and it is also known that excessive quantities of ingested alcohol can cause a diffuse gastritis. It is doubtful whether it is necessary to forbid the taking of alcohol altogether, but patients should avoid spirits and should not take any alcohol when fasting.

Drugs

Alkalis.—Most patients find that one or other of the very numerous alkaline preparations available will give effective symptomatic relief. Perhaps the most popular remedies contain aluminium hydroxide, phosphate, silicate, or glycinate, magnesium trisilicate, hydroxide, or carbonate, calcium carbonate, or bismuth aluminate. It is common clinical experience that though some preparations enjoy a fairly wide popularity among duodenal ulcer patients there is considerable variation in the apparent effectiveness of different drugs and mixtures from one individual to another. Again it is often found that whereas one alkaline preparation will regularly afford relief for months or years it may eventually lose in usefulness and the patient will switch to another preparation which apparently then proves superior. This in turn through time may eventually be superseded by yet another antacid, and yet all three

preparations might have virtually the same capacity to neutralize acids. It is often surprising how rapid and prolonged is the relief obtained from a relatively small dose of an alkaline preparation, a dose which would be able to neutralize only a very small quantity of acid. It seems that the symptomatic relief afforded by alkalis is not solely explained by their acid-neutralizing properties, since the quantities theoretically required to keep the stomach contents at an alkaline pH for prolonged periods throughout the day are many times the doses normally taken by duodenal ulcer patients.

Since the aim of giving antacid preparations is simply to give temporary symptomatic relief and not to secure continuous acid neutralization, the alkali should be taken by the patient only as and when required for relief of pain. There seems no virtue in taking doses regularly throughout the day at set times or in relation to meals, and there is no justification for giving alkalis during a period of remission in the hope that they will minimize the chance of recurrence of symptoms.

To some extent side-effects will dictate the choice of an antacid preparation. Those containing magnesium tend to cause mild diarrhoea, whereas aluminium hydroxide may have the opposite effect. If taken in very large dosage calcium carbonate and bicarbonate and sodium bicarbonate may cause alkalosis.

Anticholinergic Drugs.—Though not so popular as alkalis anticholinergic drugs are also widely used in the symptomatic treatment of ulcer dyspepsia. If given in adequate dosage it can be shown that such drugs will both reduce gastric acid and pepsin secretion and also diminish gastric motility. For this last reason the anticholinergic drugs have often been referred to as "antispasmodics," there being a belief that muscular spasms may cause or contribute to duodenal ulcer pain. Among the most commonly prescribed anticholinergic agents are atropine and hyoscine and their derivatives, poldine, propanthelene, dicyclomine, and glycopyrrolate. It is probably fair to say that such agents are not as commonly effective as the antacid preparations, but a proportion of patients do find anticholinergic drugs completely effective in obtaining prompt relief. This variation in the usefulness of different symptomatic remedies may reflect individual variation in the mechanism of ulcer pain.

There is evidence⁸ that anticholinergic drugs should be given in maximal tolerable dose in order to obtain significant relief of symptoms. Dryness of the mouth, blurring of vision, and occasionally difficulty in emptying the bladder may occur if excessive dosage is taken, and it may not always be possible to obtain satisfactory relief of the dyspeptic symptoms with a dose which does not cause these unpleasant, and at times risky, side-effects.

Sedatives.—The idea behind giving sedation to patients with duodenal ulcer arose from the concept that patients with this disorder were unduly prone to worry excessively, to be over-active, agitated, and introspective, and that this pattern was in some way causally related to their duodenal ulcer. It was also argued that, since a period of rest in bed would virtually always result in the disappearance of even the most severe ulcer symptoms, sedation might go at least some way towards achieving a more tranquil background for the patient and so encourage the healing of his ulcer. Small doses of sedatives, notably phenobarbitone, are commonly added to proprietary antacid preparations. There is, however, no good evidence that sedatives improve the chances of obtaining satisfactory remission or prevent further symptoms. However, such drugs may be useful in a selected minority of patients displaying marked nervous excitability.

Over the years the effect of oestrogens has been noted in the duodenal ulcer, following the reasoning that the lower incidence of duodenal ulcer in females might be due to the sex hormone might protect against the disease. Truelove⁹ in a carefully controlled trial of 0.5 mg. b.d. exerted a

beneficial effect on the symptom course and on healing rates in men with duodenal ulcers. Unfortunately, as might be expected, a relatively high incidence of feminizing side-effects weighed heavily against widespread use of such treatment. A few further recent attempts have been made to evaluate oestrogen preparations with less feminizing side-effects, but results have been inconclusive. While further evaluation is awaited with interest, there seems no indication at present for oestrogen therapy in the routine management of duodenal ulcer patients.

Carbenoxolone.—Carbenoxolone is an anti-inflammatory agent isolated from liquorice extract, and a variety of similar preparations have been used for many years in the medical management of peptic ulceration. While there is some evidence that carbenoxolone may facilitate the healing of gastric ulcer in ambulant patients, there is at present no indication that it exerts a favourable influence in duodenal ulcer. Most liquorice preparations, including carbenoxolone, cause retention of water and sodium when given in moderate or high doses, a property incidentally shared by oestrogens. It may well be that this fluid-retaining property is an essential aspect to the therapeutic value of these drugs.

Anti-pepsin Agents.—A number of agents have been found to inhibit the proteolytic enzyme action of pepsin under laboratory conditions. However, to date none has been shown to perform this role satisfactorily *in vivo*, and such a therapeutic approach is not promising.

General Aspects

Rest.—It is common experience that peptic ulcer symptoms rapidly remit when the patient is put to bed. Whether the physical inactivity or the isolation from "stresses" of occupational, social, domestic, and other responsibilities is the more important factor is uncertain. Whereas it is not always practical or indeed possible for a patient in relapse of duodenal ulcer symptoms to take to bed, it is on occasion worthwhile advice to a patient who is having increasingly severe pain which proves intractable to other measures. The response of symptoms to a short period of bed rest is also sometimes used to determine whether the pain is genuinely due to duodenal ulcer or some other lesion. If the pain does not subside when the patient is confined to bed this is usually taken as an indication that the pain is not due to peptic ulceration. While this is not an absolute rule it is often a useful guide.

Psychological Factors.—The importance of psychological factors in the aetiology and natural course of duodenal ulcer remains uncertain and controversial. Opinions vary from the extremes of the belief that virtually all peptic ulcers are the expression of emotive disorder and conflict, to the view that any expressions of reaction or behaviour abnormalities are the consequences of the peptic ulcer state. The compromise view is that psychic disturbance is of importance in a proportion of patients only. Many clinicians can readily recall patients whose symptoms regularly flared up on exposure to a particular emotional problem and promptly settled once more on the problem being overcome. Where such factors can be clearly recognized it may be possible to help the patient avoid exposure to the precipitating factors by some simple commonsense advice, or to modify the patient's reaction to the particular circumstance by enlisting the aid of the professional psychotherapist. In many instances, however, though there may be aggravating work or social factors, it may be quite impractical to alter the situation.

Smoking.—There are many good reasons for advising a cigarette smoker to give up the habit, and these apply no less in the duodenal ulcer patient than in any others. Doll, Jones, and Pygott¹⁰ showed in 1958 that stopping smoking accelerated the healing of gastric ulcer. There is still a surprising lack

of information on the effects of cigarette smoking on the course of duodenal ulcer. At present, therefore, any advice to stop smoking is based on general grounds.

Gastric Freezing.—The initial enthusiasm for gastric mucosal freezing has not been sustained. Clinical experience with this technique has been reviewed by Forrest,¹¹ who concludes that there is no place for this method of treatment in the management of chronic duodenal ulcer at the present day.

(This article will be concluded next week with an account of the surgical management of duodenal ulcer together with a list of references.)

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Analgesics and Monoamine-oxidase Inhibitors

Q.—What untoward reactions may occur when analgesic drugs are given to patients who have been taking a monoamine-oxidase inhibitor drug? How may severe pain of acute onset be treated in such patients?

A.—There have been a number of reports of untoward reactions when analgesics have been given to patients who were receiving monoamine-oxidase inhibitors such as iproniazid, phenelzine, nialamide, pargyline, and tranlylcypromine.¹⁻³ In most of the reported cases the analgesic concerned has been pethidine.

The more alarming type of reaction occurs within minutes of the administration of pethidine. The patient becomes restless, even violent, with twitching of muscles, sweating, cyanosis, hypertension, increased tendon reflexes, extensor plantar responses, and Cheyne-Stokes respiration. In some cases, however, the narcotic and hypotensive effects of pethidine are potentiated, and the patient has a prolonged period of unconsciousness with hypotension.⁴ In at least three cases death has been attributed to the interaction of the two drugs.⁵

An additional hazard concerns the administration of compound preparations which contain both an analgesic drug and a sympathomimetic drug such as amphetamine or one of its derivatives. The Committee on the Safety of Drugs issued a warning,⁶ directed particularly to dentists, about the dangers of using these preparations in patients who have been taking monoamine-oxidase inhibitors.

Therefore for the treatment of severe acute pain in a patient who is known to be receiving or to have recently had a monoamine-oxidase inhibitor both pethidine and compound preparations containing sympathomimetic agents should be avoided. Other narcotic analgesics may be used with caution. Morphine has been given without untoward effect to a patient who subsequently had an alarming reaction to pethidine.¹ The smallest therapeutic dose should be used and the patient watched carefully for 15 to 20 minutes after the analgesic has been given. If nothing untoward happens within this time an acute reaction is unlikely, but the patient may have a more prolonged sedative response than is usual. Should an acute

reaction occur prednisolone 25 mg. should be given intravenously. The other measure which has been recommended is the prompt acidification of the urine to increase the elimination of pethidine. The action of ammonium chloride given orally is too slow for this purpose, and the intravenous administration of sodium acid phosphate or lysine or arginine hydrochloride is suggested.⁵

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Inheritance of Ankylosing Spondylitis

Q.—What are the chances of a man affected with ankylosing spondylitis having a child who will also be affected?

A.—Ankylosing spondylitis has a multifactorial aetiology, and shows a definite concentration within families. There are not enough empirical data to give a risk for the children of affected males, but data from sibs¹⁻³ indicate that the risk will be of the order of 3%, whereas the incidence in the general population is of the order of 0.5 per 1,000. The risk is likely to be higher for sons than for daughters, and higher when the mother (and not, as in this case, the father) is the affected parent.

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Antidepressant Drugs and Muscular Weakness

Q.—Imipramine given for depression in a case of progressive muscular atrophy seems to increase the muscle weakness. Which group of antidepressants are least likely to affect muscle power in these cases?

A.—Muscular weakness is recognized as a side-effect which may occur in some patients treated with imipramine or other antides-

sant drugs of the dibenzepine (tricyclic) group such as amitriptyline. It is not therefore surprising that a patient with progressive muscular atrophy should respond in this way. One of the other drugs which have antidepressant properties, such as phenelzine (a monoamine-oxidase inhibitor) or a small dose of amphetamine (a sympathomimetic drug), might be tried, but it may be questioned whether in this case the use of antidepressant drugs is the correct approach to the problem. Presumably the patient's depression is secondary to his organic disease, and the response to antidepressant drugs in such cases is not likely to be as favourable as in endogenous depression.

Notes and Comments

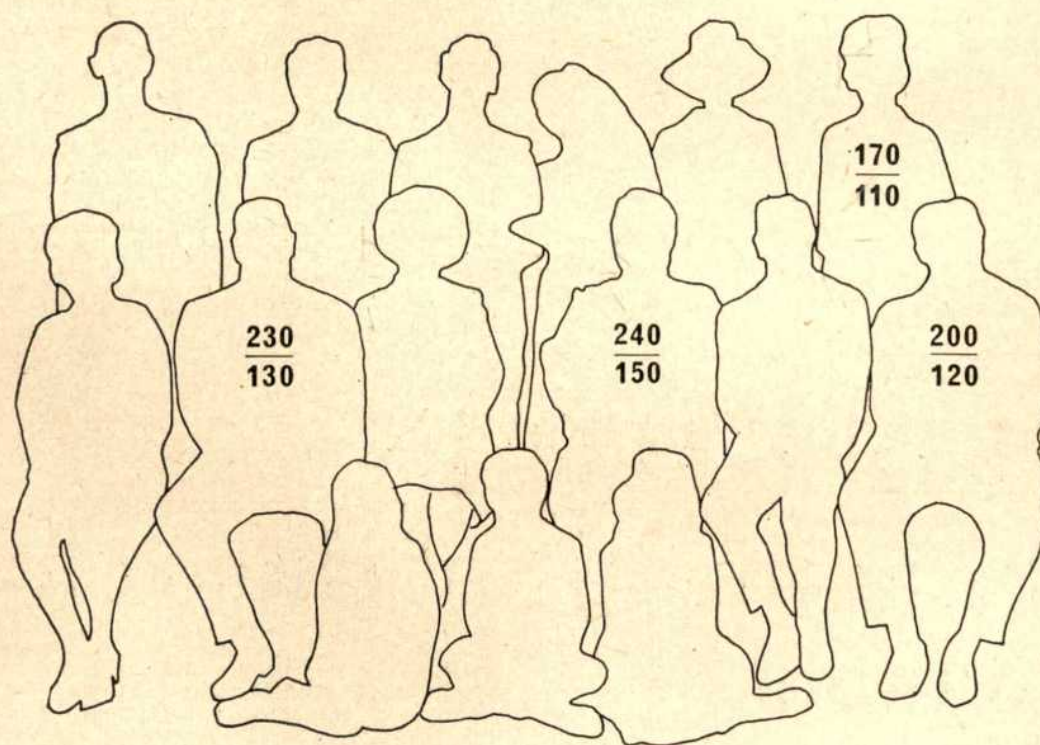
Treatment of Chronic Brucellosis.—Surgeon Commander H. M. DARLOW (Microbiological Research Establishment, Porton, near Salisbury, Wilts) writes: The value of ampicillin in the treatment of chronic brucellosis ("Any Questions?" 30 September, p. 847) was dismissed as a failure on the strength of two cases. I have been involved with two mild and one severe case which were successfully treated with this antibiotic given in doses of 250 mg. four times a day for 28 days. The result was particularly dramatic in the severe case. The patient had been a semi-invalid for several years with frequent bouts of pyrexia and spinal changes. She has been symptom-free now for four years and leads a normal life.

While not disputing the possibility that the tetracycline-streptomycin regimen is the sheet anchor in the treatment of this distressing complaint, it is not infrequently ineffective, and one wonders if it really is superior to ampicillin or to other antibiotics and nalidixic acid, not quoted in the article, which have been used less frequently but nevertheless with some success. In view of my own experience I think that ampicillin should be given a fair trial, and I should be interested to hear through your pages of the opinions and experiences of others with this antibiotic.

OUR EXPERT replies: Claims for the success of other agents rest on reports of small numbers of individual cases such as Surgeon Commander Darlow gives. They are difficult to assess without more details of criteria, length of follow-up, and total number of patients treated. It is relatively unusual to find similar reports of individual failures, and it is unfortunate for ampicillin (which looks, on the basis of in-vitro studies, a very promising agent) that a few failures have been reported but not a few successes. Surgeon Commander Darlow is quite right: what is needed is a fair trial—if by that he means a properly conducted comparison of the tetracycline-streptomycin regimen (the only one so far submitted to extended critical examination) with other likely-looking agents.



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Book Reviews

The State, Health, and Finance

Is There an Alternative? From the *British Medical Journal*. (Pp. 73. 7s.) London: British Medical Association, 1967.

It must be assumed that the National Health Service is here to stay. Conceived in the years of depression and war to serve the poor as well as the rich, its Civil Service management is showing many signs of failure to cope with the vast and growing complexity of medical needs and developments. The extremes of poverty which it was partly designed to alleviate have now largely vanished. The advance of diagnostic technology and complex therapeutic methods are outstripping the capacity of our health service organizers to undertake the necessary rapid modernization.

Professor Henry Miller highlighted the problems in trenchant terms,¹ and his subsequent dialogue with Mr. Enoch Powell raised many questions which this collection of articles by physicians, economists, and administrators is designed to consider if not to answer. Can the basic quality of the service—indeed a great achievement—be improved? Alastair Cooke in the *Guardian*² points out the travail and troubles now besetting "Medicare" in the U.S.A., where the available service is far more uneven than in our own society. Thus national wealth, prosperity, insurance, and medical financing based on private practice cannot meet all the needs. Indeed, the affluent society has promoted by television and journalistic propaganda a public demand which it cannot now satisfy.

Lord Brain's posthumous article points out that a controlling corporation structure (like the B.B.C.) is far from a happy arrangement.

An even quality of service in all hospitals may be a political slogan but it is in practice unobtainable, especially in the smaller units which are uneconomic. Furthermore, the concentration of spearheads of knowledge, the pursuit of research, teaching, and the establishment of exemplary standards are an essential feature which must be sustained in our teaching hospitals. Without unlimited money such local concentration of selected talent is unavoidable.

Regionalization of control, possibly increasing the interest of the local public, could be helpful in one way, but it would contain within it the dangers of reversion to the intolerably low standards of the old municipal hospitals while adding to the unevenness of financial support according to the wealth or poverty of particular areas. Sir Robert Aitken, in an excellent summing up, suggests the possibility of quinquennial budgeting and delegation of independent management to the controlling regional or teaching hospital boards within the total financial allocation. He points out that university building programmes under the University Grants Committee five-year budgeting system are more effectively pursued to completion than hospital building. Such devolution of management could stimulate better attention to priorities by local awareness of relative needs than is possible by referring everything to a cumbersome, gigantic Ministry overwhelmed by its responsibilities for the regulation and control of £1,500m. annually.

Professor G. A. Duncan, a Dublin econo-

mist, points out that pools and sweepstakes as sources of extra finance make a relatively trivial contribution to costs of a health service. It is perhaps worth noting that in Britain the amount of money available for research, on which the quality and efficiency of the service will ultimately be based, is far too small, and is largely dependent on bodies external to the N.H.S. The research supporting charities and the Medical Research Council together spend about £20m. a year on such developments, while the universities, through their teaching staffs and laboratory endeavours, contribute perhaps a similar amount out of their too exiguous budgets. In an expanding and increasingly costly service these amounts, perhaps totalling 2½% of the gross N.H.S. budget, remain much too small.

Monolithic control has become too huge and unbalanced. Cross consultation between Government and the profession, though actively pursued, may fail in imagination as committees usually end in compromise and half-measures. The public remains curiously apathetic about the state of our antiquated hospitals. Until they realize from personal experience the possible misery there is little that can be done by public outcry. But those who could shout loudest still shield themselves in private and expensive comfort. Thus as a profession we have to go on with our struggle and seek the support of those who are intelligent enough to appreciate our motives and comprehend our continuing dilemmas. This book should help them.

J. McMICHAEL.

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Writings of Aubrey Lewis

The State of Psychiatry. Essays and Addresses. By Sir Aubrey Lewis. (Pp. 310 +ix. 63s.) London: Routledge & Kegan Paul, 1967.

Inquiries in Psychiatry. Clinical and Social Investigations. By Sir Aubrey Lewis. (Pp. 335+vii. 63s.) London: Routledge & Kegan Paul, 1967.

In 1928 Aubrey Lewis joined the staff of the Maudsley Hospital, where later he became clinical director, director of the Institute of Psychiatry, and in 1945 professor of psychiatry in the University of London. Under his leadership the Maudsley Hospital, later combined with the Bethlem Royal Hospital, became a teaching centre known the world over. To mark the change of role to emeritus professor, his students at that time arranged the issue of these volumes containing 34 of his papers. Lewis was a prolific writer, and it was an exacting task for the editors to select material from a bibliography of over 100 articles. They have chosen well.

We have here his complete work on melancholia, covering the history, the clinical and

aetiological differentiation, and the prognostic aspects of depressive states. Running to 150 pages with almost 300 references, this in itself is a notable contribution. "The Psychopathology of Insight" was also an admirable choice. "Insight is not a word of plain and single meaning." What then does it mean? A temporary definition is offered—"a correct attitude to a morbid change in oneself"—and used as a convenient text from which to discuss the four words "correct," "attitude," "morbid," "change in oneself." All this suggests the Monday conferences at the Maudsley, so well remembered by his junior and senior colleagues.

The State of Psychiatry is in three sections: history, education, and addresses. Of the work and influence of Henry Maudsley we read: "He had something important to say on many topics that are fundamental for psychologists and psychiatrists, and he said it insistently. . . ." How true this is of Lewis himself. Among the addresses, to mention a few, we find the Manson Lecture "Philosophy and Psychiatry"; the Bradshaw Lecture "Between Guesswork and Certainty in Philosophy"; the Adolf Meyer Research Lecture "The Study of Defect"; the Hobhouse Memorial Trust Lecture

"Agents of Cultural Advance"; the Bertram Roberts Memorial Lecture (Yale University) "Ebb and Flow in Social Psychiatry"; the Harveian Oration "Medicine and the Affections of the Mind"; and by way of contrast, a B.B.C. talk "The Psychology of Shakespeare."

Inquiries in Psychiatry, covering clinical and social investigations, includes many original contributions, such as "The Experience of Time in Mental Disorder," a paper based on case records in which examples of change in the sense of time indicate significant features in psychopathology. Two papers on "Obsessional Illness" will reward the attentive reader, and so will "Demographic Aspects of Mental Disorder," delivered to a meeting of the Royal Society.

A collection of lectures and addresses cannot give continuity of theme; but this is a treatise, not a textbook, and it provides a series of well-written, well-documented studies, each in the top rank. Independent thought with clear presentation such as this is rare in psychiatric literature. We may hope that a further compilation of Lewis' work will follow.

E. A. BENNET.

Surgery in a Paperback

A Short Textbook of Surgery. By Selwyn Taylor, D.M., M.Ch., F.R.C.S., L. T. Cotton, M.Ch., F.R.C.S., and J. G. Murray, Ch.M., F.R.C.S.(Ed.). (Pp. 628+x; illustrated. 42s. Paper 30s.) London: English Universities Press. 1967.

In these days of minicars and miniskirts it was perhaps inevitable that sooner or later we should also have mini-textbooks, such as those in the University Medical Texts series, of which the latest to appear is *A Short Textbook of Surgery*, by Selwyn Taylor, Leonard Cotton, and Greig Murray. At first sight it might seem hard to believe that this slim volume—a paperback, corresponding in size to two Penguins with rather larger pages, and costing only 30s.—could adequately fulfil the authors' ambition to provide a complete text for undergraduates and practitioners. But, almost miraculously, it does, and very thoroughly too on all aspects of surgery (except E.N.T. and eye surgery and anaesthetics). This feat has been achieved by dint of very succinct and readable writing and by the sparing use of illustrations, all 87 of which are simple line-drawings. Moreover, for the guidance of those who wish to pursue various subjects farther, there are helpful references to specialist texts at the end of many of the chapters.

The result is a most refreshing book which cannot fail to give students a modern view of surgery likely to arouse their interest. Whether it will achieve its declared objective of establishing the habit whereby students will buy a cheap disposable text of this kind and discard it in favour of a newer edition every few years is less certain. For the tradition by which a student purchases a textbook at the beginning of his undergraduate clinical career and continues to rely on it, with supplementary reading, for the rest of his professional life is deeply ingrained. But this short textbook is unquestionably one of the most

exciting developments in the field of textbook publishing and I wish it every success.

J. C. GOLIGHER.

Panorama of Internal Medicine

Cecil-Loeb Textbook of Medicine. 12th edition. Edited by Paul B. Beeson, M.D., and Walsh McDermott, M.D. (Pp. 1738+xxxix+liv; illustrated. Single volume £7 3s. 6d. Two-volume set £8 11s. 6d. De luxe edition £10 10s.) London: W. B. Saunders. 1967.

There are many who believe that the day of the large textbook of medicine is past. They acknowledge, of course, that undergraduates and family doctors (who are supposed to know something about everything) require a concise text containing the essentials of medicine as a framework on which to build their knowledge. Such a book should be cheap, and, owing to the fantastically rapid advance of medical science, new editions of it should appear every two or three years. When knowledge in depth of any subject is required, however, they think it should be studied in monographs and original papers rather than in large textbooks which are bound in some respects to become out of date in a few years, and sometimes even in the considerable period which must elapse during the slow, elaborate process of their publication. There must be many who disagree with these views, for the demand for large and very large textbooks of medicine seems to be greater than ever.

This is the twelfth edition in 40 years of this immense lexicon which surveys the whole panorama of internal medicine, including dermatology and the psychoses. Dr. Cecil (who died in 1965) and Dr. Loeb made the

work famous, and, after the 10th edition, handed on the editorial torch to Dr. Paul Beeson (now Nuffield Professor at Oxford) and Dr. Walsh McDermott, of Cornell, assisted by five associate editors. They have chosen 169 contributors, 52 of whom are new to this edition so that much of it has been entirely rewritten. Apart from Sir Aubrey Lewis, of the Maudsley, and Professor Ronald Christie, of McGill, the contributors are all drawn from American schools and represent a large proportion of the flower of its medicine. The book weighs some 6 lb. (or 3 kg., as we should say nowadays), and like a great, handsome family bible is somewhat unwieldy to handle, but is available, at greater expense, in two more manageable volumes. It is none the less 100 pages shorter than its predecessor—no mean editorial achievement—but is seven shillings dearer, which roughly represents the rise in the cost of living in four years.

It is unlikely that many doctors will buy a new expensive edition of Cecil and Loeb every time one is published; they will prefer to consult it as an authoritative work of reference in libraries and university departments, which should always possess a copy. Nevertheless, there is much in medicine which is not ephemeral, and the possession of any edition of this book will be of permanent value to any doctor. It would be an affectation to pretend that I have perused more than the few portions of it with the contents of which I can still claim a slight nodding acquaintance, but I have found those parts which I have studied to be impressively authoritative, discriminating, wise, and up to date. One of the forewords by Dr. Atchley—sometime of the Presbyterian Hospital—on patient-physician communication would repay reading by all medical men. This probably represents the best great textbook of medicine in the English language.

DERRICK DUNLOP.

Books Received

Review is not precluded by notice here of books recently received.

A Short Textbook of Psychiatry. By W. L. Linford Rees, B.Sc., M.D., F.R.C.P., D.P.M. (Pp. 305+x; illustrated. 35s. Paper 25s.) London: English Universities Press. 1967.

Feminine Psychology. By Karen Horney. Edited and with an Introduction by Harold Kelman, M.D. (Pp. 269. 30s.) London: Routledge & Kegan Paul. 1967.

Science and E.S.P. Edited by J. R. Smythies. (306+viii. 42s.) London: Routledge & Kegan Paul. 1967.

The Know-How of Infant Care. By Sylvia Close, S.A.N.C.Med. and Surg.(Hons.), S.A.N.C. Midwifery(Hons.). (Pp. 49. 5s.) Bristol: John Wright. 1967.

L'Année Endocrinologique. 19th year. By M. Albeaux-Fernet, L. Bellot, L. Canet, J. Deribieux, M. Gelinet, and J. D. Romani. (Pp. 215. 42 F.) Paris: Masson. 1967.

Ganglion-Blocking and Ganglion-Stimulating Agents. By Professor D. A. Kharkevich. Translated by Dr. R. Crawford. Edited by W. D. M. Paton. (Pp. 367+xi; illustrated. 90s.) Oxford: Pergamon. 1967.

Submicroscopic Structure of the Inner Ear. By Salvatore Iurato. (Pp. 367+xii; illustrated. £7.) Oxford: Pergamon. 1967.

Précis de Pathologie Médicale. Vol. 1. Généralités. Maladies Infectieuses. By Henri Péquignot et al. (Pp. 734+viii; illustrated. 65 F.) Paris: Masson. 1967.

Précis de Pathologie Médicale. Vol. 7. Maladies Métaboliques. Maladies des Reins. Intoxications. By Henri Péquignot et al. (Pp. 631+vi; illustrated. 62 F.) Paris: Masson. 1967.

L'Ostéomalacie. Symposium. Edited by D. J. Hioco. (Pp. 415; illustrated. 80 F.) Paris: Masson. 1967.

Rekonstruktive Chirurgie der Arterien. By Dr. J. Vollmar. (Pp. 416+xii; illustrated. DM. 148.) Stuttgart: Georg Thieme. 1967.

La Transparence de la Cornée. Les Mécanismes de ses Altérations. By P. Payrau, Y. Pouliquen, J.-P. Faure, and G. Offret. (Pp. 764+xii; illustrated. 130 F.) Paris: Masson. 1967.

Essentials of Otolaryngology. By R. S. Lewis, M.A., M.B., F.R.C.S., S. R. Mawson, M.A., M.B., F.R.C.S., W. G. Edwards, M.A., B.M., F.R.C.S., and Harold Ludman, M.A., M.B., F.R.C.S. (Pp. 380+vii; illustrated. 55s.) London: William Heinemann. 1967.

Designing for the Disabled. 2nd edition. By Selwyn Goldsmith, M.A.(Cantab.), A.R.I.B.A. (Pp. 207; illustrated. £3 10s.) London: Royal Institute of British Architects. 1967.

A View of the Brain. By J. S. Griffith. (Pp. 79. 15s.) Oxford: Clarendon Press. Oxford University Press. 1967.

Bedside Medicine. 2nd edition. By I. Snapper, M.D., and Alvin I. Kahn, M.D. (Pp. 824+xxvii. £7.) London: William Heinemann. 1967.

Textbook of Anatomy. 2nd edition. By W. Henry Hollinshead, Ph.D. (Pp. 994+ix; illustrated. \$18.75.) New York: Hoeber. 1967.

The Technique of Psychotherapy. 2nd edition. By Lewis R. Wolberg, M.D. (Part 1: pp. 721+xiv. Part 2: pp. 722-1411+x. £11 4s. per set of 2 books.) London: William Heinemann. 1967.

Clinical Vectorcardiography. By Te-Chuan Chou, M.D., and Robert A. Helm, M.D. (Pp. 314+xi; illustrated. \$12.50.) New York and London: Grune & Stratton. 1967.

Work Done in India on Viral and Rickettsial Infections of Vertebrates. A Bibliography. Compiled by Surendar Mohan and T. R. Srinivasan. (Pp. 339+xii. No price given.) Delhi: Indian National Scientific Documentation Centre. 1967.

Middle Articles

GENERAL PRACTICE OBSERVED

Survey of General-practitioner Maternity Units in England and Wales

M. S. T. HOBBS,* M.B., M.R.A.C.P.

Brit. med. J., 1967, 4, 287-290

This paper is one of a series describing an investigation into the organization of the obstetric services in England and Wales (Acheson and Feldstein, 1964; Hobbs and Acheson, 1966a, 1966b). Previous studies in the series had shown that in the Oxford area general-practitioner maternity units are used as an alternative to consultant care for mothers with both high and low risks of perinatal mortality. Furthermore, the proportion of high-risk mothers booked for consultant care decreases sharply as the distance from the nearest consultant unit increases when general-practitioner beds are available as an alternative, but no similar decrease is observed when such beds are not available. Though the number of G.P. units in the area available for study was small, there was a suggestion that the proportion of high-risk mothers selected for delivery in consultant units was greater when the G.P. beds were incorporated in a consultant unit or when the G.P. unit was visited regularly by a consultant for antenatal consultations. In view of the possible implications of these findings for planners of the maternity services, it was felt that additional information about G.P. maternity units should be obtained from a national survey.

The objectives of the survey were as follows: (1) to examine the geographical relation of G.P. units to consultant units; (2) to examine the extent to which direct liaison exists between consultant maternity units and G.P. maternity units for selection of cases, provision of antenatal care, and management of complications in labour; and (3) to assess the standard of equipment and other facilities of G.P. maternity units necessary to deal with obstetric emergencies and resuscitation of the newborn.

Material and Method

In 14 of the 15 hospital regions of England and Wales the permission of the senior administrative officer was obtained to send postal questionnaires to the G.P. maternity units within the region. Permission was granted to send these direct to the matrons in seven regions, and through the group secretaries concerned in six regions, with the request that the forms be completed with the assistance of the matrons. In the remaining region completion of the forms was undertaken by the regional hospital board concerned.

Replies were received from 274 of the 288 units to which the form was sent. The information recorded on the forms was transferred to 80-column punch cards, and the subsequent

analyses were carried out with the aid of standard business machines.

Geographical Relation of G.P. Units to Consultant Units

Distance from Nearest Consultant Unit.—In Fig. 1 the distribution of units by distance measured in miles from the nearest consultant unit is shown. Eight units (2.9%) were completely integrated with consultant units, and five further units (1.8%) were situated at distances of less than half a mile (800 m.) from the nearest consultant unit, making a total of 13 (4.7%) situated in close proximity to a consultant unit. Seventy-five units (27.4%) were situated from half to five miles (0.8 to 8 km.) distance, 66 (24.1%) from 5 to 10 miles distance (8 to 16 km.), and the remaining 120 units (43.8%) were situated more than 10 miles from the nearest consultant unit.

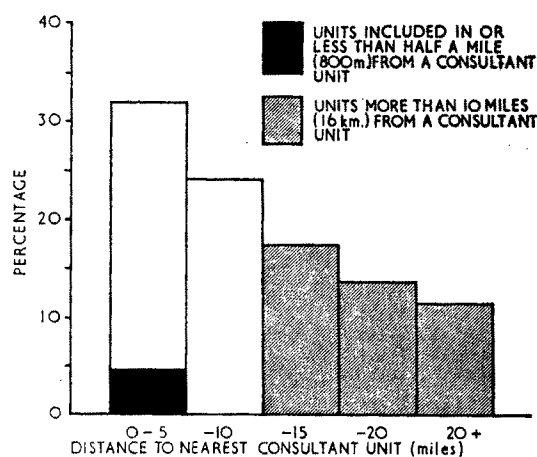


FIG. 1.—Distribution of G.P. maternity units according to distance in miles from the nearest consultant unit.

This finding suggests that in a large proportion of G.P. units a considerable interval may elapse when it is necessary to transfer obstetric emergencies to consultant units. Correct initial selection to avoid such situations is therefore of great importance.

Contact with Consultant Obstetricians

In G.P. units which are physically integrated with consultant units on the same site close liaison between consultants and general practitioners using the units can be assumed to exist. The analyses which follow are therefore confined to the remainder—that is, the self-contained general-practitioner maternity units.

* Formerly Lecturer in Medicine, Oxford Record Linkage Study and Unit of Clinical Epidemiology, Nuffield Department of Clinical Medicine, University of Oxford.

Requests for reprints should be addressed to the Medical Director, Oxford Record Linkage Study, Oxford Regional Hospital Board, Old Road, Headington, Oxford

Contact in Antenatal Period

The inquiry was directed towards determining in which units (i) a consultant obstetrician is responsible for selecting cases for delivery in the unit; (ii) a consultant reviews the progress of all women selected for delivery in the unit in late pregnancy; (iii) a consultant visits antenatal clinics held at the unit to review complicated cases only; and (iv) no special arrangement for consultation exists apart from the referral of the complicated case to a consultant antenatal clinic by the G.P.

The extent to which units have some special arrangement for consultant obstetricians to see cases in the antenatal period—that is, i-iii—referred to as “consultant contact during the antenatal period,” is shown in Fig. 2. In 66 units (24.8%) a consultant obstetrician selects the cases to be delivered in the unit and also reviews their progress at a later stage of pregnancy. In a further 17 units (6.4%) the consultant selects the cases for delivery in the units but reviews only those with complications of pregnancy. In 15 units (5.6%) selection for delivery is made by general practitioners, but the consultant reviews all cases at least once during pregnancy. A consultant obstetrician thus sees all cases at some stages of pregnancy in 36.8% of units. In a further 54 units (20.3%) a consultant obstetrician visits the unit antenatal clinic to see complicated cases selected by the general practitioner. In the remaining 114 units (42.9%) no special arrangements exist between consultants and general practitioners for contact in the antenatal period.

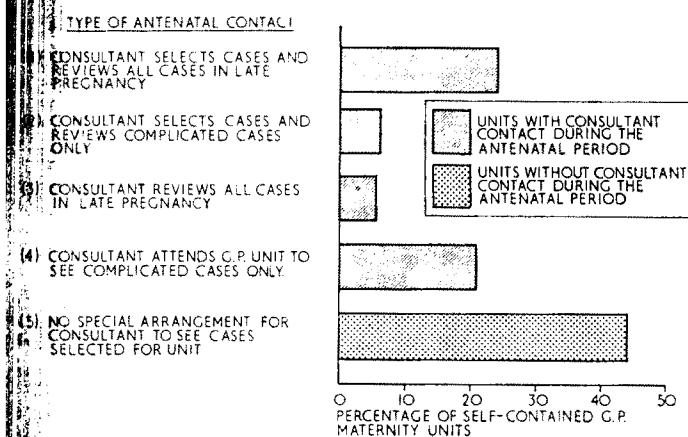


Fig. 2.—Distribution of self-contained G.P. units according to type of arrangements which exist for contact with a consultant obstetrician in the antenatal period.

Factors affecting consultant contact in the antenatal period:

(a) *Existence of Antenatal Clinics.*—The relation between the existence of antenatal clinics and the frequency of consultant contact in the antenatal period is shown in Table I. Of the 266 units 140 (52.6%) have antenatal clinics supervised by medical practitioners. (A further 22 units have antenatal or booking clinics supervised by midwives alone which have been excluded from this group.) In these a consultant sees all mothers for selection or review in 56 (40.0%) and visits to see complicated cases selected by the general practitioner in a further 54 (38.6%). Consultant contact during the antenatal period thus exists in 78.6% of units with antenatal clinics. In contrast, only 42 (33.3%) of the 126 units without clinics have formal arrangements whereby mothers visit a consultant clinic elsewhere for selection or review. The difference, which is significant at the 0.001 level, strongly suggests that the existence of antenatal clinics may be an important factor in determining whether or not units have close liaison with a consultant in the antenatal period. Moreover, the opportunity for personal contact between consultants and general practitioners should be much greater where consultants visit G.P. units than in the case where mothers attend a special consultant clinic elsewhere. However, it is notable that of the units with antenatal clinics 22 (15.7%) had clinics attended by a consultant only, and that in only 18 (12.9%) did all general practitioners using the unit also attend the antenatal clinics. Personal contact between consultant and general practitioner is therefore by no means certain even in the

units visited by a consultant. Nevertheless, the finding that only 52.6% of units have antenatal clinics is unsatisfactory.

TABLE I.—Relation Between Consultant Contact in the Antenatal Period and the Existence of Antenatal Clinics in Self-contained G.P. Maternity Units

Nature of Contact	Units with Antenatal Clinics		Units without Antenatal Clinics		All Units	
	No.	%	No.	%	No.	%
Consultant selects or reviews all cases for delivery in G.P. unit	56	40.0	42	33.3	98	36.8
Consultant visits antenatal clinic at G.P. unit to see complicated cases	54	38.6	—	—	54	20.3
No special arrangement for consultant to see cases	30	21.4	84	66.7	114	42.9
Total	140	100.0	126	100.0	266	100.0

(b) *Regional Differences.*—In Table II the hospital regions have been ranked according to the proportion of units with special arrangements for consultant contact in the antenatal period. Because of the small number of units in many regions categories 1–4 in Fig. 2 have been here grouped together. Consultant contact for antenatal care is seen to range from 82.3% for region A to 33.3% for region N. This considerable variation suggests that there may be important differences between the regions in policy regarding the relation between consultant obstetricians and general-practitioner maternity units.

TABLE II.—Proportion of Self-contained G.P. Maternity Units with Special Arrangement for Consultant Contact in the Antenatal Period in 14 Hospital Regions in England and Wales

Hospital Region	All Units	Units with Consultant Contact in Antenatal Period	
		No.	%
A	34	28	82.3
B	4	3	75.0
C	30	21	70.0
D	13	9	69.2
E	3	2	66.6
F	28	17	60.7
G	18	10	55.5
H	19	10	52.6
I	25	13	52.0
J	10	5	50.0
K	11	5	45.4
L	9	4	44.4
M	47	20	42.6
N	15	5	33.3
All regions	266	152	57.1

(c) *Distance from Nearest Consultant Unit.*—When the effect of the distance in miles from the nearest consultant unit on consultant contact in the antenatal period was examined it was found that there were no important differences between those units nearest a consultant unit and those most distant.

Consultant Contact During Labour

In addition to questions about the extent to which consultants are involved in antenatal supervision, an inquiry was made whether a consultant obstetrician (other than with the flying squad) visits the unit to see complicated cases during delivery (referred to as “contact during labour”). A positive answer to this question was given in 197 units (74.1%).

The extent to which consultant contact during labour and contact in the antenatal period are related is shown in Table III.

TABLE III.—Relation Between Consultant Contact in the Antenatal Period and for the Management of Complications of Delivery

	Consultant Contact in Antenatal Period	No Consultant Contact in Antenatal Period	All Units
Consultant visits to see complicated cases in labour	127 (64.5%)	70 (35.5%)	197 (100%)
Consultant does not visit to see complicated cases in labour	25 (36.2%)	44 (63.8%)	69 (100%)
All units	152 (57.1%)	114 (42.9%)	266 (100%)

Special arrangements for consultant contact in the antenatal period exist at 127 (64.5%) of the units where a consultant visits to see complicated cases in labour, but in only 25 (36.2%) of the units where such visits are not made. This difference, which is highly significant ($\chi^2=12.77$; d.f.=1; $P<0.001$), indicates that consultant contact during labour and contact in the antenatal period are closely related.

The effect of distance on consultant contact during labour is shown in Fig. 3. It is seen that consultant contact decreases from 80.09% when units are less than five miles (8 km.) from the consultant unit to 52.9% when over 15 miles (24 km.) distant. In contrast to contact between consultant and G.P. units for antenatal care it is thus seen that consultants visit less often to see complicated cases during labour as the distance

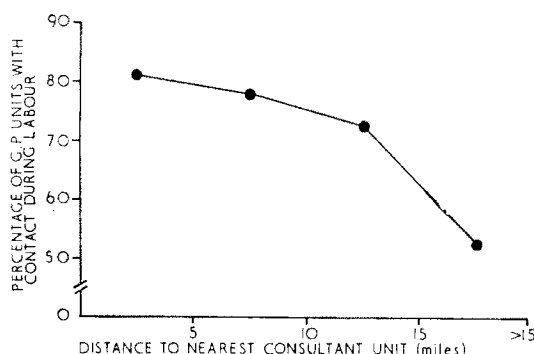


FIG. 3.—Proportion of self-contained G.P. maternity units with consultant contact during labour according to distance in miles from the nearest consultant unit.

increases. This finding, which is statistically significant ($\chi^2=9.44$; d.f.=3; $0.05>P>0.02$), emphasizes the importance of correct selection of mothers for delivery in those units most distant from a consultant unit.

Equipment and Facilities for Management of Obstetric Emergencies

General Anaesthesia

A detailed inquiry was made about anaesthetic equipment. The actual value of such equipment obviously depends on all items required for a particular technique being available. A points score for anaesthetic facilities has therefore been constructed with the advice of a consultant anaesthetist which takes into account both the functional effectiveness of the equipment and the quality of the anaesthesia that could be administered. With regard to the latter, the advice that we received stressed the fact that, while mothers were in general young and healthy, the mechanical problems of pregnancy may make the administration of anaesthetics particularly difficult. Ideally they should only be undertaken when the following facilities are available: (a) adequate suction; (b) a table (or bed) which can be tilted to the head-down position; and (c) equipment for intubation and controlled ventilation.

Of the above, mechanical suction is virtually mandatory, but provided this is available general anaesthesia may be given in emergencies with either an anaesthetic machine and face-mask or an open anaesthetic mask. Following these principles points were allotted as follows:

Equipment	Points
(1) Mechanical suction	2
(2) Complete equipment for intubation anaesthesia (including laryngoscope, endotracheal tubes, rubber face-mask, bag and connexions, anaesthetic machine)	2
(3) Access to operating-theatre* (or operating-table)	1
(4) Anaesthetic machine plus rubber face-mask, bag and connexions, or open anaesthetic mask	1

* This question was intended to identify units where patients could be tilted to the head-down position. Unfortunately it does not take into account units with obstetric beds which can be tilted head down. Units with such beds may thus be underscored in this respect.

The total points score possible is five. Examples of possible scores are as follows:

Equipment	Score
Intubation anaesthesia, suction, tilting table	5
Intubation anaesthesia and suction, or simple machine anaesthesia (or open anaesthesia) plus suction and tilting table	4
Simple machine anaesthesia (or open anaesthesia) plus suction	3
Simple machine anaesthesia (or open) plus tilting table	2
Simple machine anaesthesia (or open) alone	1

It will be noted that units with a score of less than 3 do not possess suction equipment. Their equipment is therefore inadequate for safe anaesthesia. A score of 3 indicates minimal facilities for safe anaesthesia, a score of 4 indicates good facilities, while 5 indicates optimum facilities. The distribution of anaesthetic facilities classified in this way is as shown in Table IV. In 57 of the units (21.4%) no adequate facilities for general anaesthesia were available.

TABLE IV.—Distribution of Anaesthetic Scores for Self-contained G.P. Maternity Units

Anaesthetic Facilities	Score	No. of Units	% of Units
Inadequate	0-2 points	57	21.4
Minimal	3	39	14.7
Good	4	90	33.8
Optimal	5	80	30.1
All		266	100.0

When anaesthetic scores were examined according to whether or not units had contact with a consultant for intrapartum complications (Fig. 4) it was found that in units with consultant contact the facilities were inadequate or minimal in 30.1% of units and good or ideal in 69.9%. In units without contact the facilities were inadequate or minimal in 52.2% (for the differences in anaesthetic facilities $\chi^2=9.73$; d.f.=1; $0.01>P>0.001$). Similar but less marked differences in anaesthetic facilities were observed according to whether or not units had consultant contact for antenatal care.

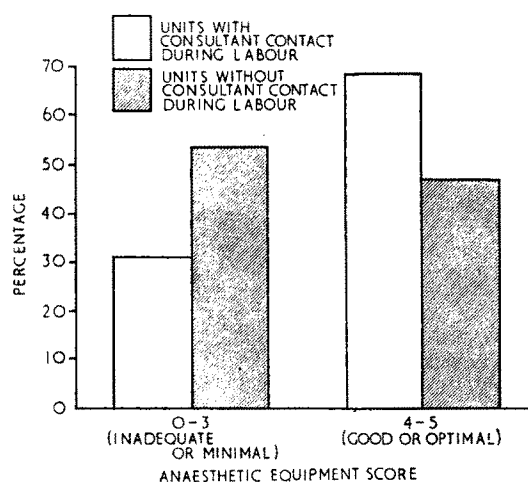


FIG. 4.—Distribution of anaesthetic facilities scores for self-contained G.P. units with and without consultant contact during labour.

Care of Newborn

Several questions relating to the care of the newborn were asked in the inquiry. These included questions about nursery facilities, visits from consultant paediatricians, and equipment for the resuscitation of the newborn. In this paper, however, attention is confined to equipment for resuscitation of the newborn, which was thought to be the most important aspect of this part of the inquiry.

The general introduction of intubation and controlled respiration for the resuscitation of anoxic babies has been in

significant advance in the care of the newborn (Hodges *et al.*, 1963; Barrie, 1963). Moreover, as both the technique and equipment required are simple, it should be possible for this method of resuscitation to be used in G.P. units should the occasion arise.

Units were considered to have equipment for intubation of newborn when both infant endotracheal tubes and a laryngoscope were available (whether infant or adult). This equipment was not available in 34.0% of units. When assessed in relation to contact with consultant obstetricians it was found that equipment for intubating the newborn was present in 57.1% of units with contact during labour, but in only 52.2% of those without contact ($\chi^2=6.49$; d.f. = 1; $0.02>P>0.01$).

Access to Operating-theatres

A total of 106 units (39.8%) were stated to have access to an operating-theatre. The proportion of such units visited by a consultant to see complicated cases during labour, 78.3%, was significantly greater than those without access to an operating-theatre, 71.8%, but this difference is not statistically significant.

Obstetric Equipment

No relation was found between the possession by units of various items of obstetric equipment and visits by a consultant to see complicated cases during labour.

Discussion

The importance of a close working relation between G.P. maternity units and consultant obstetricians has been stressed by many authorities (Ministry of Health, 1959; Baird, 1960; C.O.G., 1962; Stallworthy, 1964; Stirling, 1963). That such arrangements are not only desirable but may also be essential has also been emphasized by general practitioners who have had first-hand experience of working in units with a consultant liaison (Jameson and Handfield-Jones, 1954; Jameson, 1961; Stewart-Hess and Green, 1962). It is therefore not surprising that in almost half (42.9%) of the self-contained G.P. units in England and Wales in 1966 there was no special arrangement for a consultant obstetrician to see during pregnancy mothers booked for delivery in the units. The absence of facilities to contact antenatal clinics appears to be one important factor underlying this finding; differences between regional hospital boards in policy regarding the relation between consultant obstetricians and G.P. maternity units may be another.

Under the hospital plan announced by the Ministry of Health (1962) it is envisaged that the majority of G.P. maternity beds will eventually be incorporated in district hospitals, where close co-operation between consultants and general practitioners should be the rule. However, in 1966 fewer than one in 30 G.P. units were physically integrated with a consultant unit, and it thus seems likely that it will be many years before this ideal is achieved. It therefore seems important that in the meantime steps should be taken to ensure that all G.P. units have the facilities to conduct antenatal clinics, and that there should be a policy whereby these are visited regularly by a consultant obstetrician to see complicated cases and to advise on the selection of cases suitable for delivery in the unit.

Another matter of policy raised by this survey is the quality of equipment and facilities required in G.P. units for dealing with obstetric and paediatric emergencies. There can be little doubt that all units should contain efficient equipment for the resuscitation of the newborn, but in the matter of anaesthetic

and obstetric equipment the issues are less clear. Many authorities may feel that G.P. maternity units have no need of sophisticated equipment, as emergencies are now efficiently and safely dealt with by transfer to a consultant clinic. On the other hand, the delays involved in transferring such cases may in some instances make this course impracticable or more hazardous. Local circumstances rather than a general rule should therefore direct what is desirable in the type of anaesthetic and obstetric equipment in G.P. units. It is nevertheless of considerable interest that the quality of equipment is related to whether or not a consultant visits the unit to see complicated cases in labour.

Summary and Conclusions

This paper reports the results of a national postal survey of general-practitioner maternity units, involving 274 (95%) of the 288 units to whom the questionnaire was sent. The following are the main findings:

(1) About one in 20 (4.7%) of the units are integrated with or in close proximity to consultant units. Almost half (43.8%) are situated more than 10 miles (16 km.) from such units. As transfer of obstetric emergencies from such units is likely to involve considerable delay, selection of low-risk mothers for delivery there is of obvious importance.

(2) When the degree of contact between the units and consultant obstetricians was examined it was found that in almost half (42.9%) there was no formal arrangement for antenatal consultation with a consultant obstetrician. However, in nearly three-quarters of the units (74.1%) a consultant visited to see complicated cases during labour.

(3) The frequency of formal arrangements whereby a consultant sees cases antenatally was found to be associated with the existence of antenatal clinics. Three-quarters of the units with antenatal clinics had an arrangement, while one-third of units without clinics had no such arrangement.

(4) When the equipment of the units was studied it was found that about one in five (21.4%) did not have facilities to give an anaesthetic safely and one in three (34%) did not have equipment for intubating the newborn. The likelihood of possessing both types of equipment was associated significantly with an arrangement for a consultant to visit during labour.

(5) These findings suggest that in self-contained G.P. maternity units both formal arrangements for contact with a consultant obstetrician and the existence of antenatal clinics are highly desirable.

I wish to thank the senior administrative medical officers of the hospital regions in England and Wales for their permission to conduct this survey, the matrons and group secretaries of the units concerned for their co-operation in completing the questionnaires, Dr. D. C. Hodgson for his advice in constructing the anaesthetic equipment scores, and Dr. E. D. Acheson for his advice in the design of the survey and preparation of this paper.

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Medical Management in Hospitals

In December 1965 the Secretary of State for Scotland set up a Working Party of doctors and hospital service administrators "to consider what developments in the hospital service are desirable in order to promote efficiency in the organization of medical work." In 1966 a Joint Working Party was appointed by the Ministry of Health and the Joint Consultants' Committee with the same terms of reference. The two Working Parties have published their first reports^{1,2} this week. Printed below is a summary of the recommendations.

Scotland*

The Working Party set up subgroups to consider four aspects of the subject—namely, clinical organization and staff committee systems, medical staffing, alternatives to traditional systems of hospital care, and operational research. The parent Working Party nevertheless makes it clear that it could not consider hospital work in isolation from the other branches of the N.H.S., and it recommends that the Secretary of State should set up another Joint Working Party with wider terms of reference to consider the organization of medical work in the N.H.S. as a whole.

Within the hospital service the report proposes that clinical organization should be based on larger groups than at present. The new administrative entity proposed is the "division" made up of "consultancies" consisting of a consultant and that part of the hospital staff and resources available to him. Divisions would be formed by the grouping together of specialties falling into the same broad categories, such as general surgery, the laboratory services, and so on. Divisions should organize and encourage evaluation of the care of patients and would also co-ordinate the use and the training of hospital junior staff. The chairmen of all divisions within a hospital should form a committee to deal with professional matters concerning the interest of more than one division or the hospital as a whole. This committee of chairmen would be able to give advice to the regional hospital board. Clinical staff at all levels of training should receive guidance in organization and administration.

Medical Staff

The shortage of medical manpower was being accentuated by emigration, says the report, and no increase in output could be expected from medical schools in the next 10 years. The morale of junior staff had

been affected by the anxiety felt by registrars about their career prospects. The report recommends that a planned registrar establishment should be created related to career prospects in the N.H.S. The reduction of the registrar establishment made necessary by this change would be made up by an increase in the numbers of medical assistants. The report warns against the possibility of medical assistants carrying out work with specialist responsibility, and also draws attention to the disincentive for general practitioners to undertake sessional work as part-time medical assistants under present financial arrangements.

More effective use of medical manpower can also be made by the provision of adequate secretarial assistance, says the report, and the provision of adequate numbers of ancillary staff should be the subject of urgent attention.

Alternative Systems of Hospital Care

Hospital care based on medical "firms" and the retention of patients in the same ward at all stages of illness lead to inefficiencies, suggests the Working Party. The report advocates the separation of beds for emergency cases from those for patients on the waiting-list. A number of beds would be allocated for routine admission, investigation, and treatment of patients, and their time of admission and length of stay in hospital planned in advance. Patients admitted in this way should reach hospital only after all possible investigations and treatment which could be carried out as an outpatient had been completed. The report also recommends that the advantages and disadvantages of techniques used in routine investigations should be examined.

The Working Party recommends that acute beds should be divided into intensive nursing care beds, intensive therapy beds, and short-stay beds. This last category would include overnight and observation beds and five-day beds, which could be used to accommodate patients whose condition could be investigated and treated during the course of a five-day week. These beds could close at week-ends, which would facilitate their staffing by part-time married nurses. Planned early discharge could be made easier by co-operation between hospital, general practitioner, and local authority services.

Operational Research

The report asserts that effective use of limited resources can be made only after operational research has been carried out, and that clinicians should be presented with readily intelligible accounts of work

done. An evaluation of patient care should be introduced and studies undertaken to find out what modifications to American techniques may be necessary.

The Working Party proposes to continue its meetings and to issue a further report. Implementation of the present proposals will require consultation among all concerned, but the report recommends that immediate steps be taken to work out the planned registrar establishment and its introduction with the agreement of the profession and the hospital authorities.

England and Wales†

The English Joint Working Party's report is concerned mainly with the reform of the clinical organization of medical staff in hospitals and hospital groups. This report, like that from Scotland, recommends the grouping together of categories of specialties to form divisions. Each division would have a chairman, and a small medical executive committee would be formed in each hospital with representatives from each division. The chairman of the executive committee would have time for administrative duties included in his contract. Chairmen of divisions and of the executive committees would be appointed by boards of governors or by regional boards in consultation with hospital management committees and consultant staff. (This contrasts with the recommendations of the Scottish report, which suggests that chairmen of divisions should be elected by their colleagues.) The chairman of the executive committee would be an experienced clinician, but he would act in his administrative capacity for five years or more. He would be the chief medical spokesman of the hospital in its relationship with the regional board and would speak for medical staff to other bodies. The report makes it clear, however, that it does not propose to resurrect the medical superintendent. (In Scotland, where medical superintendents have been retained, no post of chairman of executive committee has been proposed.) The functions of the executive committee will be to receive reports from divisions, to consider medical policy in planning, and to co-ordinate the medical activities within the hospital.

The report suggests that hospitals should go ahead with reorganization. It envisages that staff accommodation will be needed by the divisions and executive committee and that chairmen of the executive committees and other medical staff will need training in administration.

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- ¹ *Organization of Medical Work in the Hospital Service in Scotland, 1967.* H.M.S.O. Price 6s. 3d.
- ² *First Report of the Joint Working Party on the Organization of Medical Work in Hospitals, 1967.* H.M.S.O. Price 2s. 9d.

* The members of the Working Party were: Dr. J. H. F. Brotherston (Chairman), Dr. C. Bainbridge, Dr. F. D. Beddard, Sir John Bruce, Dr. C. W. Clayton, E. U. E. Elliott-Binns, Esq., Dr. G. D. Forwell, Dr. J. G. M. Hamilton, Mr. D. McKay Hart, Mr. Neil G. C. Hendry, Mr. Arthur H. Jacobs, Dr. I. M. Macgregor, Dr. S. J. Hadfield (Observer), Dr. John Smith (Observer), and J. E. Tinkler, Esq. (Secretary).

† The members of the Joint Working Party were: Sir George Godber (Chairman), Dr. J. O. F. Davies, Mr. H. G. Hanley, Mrs. J. A. Hauff (succeeded Mr. T. B. Williamson in February 1967), Dr. T. Rowland Hill (Deputy Chairman) (died on 14 April 1967), Mr. H. H. Langston, Mr. T. L. T. Lewis (designated successor to Sir Arthur Porritt in May 1967), Dr. R. Mayon-White (succeeded Dr. T. Rowland Hill in April 1967), Mr. G. McLachlan, Mr. G. A. Phalp, Sir Arthur Porritt (appointed Governor General of New Zealand in January 1967), Sir John Richardson, Dr. K. Robson, Mr. T. B. Williamson (retired in February 1967 from the Joint Working Party because of illness), Dr. H. Yellowlees, Dr. I. T. Field (Joint Secretary), and Dr. G. R. Ford (Joint Secretary).

Correspondence

Letters to the Editor should not exceed 500 words.

Obstetric Forceps or Vacuum Extractor?

SIR,—Your leading article on the above subject (23 September, p. 753) has just come to my notice. Although it appears to be based on the paper by Schenken and Serr,¹ the conclusions which it draws seem to be wholly at variance with those of the authors quoted.

This paper deals with a study of some 300 cases delivered with the vacuum extractor compared with a similar number delivered with forceps. Foetal distress was the indication in 10% of the vacuum-extractor cases and 29.6% in the forceps cases, the difference not being significant. In 10 cases foetal distress increased during the delivery with the vacuum extractor partly because of absolute or relative shortness of the second stage. In our experience this change of opinion would appear to have been unfounded. Much has been made of the slow rate of extraction with the vacuum extractor, but in the series quoted the duration of extraction was less than 20 minutes in more than half of the cases, and in four did it reach 20 minutes. The authors show that in the vacuum extractor series 10% of the cases in 300 died. In two of these intracranial haemorrhage was the cause and in both cases traction was prolonged beyond 20 minutes. In the forceps series seven infants died and in four of these cerebral haemorrhage and tentorial lacerations were found. There was evidence of central nervous system damage in 1% of the vacuum-extractor series and 1.3% of the forceps series. The frequency of cephalohaematoma and scalp laceration was the same in both groups, and 95% of these cleared up within five days. In the forceps series there were four facial palsies and one fractured skull. No similar lesions were found in the vacuum-extractor group.

In view of the above figures it is quite clear that the danger to the foetus of forceps delivery is greater than that of vacuum extraction. Your suggestion that forceps delivery would be quicker is probably true, but I would deny absolutely that the preparations for the use of the vacuum extractor take at least a quarter of an hour. Many of our cases have been delivered within five minutes of setting out to rescue a distressed child, and with the recent use of the Einar Egnell vacuum pump we have been able to produce an adequate chignon on the scalp within two to three minutes and to complete the delivery very rapidly thereafter. Schenken and Serr have shown clearly the danger of attempting delivery in a high station in the pelvis and of prolonged traction. We believe that where the head lies more than one fingerbreadth above the ischial spines caesarean section is the better alternative and that delivery from a high station is unjustifiable in present-day obstetrics. The argument that the position of the occiput should be checked before forceps is applied applies equally to the application of the vacuum extractor. The results of failure to orient the head exactly are much

more likely to be disastrous with the forceps than with the vacuum extractor, and it must be reiterated that a failed vacuum extraction cannot be equated with a failed forceps operation. I would agree that properly applied obstetric forceps should not damage the brain, but in the series quoted brain damage, fatal or non-fatal, was materially more frequent in the forceps group than in the vacuum-extractor series, and our results here in over 1,000 vacuum extractions confirm the much greater safety of the vacuum extractor. Furthermore, in malrotation of the occiput the vacuum extractor can achieve rotation of the head from either the occipito-posterior or transverse position very much more easily than can forceps or manual rotation, with increased safety for both mother and child.

In view of the foregoing figures derived from the article you have reviewed, your conclusion that the vacuum extractor has no place on the district or a general-practitioner maternity unit is very difficult to understand. The place of instrumental delivery in domiciliary obstetrics and in the general-practitioner maternity unit must always be limited, and present conditions throughout most of this country indicate that all but the simplest instrumental deliveries, whether by vacuum extractor or other means, should be carried out in a specialist unit. Even in this country, however, there are remote areas where this is not practicable, and in parts of the world less generously equipped with hospitals this applies even more strongly, and so intervention has to be undertaken outside a specialist unit. Where this is the case, we believe that the vacuum extractor is safer for the mother, since there is less need for general anaesthesia, less risk of introducing ascending infection, and less risk of trauma to the vagina and cervix. It is safer for the child in that there is less risk of intracranial trauma and less likelihood of applying excessive traction than with the forceps. The figures of the foetal trauma quoted by Schenken and Serr (who as you point out are practising obstetricians) show that even in the hands of the specialist intervention with the head high in the pelvis carries a considerable risk, and except in the case of a second twin almost all such cases are better dealt with by caesarean section. Where the head is little above mid-cavity, however, the vacuum extractor can be used by the experienced obstetrician effectively and safely and even the occasional operator is likely to do much less harm with this than with the forceps. For this reason I would disagree completely with your conclusion about the place of the vacuum extractor outside the specialist unit. I would not wish to advocate heroic use of this or any other instrument, but in properly selected cases it has been shown by Cavenagh² that it can

make a very real contribution to the work of the general practitioner.—I am, etc.,

J. A. CHALMERS.

Worcester Royal Infirmary,
Worcester.

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SIR,—I should like to express my most profound disagreement with some of the views in your leading article on the vacuum extractor (23 September, p. 753).

I have used the vacuum extractor in over 60 domiciliary deliveries in general practice. In no case has there been a stillbirth, neonatal death, or any evidence of cerebral injury. In a few cases there have been small lacerations of the scalp due to the use of the smallest cup, not to prolonged traction. I have not used forceps in domiciliary deliveries for many years. I use the vacuum extractor to prevent delay or foetal distress in the second stage. This is accomplished by applying the instrument after one hour in primigravida and 20 minutes in multigravida unless delivery is imminent.

You state that delivery with forceps will be quicker than with the vacuum extractor; this ignores the time required for getting an anaesthetist and giving an anaesthetic or alternatively using some form of local or spinal anaesthetic. The vacuum extractor can be used without an anaesthetic, so that unless the patient was already anaesthetized the vacuum extractor would be the quicker instrument to use.

"Secondly, delivery is safer because a doctor cannot hope to apply the forceps correctly. . . ." The operative word here is "hope." Surely one hopes to apply the cup correctly too. If one's hopes are not matched by one's achievements a failed or difficult vacuum extraction is less likely to injure the foetus than a failed or difficult forceps delivery.

Your penultimate paragraph is the most insulting I have read for a long time. Your writer ignores the fact that a large number of general practitioners are highly skilled obstetricians. A few are members and a great number diplomates of the Royal College of Obstetricians and Gynaecologists. It is surely ridiculous to suggest that an obstetric house-officer is more competent than an experienced obstetrician who uses his skill in the sphere of general practice.—I am, etc.,

Croydon, Surrey.

THOMAS WHITE.

SIR,—Your leading article on obstetric forceps or vacuum extractor (23 September, p. 753) raises many debatable points. I will confine myself to comment on a few. Generalizations seem inappropriate in the discussion of the relative merits of these two important obstetric tools.

What is meant by foetal distress? The degree of distress will obviously influence the method of delivery, and so will the location

of the patient at the time. What is a trained obstetrician? Is he the same as "a doctor," referred to in the next sentence, or "a general practitioner obstetrician," referred to in the final sentence.

By amalgamating the two indications for assisted delivery—that is, delay and distress—the writer of your leader confuses the issue. Most obstetricians would agree that forceps delivery is preferable to vacuum extraction in cases where rapid delivery is required in the second stage of labour, when foetal distress occurs with the foetal head fully engaged, because there is no doubt that the application of and delivery with the vacuum extractor does take longer than forceps delivery. However, delivery does not require to be excessively rapid if there is no foetal distress, so the question arises whether forceps delivery is really preferable to vacuum extraction for delay in advance of the foetal head in the second stage of labour. My own experience leads me to doubt it, even though I feel that my skill with the obstetric forceps is at least average.

The statement is made that "delivery is safer [with forceps] because a doctor cannot hope to apply the forceps correctly and effectively until he has checked the position of the occiput," and that "properly applied obstetric forceps should not damage the brain." Not all general practitioners are skilled in assessing the position of the occiput from pelvic examination, and fewer still have the necessary experience and skill to correct malpositions of the foetal head. The doctor who cannot diagnose occipito-posterior position of the occiput from his pelvic examination (and this is by no means always easy to the expert, in the presence of a large caput and deep engagement of the foetal head) will be an even greater menace to the unborn child with faulty application and attempted delivery with forceps than he would be with an attempted vacuum delivery, even if the latter fails, provided that he uses the vacuum only to assist uterine contractions and associated maternal effort, and is prepared to desist from any further attempts at delivery if this has not been effected within 20 minutes. Most of the misfortunes attributed to the vacuum extractor have been due to impatience or unduly prolonged application of the vacuum in cases where minor disproportion exists.

I would dispute the leader writer's conclusion that "the vacuum extractor has no place . . . in a general practitioner maternity unit." Given the assurances indicated above, I feel that it can be a safer instrument than forceps in the hands of the relatively inexperienced obstetrician.—I am, etc.,

W. H. LAIRD.

Mid-Antrim Hospitals Group,
Waveney Hospital,
Ballymena, Co. Antrim.

SIR,—Your leading article (23 September, p. 753) on the use of the vacuum extractor and the obstetrical forceps states that neither instrumental technique has any place if the foetal head is not engaged in the pelvis. In the delivery of a second twin with the vertex presenting, where foetal distress occurs, may not the vacuum extractor cup be applied to a head which is not engaged and delivery be expedited? If necessary, external pressure might be applied to the uterine fundus to fix the head. This method of delivering a

second twin in such a case may be safer than version and breech extraction, and quicker than caesarean section.—I am, etc.,

New Pitblago,
Aberdeenshire.

R. J. BENZIE.

Psychotropic Drugs

SIR,—As one of the senior registrars at St. Thomas's my views on the efficacy of the monoamine-oxidase inhibitor drugs may be regarded as prejudiced, but I feel there is something helpful that I can add to the controversy (30 September, p. 861, and 14 October, p. 108).

When I first started my psychiatric training in 1962, in a Bristol hospital, Parstelin (tranylcypromine and trifluoperazine) was being widely used there in the treatment of non-endogenous, neurotic-type depression, and I had no doubt that this was an effective drug in this type of illness. When its use was curtailed there by the cheese-reaction scare the loss of this valuable drug was very noticeable clinically. I then moved to another teaching hospital in London, where, although isocarboxazid was sometimes used, Parstelin was regarded as too dangerous and phenelzine deemed useless.

On taking up my present post two years ago I of course knew that Dr. W. W. Sargent and others regarded phenelzine and the other monoamine-oxidase inhibitor group as very useful drugs in selected patients, but I must admit that at that time I had now become sceptical of their value from what I had been taught. However, I again started to see, as I had done in Bristol, many patients with quite long histories who had failed to respond to other treatments show quite remarkable improvement, but what was even more surprising was the large number of patients with phobic anxiety states improving on the phenelzine regimen.

One of the major criticisms levelled at Dr. Sargent's treatments is that it is his forceful personality and not the drugs that is most effective. This, however, does not explain why the combination of "Gundy and phenelzine" is quite as successful as "Sargent and phenelzine"; nor does the personality factor explain why this improvement may start only 2–3 weeks after commencing the drug and not after the initial interview, and also if the drugs are discontinued it takes a week or so for the condition to return.

One case (treated solely by myself) which convinced me most was that of a man aged 49 who had been phobic since the age 13—that is, 36 years. He became completely symptom-free three weeks after taking phenelzine, and when his drugs were stopped for a blood-flow test his symptoms returned a week or so afterwards.

A very large number of cases seen since has confirmed my belief that phenelzine is a very effective drug for this condition, and in many hundreds of cases I have seen no serious side-effects, taking reasonable precautions.—I am, etc.,

Department of Psychological
Medicine,
St. Thomas's Hospital,
London S.E.1.

G. H. GUNDY.

SIR,—The M.R.C. trial, like most trials conducted on the depressive illnesses seen in inpatients, showed the tricyclic antidepressants

to be superior to the monoamine-oxidase inhibitors. However, Dr. P. Leyburn and his colleagues (14 October, p. 108) imply that they are therefore of little value in the quite different types of depression seen in the outpatient departments of general hospitals.

In a recent review of over 10,000 patients subjected to clinical trials such a protagonist of the tricyclic antidepressants as Dr. I. F. Bennett¹ has confirmed that the monoamine-oxidase inhibitors are at least as effective as the tricyclic drugs in the outpatient type of case. This surely is added confirmation that there are at least two types of depression, and that some patients will only respond to the monoamine-oxidase inhibitors.^{2,3}

Like all potent drugs, the monoamine-oxidase inhibitors have side-effects and must therefore be used with caution, and only in patients whose disability warrants such risks. Even so, fatalities are rare, and with even the most "dangerous" drug, iproniazid, the mortality of 1 in 20,000 patients compares favourably with the 1 in 200 mortality accepted for the surgical treatment of, say, peptic ulcer.—I am, etc.,

C. M. B. PARE.

Department of Psychological Medicine,
St. Bartholomew's Hospital,
London E.C.1.

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- 2 Pare, C. M. B., Rees, L., and Sainsbury, M. J., *Lancet*, 1962, 2, 1340.
- 3 Rees, W. L., *Prescribers' Journal*, 1967, 7, 13.
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Massive Overdose of Adrenaline

SIR,—While we agree with Dr. M. A. Lewis (7 October, p. 38) that the effect of very large doses of adrenaline must in part be open to speculation, we feel that what is known about the effect of smaller doses should be taken into consideration in the rational treatment of overdose.

In the first instance there appears to be no justification for the use of a ganglion-blocking drug. Arterial pressure normally depends to a considerable extent on the presence of vasoconstrictor tone mediated by sympathetic nerves, and interference with these nerves will cause a fall in arterial pressure in the normotensive subject. However, baroreceptor reflexes work in both directions, and when arterial pressure is increased there is reflex slowing of the heart and release of vasoconstrictor tone in an attempt to return arterial pressure to "normal." It is well known that such reflexes reduce to some extent the pressor effect of noradrenaline, and we have experimental evidence in man that the pressor response to small doses of adrenaline is potentiated by ganglion blockade.

We would suggest that the rational treatment of adrenaline overdosage must include the administration of a beta-receptor antagonist such as propranolol in addition to the alpha-receptor antagonist used by Dr. Lewis. This would control the cardiac stimulation caused by adrenaline and reduce the great risk of cardiac arrhythmia. The importance of both alpha- and beta-receptor antagonism has been recognized in the management of patients with phaeochromocytoma (another

of adrenaline overdosage), and this treatment and its rationale has been well described by Dr. E. J. Ross and his colleagues.¹

In cases of accidental overdosage we suggest the following treatment. Intravenous injection of phenoxybenzamine 20 mg. (to antagonize the vasoconstrictor action of adrenaline), followed by intravenous injection of propranolol 5 mg. (to antagonize cardiac stimulating effects of adrenaline). The propranolol should not be given first, as reduction of the vasodilator action of adrenaline may potentiate its vasoconstrictor action, resulting (in the absence of alpha-receptor blockade) in a further rise in arterial pressure. The subsequent dosage of phenoxybenzamine should be judged from the diastolic pressure, and of propranolol from the heart rate.

Dr. Lewis suggested that the hypotension following the episode may be explained when we have some information on the relative duration of action of alpha and beta effects. We have found that the beta (vasodilator) action of adrenaline in the human forearm is more persistent than the alpha (vasoconstrictor) action and that this prolonged vasodilator action can be abolished by beta-receptor blockade.² It is possible that a persistence of the peripheral vasodilator action of adrenaline may have contributed to the hypotension observed in this case.—We are, etc.,

W. E. GLOVER.

Department of Physiology,
Queen's University,
Belfast.

R. G. SHANKS.

Department of Therapeutics
and Pharmacology,
Queen's University,
Belfast.

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National Kidney Centre

SIR,—I cannot allow some of the comments of Drs. M. H. F. Coigley and I. R. McWhinney (14 October, p. 112) to pass unchallenged. But firstly I must support them in acknowledging the indebtedness of all who practise intermittent haemodialysis to Dr. S. Shaldon, and particularly to his pioneering of home dialysis.

Your correspondents are, however, out of touch with the times when they infer that N.H.S. units are not home-orientated. Within 25 miles (40 km.) of their practice are two renal units within the N.H.S. with active home dialysis programmes, one of which (the Queen Elizabeth Hospital) had patients dialysing themselves at home before the National Kidney Centre opened. Without capable staff, thoroughly conversant with problems of dialysis and able to pass their knowledge on to others, one cannot teach patients self-dialysis. It has been the finding and training of such staff which has delayed most units from starting home dialysis. On a recent visit to North America I found nothing to support Dr. Coigley's suggestion that chronic dialysis programmes there are overall more orientated towards home dialysis than are those in Britain. Nephrologists on both sides of the Atlantic recognize Shaldon's and Dr. Scribner's achieve-

ments and appreciate that the logical extension of intermittent dialysis programmes is into the patients' homes.

Your correspondents, possibly because they are not directly involved in dialysis units themselves, underestimate the difficulties. I do not believe that any responsible renal physician would wish to conduct home dialysis without access to hospital facilities. In spite of your correspondents' claim, I can assure them that complications such as haemorrhage or septicaemia do occur on chronic dialysis programmes, even though they may be less common at home than in hospital dialysis. We have recently had occasion to witness the difficulties which may arise when responsibility for medical care is shared between a dialysis centre and another hospital centre. This is not an indictment of the remarkable achievements of the National Kidney Centre, but a recognition of the need for such a centre if it is to continue to have proper access to full hospital facilities. I am sure the Director would agree with this, and it is unfortunate that it has not been possible to make suitable arrangements to this end.—I am, etc.,

B. H. B. ROBINSON.

Renal Unit
East Birmingham Hospital,
Birmingham 9.

Cancer Chemotherapy

SIR,—Apart from experimental and pharmacological data very little is known about 5-fluoro-2-desoxyuridine (5-FudR). Indeed, the advantages of this preparation as compared with the concurrently used 5-fluorouracil (5-FU), which is much cheaper and has a similar spectrum of response in human tumours, seem still debatable,¹ and this has not encouraged the producers to give a large supply of the drug to clinical investigators. As we have had the chance to make some direct observations with 5-fluorouracil since 1961,² and with 5-FudR since 1964 (unpublished), it may be helpful to report briefly on our studies on 5-FudR.

Twenty-eight adult patients with various forms of disseminated cancer were admitted to the clinical trial of 5-FudR. They included 20 patients with mammary cancers; three patients with rectum or large-bowel cancer; one patient each with cancer of skin, tongue, pancreas, and prostate; and one patient with an adenocarcinoma with site of the primary unknown and multiple skin deposits. The administration schedule in 26 cases was: eight-hour venous drip of amounts varying between 50 and 100 mg. daily for 7 to 30 days (dissolved in 500 ml. of 5% dextrose). One case had an external carotid artery infusion, and one had an intrapleural injection.

Some degree of toxicity (mainly represented by gastralgia, vomiting, and diarrhoea) appeared in 11 of the 26 patients treated by the venous route. One of them had toxic manifestations after 10 days of treatment and all the others after more than 16 days. These side-effects reached important proportions in only six of the 11 cases (toxicity=2+ according to the Karnofsky criteria).³ In only one patient did we note frank leucopenia (1,500/cu. mm.). In nine cases leucopenia under 4,000 W.B.C./cu. mm. was found during treatment, but it must be pointed out that six of the patients showing leucopenia had begun the treatment with very low counts—namely, 2,200, 3,800, 3,100, 2,900, 3,800, 2,800/cu. mm.—and in none of these was a further drop of leucocytes noted during or after treatment. Platelet counts were not con-

sistently changed, and sometimes they increased. Only the haemoglobin content of the blood diminished almost constantly by 1 to 3 g./100 ml. This very mild damage to leucocytes and platelets is not common; our own experience does not suggest that treatment by 5-FU could have been given in such leucopenic patients.³

Clinical improvement began generally between the third and tenth days of treatment. There was an objective improvement in 12 cases and some subjective improvement in 20. Toxicity and clinical improvement were associated in only seven cases, while five objective and 13 subjective remissions were obtained without any toxicity. In some instances maintenance therapy by 5-FU on an ambulatory basis was possible after 5-FudR drip treatment, and it delayed the clinical relapse for months; otherwise relapse occurred between 15 and 45 days after stopping the treatment.

According to the described observations we suggest that 5-FudR be used instead of 5-fluorouracil by slow venous drip as a palliative anticancer drug for inducing remission in severely ill haematologically depleted patients (washed red cell transfusions being possibly added), and 5-FU be reserved for less ill patients or for maintenance therapy by weekly rapid venous injection of 10 mg./kg.²—We are, etc.,

MARIO FIORENTINO.
ENZO FINOTTO.

Departments of Radiotherapy and
of Internal Medicine,
Ospedale Civile di Padova,
Italy.

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- ² Fiorentino, M., and Conte, G., *Tumori*, 1963, 49, 379.
- ³ Karnofsky, D. A., *Clin. Pharmacol. Ther.*, 1961, 2, 709.

Safer Dental Anaesthesia

SIR,—The Ministry of Health Report on Dental Anaesthesia¹ damns with faint praise the intravenous techniques which are used in dental surgery, and many will question the statement that, "Techniques such as that advocated by Jorgensen and associates . . . do not appear to be entirely satisfactory, particularly in children under 10 years of age, but seem to provide an alternative to general anaesthesia for conservative work in certain older patients."

There are many dentists who utilize this form of anaesthesia for their daily routine work, and, like Dr. Bourne,² I have been greatly impressed by the smooth manner in which dental surgical procedures may be carried out by incremental injections of intravenous anaesthetic, and the patient at the end of the operation is still able to walk from the chair with a little help. Certainly the dentist must be adequately trained in the anaesthetic technique, and have the assistance of two experienced dental nurses. The intravenous technique is further improved by using an intravenous drip of 5% dextrose as a medium through which intermittent injections may be given, and in this manner a session of extended rehabilitative oral treatment may be carried out in one session lasting for two hours or more. Safety is of course an important prerequisite to the use of any anaesthetic. In one series of 15,000 cases dealt with by the Jorgensen and intermittent

methohexitone methods³ no immediate or late complications occurred, and in 2,000 of these the treatment lasted for one to two and even more hours. The technique is described in a film.³

A Scottish dental school has recently proposed a diploma course in dental anaesthesia. While one must deplore the creation of too many "splinter" diplomas, the suggestion in this case is worth serious consideration, particularly if the course provides adequate training in the newer intravenous techniques.

—I am, etc.,

Royal Infirmary,
Greenock.

A. LYALL.

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¹ *Dental Anaesthesia*, Report of a Joint Subcommittee of the Standing Medical and Dental Advisory Committees, 1967, Ministry of Health. H.M.S.O., London.

² Bourne, J. G., *Brit. med. J.*, 1967, 3, 616.

³ Robertson, A. B., 1967, personal communication.

Mental Handicap and the Family

SIR,—Your article, "Mental Handicap and the Family" (7 October, p. 5), gave a summary of the findings of a working party set up by the National Society for Mentally Handicapped Children. It may be of interest that a co-ordinating centre of the type described has been in existence in Glasgow for almost three years.

As a result of their investigation into the problems of the handicapped child and his family, begun in 1955, the Carnegie United Kingdom Trust made a grant of £30,000 to the Corporation of Glasgow to assist in setting up a centre at which services could be co-ordinated and parents could receive medical and social advice and support.¹ Glasgow Health and Welfare Department augmented this sum, and in December 1964 Balvicar Centre was opened. Since then 264 children have attended.

Pre-school children with all types of handicap are referred to the centre, which aims at providing all medical services other than in-hospital care. The centre is staffed by the health and welfare department, and consultants (paediatrician, orthopaedic surgeon, neurologist, ophthalmologist, otologist, child psychiatrist) are seconded from the regional hospital board to visit the centre at regular intervals. When inpatient treatment is required the consultant admits the patient to his own hospital unit. Routine hearing, vision, and psychological testing are carried out in all cases. A dentist, a psychologist, a physiotherapist, and a speech therapist also attend at the centre. An audiology unit functions within the centre. There is also a special day nursery, to which patients can be admitted for training. Play therapy groups are arranged for diagnostic and remedial purposes. Transport can be provided. General practitioners are kept fully informed of all diagnoses and treatment.

Parent guidance and support are most important. Advice on home management of patient, therapeutic apparatus, and suitable play material is given. Family planning and genetic counselling are available. Co-operation with hospital, social, and voluntary services is maintained, so that overburdened parents can be relieved by domiciliary help, housing improvement, and admission of patients for day or temporary residential care. Parents are encouraged to apply to the centre in family crises, so that prompt measures can

be taken to prevent breakdown. At intervals parents' meetings in the evening are held, with lectures, discussions, and films on relevant subjects. Continuity of care is achieved throughout the early years and the educational placing interview is conducted at the centre, where friendly and familiar surroundings reassure the parents and present the child at his best.

Even in this short space of time Balvicar Centre has proved once again the value of a multi-disciplinary team in dealing with handicapped children. The patients are assisted to reach their potential and the parents appreciate the co-ordination of advice and treatment at the centre.—I am, etc.,

Balvicar Centre,
Glasgow S.2.

LILLY C. HALL.

REFERENCE

¹ Tizard, J., and Grad, J. C., *Handicapped Children and Their Families*, Reports to the Carnegie United Kingdom Trust on the Problems of 600 Handicapped Children and their Families, 1964. Dunfermline.

SIR,—In your leader "Mental Handicap and the Family" (7 October, p. 5) you quoted the recent report of the National Society for Mentally Handicapped Children,¹ which, although in many respects was admirable, gave an erroneous impression of the procedure of legal ascertainment. To say that this process is an administrative one designed for the negative purpose of excluding children from school rather than a positive attempt to decide what is best for the child's future is a misconception of what the medical staff of a good local authority are doing to provide community care for subnormal children.

In the vast majority of local authorities the same medical staff serve both the education and health departments, and the dichotomy referred to in the report is far less real than is implied. Most mentally handicapped children are known to the local health authority before school age, and at some stage a decision has to be made about whether his needs are best met by the regimen of a training centre or by the services of a special school. Most doctors working in this field regard this as a clinical matter, involving taking a history, making a physical examination, and psychometric or developmental assessment. Clearly children vary considerably, but only a limited number of establishments can exist for their training and education, so that they have to be placed in the establishment most likely to provide for their immediate needs.

Of course on occasions mistakes will be made and on other occasions the educational needs will alter, in which case they can be rectified, but the impression given that a once-and-for-all decision is made on one medical examination is far from accurate in most progressive local authorities today, and the decision about whether the child attends school or training centre is simply an incident in his continuing care, and one which allows considerable flexibility.—We are, etc.,

B. A. SMITH.

M. BUSH.

J. BROWN.

Health Department,
Ipswich.

REFERENCE

¹ *Stress in Families with a Mentally Handicapped Child*, Report of a working party set up by the National Society for Handicapped Children, 1967. London.

SIR,—What Rip van Winkle was responsible for the leading article on the above subject (7 October, p. 5)?

Ten years ago, in accordance with the provisions of the National Health and Education Acts, Monmouthshire County Council, with the Welsh Hospital Board, had in operation a scheme for the mentally and/or physically handicapped child which, with the exception of income-tax relief, fulfilled each and every recommendation in this leading article. Moreover, some 10 years ago this scheme for the mentally handicapped child was fully reported in *The Medical Officer*,¹ a publication which would seem to have escaped your notice, but which brought visitors and correspondence from the other side of the world.

Finally, and again about 10 years ago, the members of the National Society for the Mentally Handicapped (then, I think, the Parents' Association) were told about this scheme at their own annual general meeting in London's Royal Festival Hall—told that local authorities have limited spending power, but exercise their own priorities, and advised that if they wanted a similar scheme in their own localities then they should take active steps to become elected members of their own local authority.

Truly, the prophet still has little honour in his own country.—I am, etc.,

MARY E. COCHRANE-DYET.

Maindiff Court Hospital,
Abergavenny,
Monmouthshire.

REFERENCE

¹ Rocyn-Jones, G., Cochrane-Dyet, M. E., and Fuller, A. M., *Med. Offr*, 1957, 97, 221.

Chronic Thyrotoxic Myopathy

SIR,—Dr. D. Gaan, in his interesting report of a case of chronic thyrotoxic myopathy with involvement of respiratory and bulbar muscles (12 August, p. 415), referred to doubts that have been expressed about the existence of acute "thyrotoxic myopathy" (affecting bulbar muscles) as a separate entity distinct from myasthenia gravis occurring fortuitously in a hyperthyroid patient. The case of a patient recently under my care does suggest that acute bulbar involvement may occur as the result of thyrotoxicosis alone; it is not conclusive, as he may have had acute myasthenia gravis with spontaneous remission, but this seems improbable.

The patient, a man of 73, was a proved case of thyrotoxicosis and had been treated medically for two years with apparent success. He was then lost sight of for a year, but had continued taking carbimazole in doses of from 5 to 15 mg. daily. He was referred again at the end of this time, having developed marked exophthalmos and ophthalmoplegia with diplopia, a goitre of considerable size, and typical pretibial myxoedema, none of which had been present when first seen. An edrophonium test was negative in that no appreciable improvements in ptosis or ocular movement was induced and on clinical and biochemical grounds (protein-bound iodine 4.8) he was regarded as euthyroid and suffering from typical "exophthalmic ophthalmoplegia." Carbimazole dosage was reduced to 10 mg. with a view eventually to discontinuance.

He remained well apart from the ocular condition for about three months, when he started losing weight and the P.B.I. rose to 8.1. He was complaining of general fatigue, though this was not of striking degree. Relapse of hyperthyroidism was suspected, but before treatment with radioactive iodine could be arranged he had

to be admitted to hospital as an emergency about six weeks later in a condition of extreme emaciation, his weight having dropped from eight stones (52 kg.) to under six stones (38 kg.). His voice was reduced to a feeble whisper, he could barely articulate, and was unable to swallow or cough effectively. Breathing was shallow and there were signs in the lungs compatible with inhalation of food material. There was generalized weakness of the body musculature, but not more than might have been expected in his cachectic state, and limb movements and reflexes were still present.

Iodine uptake and excretion 14 days before admission were in the "gross hyperthyroid" range and the P.B.I. was now 21.8. Urinary creatine (two estimations) was over 800 mg. per 24 hours and serum potassium lay between 2.4 and 3.1. A Gastrografin swallow, difficult to carry out, showed grossly delayed passage both at pharyngeal level and in the oesophagus. Tube feeding was attempted but proved impracticable, and the patient deteriorated rapidly, becoming semistuporous and looked like dying of inanition. Intravenous feeding was then started and later, despite a negative response to a second edrophonium test, a trial of neostigmine was made. From this time his condition changed for the better and swallowing and speech began to improve, though the response was by no means dramatic. In view of his high iodine uptake and excretion and serum P.B.I., carbimazole 60 mg. daily, as crushed tablets, was given throughout, at first by gastric tube, later orally.

Over a period of four or five days he improved to the point of being able to swallow fluid or semi-solid feeds, and neostigmine, discontinued at the end of this short period, was not required again. His subsequent gradual recovery was interrupted by severe neutropenia, thought possibly due to carbimazole, though he had been taking this drug for three years without apparent ill-effect. It was therefore stopped, with resultant partial relapse in thyrotoxicosis, and had to be reinstituted at a lower dose level, since it was believed that in this case it was literally a life-saving drug. With cortisone and transfusion the white count eventually reached normal levels and full recovery from the bulbar myopathy was achieved. He regained normal speech and swallowing and all his lost weight. When last seen, following radioiodine ablation of the thyroid and five months after the onset of the acute illness, he was well.

Neostigmine, given only for a few days, was not needed again; it is therefore difficult to regard this as a case of myasthenia gravis unless we assume that it underwent rapid spontaneous remission. If so, this occurred *pari passu* with successful control of thyrotoxicosis, which is not the sequence of events observed hitherto for true myasthenia gravis. Moreover, "limited relief of thyrotoxic myopathy with Prostigmin has been observed" and this cannot be used as a definite means of differentiation.¹ Just what part the brief period of Prostigmin therapy played in his recovery is difficult to assess, and the fact that recovery apparently began at that time may be fortuitous. It seems more likely that this case could be classed as acute thyrotoxic myopathy with the major onslaught on the bulbar muscles. There seems to have been an acute flare-up of hyperthyroidism in the few weeks prior to his emergency admission, the P.B.I. rising from 8.1 to 21.8 and the radioactive tests reaching high levels. This flare-up corresponded with the onset of bulbar paralysis. Ramsay² concludes that so-called acute thyrotoxic myopathy may simply represent one end of the spectrum of thyrotoxic muscle disorder.

The significance of the low serum potassium is uncertain; Whitfield and Hudson³ found normal potassium levels in their patients. They stressed the severity of the

hyperthyroidism in their cases, who were all "chronic," and also that men are predominantly affected.—I am, etc.,

W. M. PRIEST.

Warneford General Hospital,
Leamington Spa.

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Corrosive Poisons

SIR,—I wish to comment on the statement on the treatment of corrosive damage to the stomach made by Drs. S. C. Kennedy and A. E. Bavaki (14 October, p. 93), where the use of magnesium bicarbonate was advocated.

Corrosive poisoning by acetic acid is not a rare occurrence in Ceylon, especially in the rubber-producing areas (acetic acid being used in the coagulation of rubber latex and being available "over the counter"). Our teachers used to impress upon us that magnesium hydroxide or dilute calcium hydroxide should be used locally in the mouth and be given orally whenever the patient could swallow—which was seldom. Bicarbonates were not advocated owing to the theoretically increased risk of perforation due to the evolution of gas, which I believe is a reasonable assumption.—I am, etc.,

London S.W.4.

D. R. MUNASINGHE.

Taking Blood Samples

SIR,—Following the letter from Dr. W. Joan Ferraby (7 October, p. 52), with which I agree, I have always been amazed why most doctors and technicians use a finger rather than the ear lobe, which I have found more suitable for the following reasons:

- (1) The skin of the lobe is cleaner—thus reducing the chance of sepsis.
- (2) The circulation is more easily stimulated.
- (3) There are fewer tactile corpuscles in the lobe and the skin is much thinner; hence the prick is less vicious and less painful.
- (4) Moreover, the apprehensive patient does not move nor witness the procedure, which is a great advantage.—I am, etc.,

London W.1.

I. MARTIN-SCOTT.

Prevention of Rh-haemolytic Disease

SIR,—Professor C. A. Clarke (7 October, p. 7) gives further results of the clinical trial on prevention of Rh-haemolytic disease with the use of anti-D gammaglobulin. He convinces that "prevention" is possible. It is realized that every detail in such a complex investigation cannot be reported, but it would greatly help those likely to be concerned in any future programme of prevention to have answers to some further points.

There are now reported 21 out of 131 treated women and 26 out of 136 controls who have had second Rh-positive ABO-compatible infants. The timing of antibody tests during and after this second pregnancy is not given, nor are facts about the infants. Have they all been Coombs' negative, normal, and liveborn?

Is it known of the remaining 110 women in the treated group that they have not been pregnant? How many have aborted during a second pregnancy, and have they also been tested for antibodies? How do these findings—for example, stillbirth or abortion rate—compare with the control group? Although in the treated and control groups the incidence of second pregnancies is similar, this seems small for the time interval. How does this rate compare with Liverpool as a whole?

In the *B.M.J.* (16 October 1966, p. 907) there was mentioned an experiment with anti-Kell, in progress, designed to find out if suppression of D-immunization was specific. Are these results yet available? One speculates, if suppression of D-immunization is able to suppress other blood group immunizations, whether there might not also be some impairment of general immunity to infection. Does this not require further investigation and close-controlled follow-up of treated women? A limited search for anti-gammaglobulin antibodies is mentioned and anti-Gm(a) has been found in 1 out of 20 treated women (5%). Does this represent the true incidence in so small a number? One might speculate that anti-gammaglobulin antibodies in some cases would have adverse effects if subsequent transfusion were necessary, that they might have clinical implications for subsequent infants if some of these antibodies could cross the placenta, or even have long-term effects for the patients themselves. There has already been one unexpected and as yet unexplained result of the experimental anti-D prevention work—that is, the IgM enhancement of immunization. What is the ultimate relationship of anti-Gm in rheumatoid arthritis likely to be? Gammaglobulin used for other indications—for example, rubella in pregnancy and hypogammaglobulinaemia—has not been blood-group specific, and this use might not be comparable to the use of anti-D γ in normal non-pregnant subjects.

These speculations all concern assessment of the risks to the treated patients. There is less doubt in weighing the risks of deliberate immunization to any Rh-negative volunteers. No one would wish the continuance of exchange transfusion, the family distress in Rh-haemolytic disease, and the possibility of stillbirth for any longer than necessary. But surely an intensification of research is called for to ensure as far as possible the long-term safety of treatment before it can be unquestionably right for national use.—I am, etc.,

S. MURRAY,

Director, Region 1,
National Blood Transfusion Service,
Newcastle upon Tyne.

Salmonella in Tortoises

SIR,—I should like to draw the attention of your readers to the danger of tortoises as a cause of salmonella infection in children.

A patient of mine, a little girl aged 5, developed an attack of acute enteritis with abdominal pain, blood-stained faeces, and pyrexia. As there was no improvement following treatment, she was admitted to a fever hospital where *Salmonella typhimurium* was isolated from the stools. In the interim I discovered that the patient had a pet tortoise, which she frequently fondled, and so I suggested to the patient's mother that she should

have the faeces of the tortoise examined. This was subsequently done at the Royal Veterinary College, where *Salmonella canastota* was isolated from the faeces of the tortoise.

In order to establish the frequency of salmonella infection in tortoises I obtained the following information with the help of the Librarian of the Royal College of Veterinary Surgeons.

In 1958 Schwabe (unpublished) isolated 17 salmonella serotypes from 11 tortoises (*Testudo graeca*) imported from Morocco to Britain. In follow-up studies in Tangier 78% of tortoises examined were positive, and they yielded 15 salmonella serotypes from the terminal gut and rectum. In 1959 Bövre and Sandbu¹ isolated 19 serotypes, including two which were new, from 27 of 33 pet tortoises examined in Norway. All the strains were lethal to mice. In 1962 Boycott² reported isolation of salmonella in England from 41 of 45 *Testudo graeca* and 33 of 50 wild tortoises examined. The increasing hazard to public health was emphasized by some statistics published in 1961 by the Universities Federation for Animal Welfare,³ in which they stated that in a few years prior to 1961 46 tons of pets from Morocco were imported to Great Britain, whereas by 1961 this figure had reached 80 tons per annum.

I should therefore like to emphasize that in any unexplained salmonella infection, especially in a child, careful inquiries should be made about the possibility of a pet being the vector of the infection.—I am, etc.,

London N.W.6.

L. T. NEWMAN.

REFERENCES

- ¹ Bövre, K., and Sandbu, P., *Acta path. microbiol. scand.*, 1959, 46, 339.
- ² Boycott, J. A., *Science*, 1962, 137, 761.
- ³ Universities Federation for Animal Welfare, Annual Report, 1960, p. 12. London.

Abortion and Conscience

SIR,—The Abortion Act has now passed its final stage and is law. Because of the determination of the sponsors to have the law changed before there was a full inquiry into the facts there is still no body of reliable evidence to guide doctors or the public in the interpretation of the various clauses.

One point seems clear, and that is the new law will permit a doctor to refuse to recommend or perform an abortion on grounds of conscience. This clause was intended to protect those doctors (and nurses) with strong religious objections to abortion. There are, however, conscientious objections other than religious. There is a medical conscience which dictates that one should not interrupt the process of human life unless there is good evidence that such a measure is entirely justified in order to avert a dangerous situation. This used to mean one which was dangerous to the mother, though now we must consider danger to other members of the family and no doubt eventually to society.

A doctor's conscience should be satisfied that these dangers are real, adequately proved, and fully relevant to the patient's situation. If this evidence is not forthcoming a doctor's conscience would prevent him from taking such drastic action. That the law makes it permissive for doctors who have not got this medical conscience does not remove

from the doctor who possesses one the right to act according to it. It would be intolerable for a doctor to be pressurized into what he considers to be bad medical practice in order to conform with a new law. Parliament may well have thought that the number of "cranks" who will not abort without adequate medical indications are few and can be ignored. I question this. It has been possible for a "permissive" gynaecologist with the support of "permissive" psychiatrists to earn legally £250,000 in one year. This alone indicates that most gynaecologists, who are presumably no less competent, are not tripping over themselves to enter

this lucrative field. Their medical conscience is more important to them than wealth.

One does not wish at this stage to raise objections to a new law, but it is important to declare that a medical conscience should not require a special dispensation but is our main *raison d'être* as a profession. We must not only protect it, but try to convert our lapsed colleagues with the medical evidence. I now feel that I, too, can campaign for Abortion Law reform, but this campaign will be based on existing facts and a continuing search for truth.—I am, etc.,

Edgbaston,
Birmingham.

MYRE SIM.

Fluoridation of Water Supplies

SIR,—Dr. Ronald L. Kerr is entitled to his personal views regarding the fluoridation of water supplies (21 October, p. 176), but he must surely be aware that the evidence he has adduced in favour of his arguments has been systematically and patiently refuted during the last 10 years.

The refutations have been stated so frequently and at such length, indeed, that I would not presume to ask for further space in your correspondence columns to deal with them. Perhaps the handiest compendium of information, which includes the arguments of anti-fluoridationists, is the report of the proceedings of the Eire High Court, following which Mr. Justice Kenny delivered his now famous judgement.¹

All who have made a special study of fluoridation have included the study of the case against the measure, and, although there may be a handful of people who have doubts, the practical experience of the effectiveness and safety of this measure, supported by a mass of fundamental research, has dispelled the slightest doubt from the minds of the majority. At no time during the period in which fluoridation of water supplies has been practised in any country of the world has a single case come to light of illness caused by, or aggravated by, the consumption of water containing one part per million of fluoride.—I am, etc.,

A. J. DALZELL-WARD,

Medical Director,
Central Council for Health Education.
London W.C.1.

REFERENCE

- ¹ *Fluoridation*, judgement delivered in the High Court by Mr. Justice Kenny, Dublin, 1963 (Department of Health, Dublin).

SIR,—I was impressed by Dr. Ronald L. Kerr's letter (21 October, p. 176) with its comprehensive references, and would like to emphasize one of the points he raised.

If we allow the public water supply to be used as a means of mass medication in order to influence a small section of the community (at the same time ignoring its effect on the much greater remainder) it introduces a most dangerous precedent of dictatorship, against which tyranny this country has fought on many occasions in the past.

We may next be forced to accept somebody's whim of putting oestrogens in our drinking-water in the hope of preventing prostatic cancer in a limited number of elderly men, while ignoring its effect on the women of the country.

Surely it is time the B.M.A. had the courage to admit it has made a mistake in supporting such a blindly unscientific and dangerous policy.—I am, etc.,

East Grinstead,
Sussex.

H. TUDOR EDMUNDS.

SIR,—To Dr. Ronald L. Kerr's letter on this subject (21 October, p. 176) I would like to add a postscript, if I may, to the effect that before such a project is put into practice it is the duty of its proponents to establish their case for it doing some good, which, in my submission, they have not done. Nothing in the way of convincing evidence has so far been put forward and the "pro" case appears to rest entirely on suitably selected statistics about "60% reduction of dental caries" (whatever that means). Statistics can be made to "prove" that black is white.

The classical "control experiment" case of North and South Shields, where South Shields had water with a naturally occurring fluoride content of 1 p.p.m.—the optimum advocated by the proponents—while North Shields had none, was reviewed by the Government's own spokesman Dr. R. Weaver,¹ who showed grounds for supposing, as Dr. Kerr quotes, that dental decay in South Shields was postponed for two to three years without its total amount being affected. But there has been no hint of a reduction in the cost of dental services, or any increase in the level of general health in the latter town.

Less publicity is given to the authoritative work *Fluorine Intoxication*, by Dr. Kaj Roholm,² which is available in the British Museum library. He gives a most emphatic and unqualified warning that in no circumstances whatever should children be given fluorides in any dosage whatever.—I am, etc.,

Liskeard,
Cornwall.

W. H. SPOOR.

REFERENCES

- ¹ Weaver, R., *Proc. roy. Soc. Med.*, 1948, 41, 284.
- ² Roholm, K., *Fluorine Intoxication*, 1937. Copenhagen.

SIR,—I was most interested to read Dr. Ronald L. Kerr's most excellent letter on the subject of fluoridation of drinking-water (21 October, p. 176).

May I say how much I endorse every word of what he says. Any member of the community is free to take fluoride if he wishes to do so. Can there be any sense in denying

him the right to refuse to take it if he so wishes?—I am, etc.,

Fulmer, Bucks.

RICHARD FAGAN.

SIR,—I was pleased to see the letter on this subject by Dr. Ronald L. Kerr (21 October, p. 176), who takes up the only reasonable approach to this subject. It was a great tragedy when the B.M.A. accepted the recommendation of a subcommittee to encourage fluoridation and so erode still further what little freedom we have left. Both freedom and health are lost under fluoridation.—I am, etc.,

Glasgow.

W. HAROLD EMSLIE.

SIR,—Dr. Ronald L. Kerr's letter (21 October, p. 176) seems unanswerable on medical or ethical grounds. If fluoride against caries, why not other toxic "preventive medication" that any strong lobby might persuade the authorities to add to the water? These things always begin as the wholly beneficent intention of men who know what is good for the people.

I am not given to supporting campaigns, but I must in this important test case add my voice to protest against a piece of political arbitrariness which goes far beyond the civically or scientifically justifiable.—I am, etc.,

London W.1.

H. V. DICKS.

SIR,—The plea by Dr. Ronald L. Kerr (21 October, p. 176) for a reassessment of the question of fluoridating the water supplies is timely, and should be seriously considered by the B.M.A. Council and the Ministry of Health.

To my mind the most important aspect of all is the ethical one. It seems strange that the Ministry of Health can promote—and the B.M.A. support—a line of conduct which if practised by an individual would not be tolerated either by the public or by the Ministry itself. If a doctor gave his patients treatment against their wishes he would render himself liable to an action at law for assault. A plea that he believed the treatment to be beneficial might mitigate sentence but would not clear him of the charge. If it transpired that he knew that some of his patients so treated could not possibly benefit from it his only hope would be to plead guilty but insane.

Apart from the criminal aspect, such an offender would probably find himself in serious trouble with the G.M.C., and, should the victims be N.H.S. patients, he would risk severe penalties from the Ministry of Health acting through the local executive council.

Why can the Ministry of Health and the B.M.A. get away with it?—I am, etc.,

Brighton, Sussex.

G. R. MITCHELL.

SIR,—Surely Dr. Ronald L. Kerr (21 October, p. 176) cannot be serious in his suggestion that fluoridation is "compulsory mass medication." Every piped water supply contains some natural fluoride, in some areas at a higher concentration than one part per million. Fluoridation, which in temperate zones means the adjustment of F ions in the water to 1 p.p.m., has been achieved in some areas merely by mixing natural waters of

differing fluoride content. Can this be called "mass medication"? The fact that in this country fluoridation would usually involve the addition of F ions is immaterial to this argument. In some parts of the world, such as large areas of the Sudan,¹ a reduction in the fluoride content of well-water would be needed to produce the optimum concentration.

Fluoridation in the U.S.A. was started over 20 years ago and now is supplied to more than half the population receiving piped water. Vigilant public health authorities have confirmed that the only effects are dramatic reductions of dental decay, together with some still not fully substantiated reports of reduction in the incidence of osteoporosis of the aged.—I am, etc.,

R. D. EMSLIE,

Chairman, Dental Health Committee,
British Dental Association.

Department of Preventive
Dentistry,
Guy's Hospital,
London S.E.1.

REFERENCE

¹ Emslie, R. D., *Brit. dent. J.*, 1966, 120, 167.

Adams-Stokes Syndrome

SIR,—Congratulations to the B.M.J. for encouraging (28 October, p. 199) the use of the old-fashioned but truer name for the syncopal syndrome associated with complete atrio-ventricular block—the "Adams-Stokes Syndrome"—in preference to the now frequently used "Stokes-Adams Syndrome." The latter has been too widely adopted for the usual slovenly modern reason that it comes more easily to the tongue than the former, and so tends to be used in spoken bedside or lecture-room teaching. There can be little doubt about the primacy of Adams, who wrote in 1827, over Stokes, whose cases were described in 1846. It ought not to be overlooked that the first cases were described by Morgagni in 1762 and Spens in 1793, but perhaps the "Morgagni-Spens-Adams-Stokes Syndrome" would be in danger of becoming slurred into the "Stokes-Adams Syndrome."—I am, etc.,

Edinburgh.

J. G. M. HAMILTON.

Use of Thorotrast

SIR,—I have read the letter from Dr. G. A. Granger (14 October, p. 112) with some interest. Dr. Granger implies in his letter that the recent article by myself and Dr. E. R. D. Williamson (22 July, p. 206) indicates that Thorotrast may be used for conditions other than those specified by the U.S. Food, Drug, and Cosmetics Act, details of which are given in the literature enclosed with each vial of Thorotrast sold in the U.S.A.

I would like to point out that our article referred to the former use of Thorotrast in Britain, and that the study on which it was based was specifically undertaken, as was pointed out in the paper, to obtain information on the morbidity which may follow the use of this substance. With one exception the cases which we studied were given Thorotrast prior to 1947. As far as I am aware the clinical use of Thorotrast was discontinued in Britain at that time because of an increasing awareness of the dangers inherent in the use of a radioactive substance

which is retained indefinitely by the body. Such dangers are illustrated by reports of very extensive chromosome damage found in patients who have received intra-arterial injections of Thorotrast.^{1 2}—I am, etc.,

A. O. LANGLANDS.

M.R.C. Clinical Effects of
Radiation Research Unit,
Western General Hospital,
Edinburgh 4.

REFERENCES

- ¹ Fischer, P., Golob, E., Kunze-Mühl, E., Benhaim, A., Dudley, R. A., Müllner, T., Parr, R. M., and Vetter, H., *Radiat. Res.*, 1966, 29, 505.
- ² Buckton, K., and Langlands, A. O., *Int. J. Radiat. Biol.*, 1967, in press.

Oculogyric Crises after Phenothiazines

SIR,—The neurological complications associated with the use of perphenazine are "as yet poorly recognized," according to Drs. E. C. B. S. Keat and P. J. Toghill (30 September, p. 867). If this be the case it is my contention that the manufacturer cannot be blamed.

In 1964 a 26-year-old patient in the second trimester of her second pregnancy was given Fentazin Duolets (6 mg. perphenazine in a long-acting tablet). She had taken one tablet 12-hourly for but three days when I received a message suggesting that the patient had "lock-jaw." The patient's husband had good perception. The risus sardonius with which my patient greeted me was quite startling. Thanks to the manufacturer's information leaflet I was not side-tracked into a bizarre diagnosis. It may be argued that I was fortunate in having this information ready to hand in my "series" of one.

To plead ignorance when information has been disseminated (and indeed continues to be thus included in each original pack of tablets of the drug in question) does not seem justifiable to me.—I am, etc.,

WILLIAM J. O'CONNELL.

Fareham, Hants.

Consultant Distinction Awards

SIR,—The results of the B.M.A. ballot (*Supplement*, 21 October, p. 22) revealed very little of the opinions of consultants on distinction awards, as the questions asked were so few. They did show, however, an overwhelming majority in favour of change, and this must indicate widespread dissatisfaction. It is to be hoped that this dissatisfaction will be resolved in public and private debate. Clearly the majority favour awards as a means of acknowledging those who have made outstanding contributions to medicine, but the scheme loses its point when a very large proportion of consultants are given awards. One-third at present receive them, and in the course of a career more than a third, possibly more than a half, might receive an award at some time or other. This has three serious disadvantages.

Firstly, the further down the rank-and-file of consultants the distinction awards extend the more difficult it becomes to decide who shall get them and who not, and this is a great source of unrest. It is widely felt that the criteria on which the "C" awards are made are very slender, and if the rule of secrecy were lifted many decisions would be very difficult to defend. This is no slight

on responsible committees, but an indication of the difficulty of their task and the small amount of information they work on.

Secondly, as distinction awards are so widely attained, any committee considering consultants' salaries is bound to consider awards as part of the salary structure, to the detriment of those who do not have them.

Thirdly, by awarding a label of merit to one-third of consultants there is an immediate implication that the remainder are without merit, which puts them at an immediate disadvantage in salary negotiations. As a result there are numerous consultants who have done 10 years' postgraduate training and acquired two or three higher qualifications who earn much less than many of their general-practitioner colleagues.

The solution to this unsatisfactory pay structure is to reduce the number of merit awards and confine them to doctors of undoubted merit. The "C" award should be abolished and incorporated in the normal pay structure. Whatever happens, our negotiators must establish a proper salary structure for specialists independently of the merit awards, otherwise the non-merit-award consultants will rapidly become the Cinderellas of the Health Service.—I am, etc.,

Ashington Hospital,
Northumberland.

T. MANNERS.

Approval of Emergency Treatment Service

SIR,—The reason for the B.M.A.-sponsored Emergency Treatment Service not getting off the ground has, I submit, little to do with delay in obtaining approval (21 October, p. 176). It lies elsewhere.

Firstly, the insistence that membership of the Emergency Treatment Service shall be confined to subscribers to the Telephone Answering Service. This proviso operates to the detriment of those of us who go to great trouble to maintain standards by ensuring that our telephones are always manned, and who therefore have no need of a telephone answering service. Our reward is to be barred from membership of a B.M.A.-sponsored Emergency Treatment Service. I am impelled to ask what sort of general practice the B.M.A. is seeking to encourage. Is it the second-rate lock-up, or one where the practitioner seeks to ensure that telephone calls are properly dealt with and not left to the caprice of an inefficient G.P.O. telephone transfer service?

Is the Emergency Treatment Service not familiar with the situation where a caller hangs up in despair long before the transfer service cuts in? That is why some of us do not wish to depend on an answering service. I am not unaware of the commercial element in all this, whereby the firm running the telephone answering service looks to the income therefrom in order to provide a cushion against loss in running an emergency treatment service. This does not make the proviso any more palatable. The Central Advisory Committee should do more than pay lip service to the best standards of practice organization, and they might make a start by scrapping the requirement of Telephone Answering Service subscription.

Secondly, the Emergency Treatment Service is quite simply too expensive. Complaint to this effect is met by the organizers pointing out that the subscription is intended to cover 25

calls per month, but, Sir, apart from a few areas, this figure greatly exceeds actual numbers in the experience of most of us. I have a not inconsiderable list and my average is seven emergency calls a month, which on the Emergency Treatment Service scale would work out at £3 a call. The night call refund from executive councils makes little impact, since most night calls originate before midnight; and may I further remind the Central Advisory Committee that executive councils via the Minister have set their faces against handing over all night and weekend calls to a call service, and suggest that those wishing to do so should instead opt out of night work altogether and forgo the payment therefor. (It is in fact only by handing over all out-of-hours calls to a service that 25 visits would accumulate even in bad areas.) Further it should not be necessary for me to remind the sponsors that the use of call services is rationed by appropriate committees to so many calls per thousand patients per year as a condition of approval of use, and that it would be only enormous lists which would approach a ration of 25 calls per month. No single-handed doctor could possibly approach it.

No, Sir. The organizers must adopt a much more realistic attitude towards a viable Emergency Treatment Service.—I am, etc.,

M. MUNDY.

London W.8.

SIR,—Dr. W. P. Lambie's castigation of the Inner London Executive Council over the B.M.A.'s Emergency Treatment Service (21 October, p. 176) is as unfair as it is unwarranted. While deploring any undue interference by an executive council into a general practitioner's affairs, they do have the statutory duty of ensuring that patients are properly cared for. After the necessity of a ministerial inquiry into the workings of the B.M.A.'s Glasgow E.T.S. any executive council would proceed cautiously.

However Dr. Lambie might protest, it does not explain why the B.M.A.'s E.T.S. repeatedly stated that it would not open up in any area where there was already a satisfactory service unless the E.T.S. was sufficiently demanded; repeatedly claimed that its service was sufficiently demanded in those areas; repeatedly has its claim refuted in practice, there following disgruntled withdrawal.

In the words of the song "When will they ever learn?"—I am, etc.,

B. JOHN MAXWELL,
Medical Director,
Liverpool Locums Limited.

Liverpool 6.

Foreign Residents

SIR,—A retired American citizen applied to be on my list. I made him a temporary resident, and then inquired from my executive council what the position was regarding his entitlement to medical services. I was informed by the executive council that an American citizen now permanently resident in England is entitled to apply for acceptance as a National Health Service patient.

Are we going to accept all retired people from foreign lands who have never contributed a penny? Isn't this socialism gone

mad? There is no quid pro quo in foreign lands. Are we to look forward to an England which is to be a dumping ground for old or retired persons as well as foreign goods? By 1980 this island might well be a home for cripples and geriatrics.—I am, etc.,

London S.W.5.

O. S. THOMPSON.

Was it a Drug?

SIR,—Did my eyes deceive me? I read in the *Supplement* (9 September, p. 128), "The Minister's representative . . . maintained that the mother was responsible for the inflammation, and that she should have paid for the remedy. . . ."

This is another example of bureaucracy gone mad, and must lead the profession to fight even harder than ever before for the right to prescribe what they consider to be necessary on clinical grounds without for ever looking over their shoulders in fear of being charged for treatment given to their patients.

We are a responsible body of professionals and act on behalf of our patients with good faith. This should be made clear to the Ministry, and the offending regulations should be withdrawn.—I am, etc.,

Seven Kings,
Essex.

I. M. SEGAL.

Points from Letters

Respiratory Distress Syndrome

Dr. FRANK MARSH (Epping, Essex) writes: You state that the paramount importance of the accurately controlled administration of oxygen cannot be overstressed (9 September, p. 628). I would like to suggest the administration of humidified oxygen through a ureteric catheter made of radio-opaque material, and passed through the larynx (locally anaesthetized) until the tip is at the bifurcation of the trachea, to overcome the "dead space." . . . The catheter under certain conditions might be passed through a tracheostomy opening.

Self-expulsion of a Nasal Polyp

Mr. A. HEDLEY BROWN (London S.E.1) writes: Recent evidence (5 August, p. 372, and 19 August, p. 500) shows that nasal polypi can be expressed by the patient.

My mother, before visiting an E.N.T. specialist after a lifetime of recurrent sinusitis, had a worse attack than usual. Sniffing despairingly, she produced a pedunculated polyp the size of an acorn into her mouth, with the cure of her symptoms. The specialist did not believe her, though she was a nurse, for she had not preserved the specimen. Perhaps he will now.

Computer Miscontrol

Dr. L. C. PAYNE, Ph.D. (Shenley, Herts) writes: A letter in the *B.M.J.* under the heading of "Computer Control" (23 September, p. 802) refers to "bureaucratic dominance by computer" in which the Ministry of Social Security (according to your correspondent) would not permit a valid exception to some administrative procedure because "it would interfere with the computer programme."

This is utter nonsense. The computer is a machine which simply performs a sequence of operations specified to it by a programme, as does an automatic washing machine. . . . What your correspondent is describing, therefore, is not computer control but bureaucratic inflexibility.

Obituary Notices

H. G. GARLAND, T.D., M.D., F.R.C.P.

Dr. H. G. Garland, consultant physician in charge of the neurological department in the General Infirmary at Leeds, died at his home on 23 October. He was 64.

Hugh Gregory Garland was born in Bridlington on 8 October 1903. After receiving his early education locally he entered Leeds University Medical School, graduating M.B.,



Ch.B. with distinction in 1926 and taking the Conjoint diploma the same year. After holding resident appointments in the Leeds Infirmary he was appointed a resident at the National Hospital for Nervous Diseases, Queen Square, and later at the Brompton Hospital. On his return to Leeds,

after holding further hospital junior appointments, he became medical tutor in the Leeds Infirmary, achieving a reputation as a first-class clinical instructor. He took the M.R.C.P. in 1929, and in the following year proceeded M.D. with distinction. In 1934 he was appointed honorary physician to the Leeds Public Dispensary, where for the next three years he was associated with Professor S. J. Hartfall in the gold treatment of rheumatoid arthritis. In 1937 he was appointed honorary assistant physician to the Leeds General Infirmary. By this time he had already entered private practice, and had become well known as a neurologist. He was elected F.R.C.P. in 1939. As a territorial officer he served in the R.A.M.C. throughout the whole of the second world war. After a short spell as a battalion medical officer at the beginning of the war, he was posted to Davydhulme Military Hospital as a medical specialist. He later served in a similar capacity at the Queen Alexandra Military Hospital, Millbank, until his posting to York Military Hospital as Northern Command neurologist in 1941. In November 1943 he went out to India to become adviser in neurology to the Southern Army with the rank of lieutenant-colonel. He held this appointment until his demobilization in November 1945. During his period of service in this capacity he travelled extensively and had charge of a large neurological centre in a base hospital. After the war he returned to his post at the Leeds General Infirmary. In 1946 he founded, and became physician in charge of, the neurological department, an appointment which he held until his death. In 1948 he became senior clinical lecturer in neurology in the University of Leeds, and at the inception of the National Health Service in 1948 he also became consultant neurologist to the Leeds Regional Hospital Board.

During the course of his professional career Hugh Garland held many important

appointments. At various times he was president of the Leeds and West Riding Medico-Chirurgical Society, the neurological section of the Royal Society of Medicine, the North of England Neurological Association, and the Leeds and West Riding Medico-Legal Association. He was, in fact, a founder member and the first president of the two latter associations. He was also a founder member of the Association of British Neurologists, and a councillor during the years 1947 to 1951. A member of the British Medical Association, he was vice-president of the section of neurology at the Annual Meeting in 1950, and president in 1957.

Hugh Garland was a man of exceptional ability, embellished by a complex and colourful personality. He was an outstanding teacher, and was greatly in demand as a lecturer and speaker. In addition, he was a prolific and lucid writer, publishing over a hundred papers on a wide variety of subjects in many different journals. He was the senior editor of a textbook of medicine which was published in the early 1950s, had many novel features, and was extremely well received.

During the years 1949 to 1955 he was editor of the *Leeds University Medical Journal*. Some years later he organized a series of lectures on the scientific aspects of neurology in which a number of eminent visiting speakers took part. The lectures were subsequently published in book form. His quick grasp of essentials and his fluency of expression made him a much-sought-after administrator, as well as contributing to his success in medico-legal practice. He had an exceptionally long tenure of office as chairman of the Faculty in the Leeds Infirmary, and also served on the Board of Governors for many years. Latterly, he also became chairman of the medical advisory research committee of the Multiple Sclerosis Society of Great Britain and Northern Ireland. Although virtually his entire professional life was devoted to the service of his teaching hospital, he also acquired a world-wide reputation as a neurologist, and became well known as the leader of a tetanus treatment team. He was intensely loyal to all those whose future depended upon his patronage, and there are many who owe much to his guidance, support, and encouragement during their early formative years. Fond of good company, his reputation as a *bon viveur* was proverbial. A keen sense of humour and a ready wit enlivened his many activities. Never daunted by authority, he loved to demolish long-cherished beliefs, especially if they had flimsy foundations. Prone at times to display autocratic and dogmatic attitudes, he would delight in generalizations which sometimes seemed outrageous, yet even his sternest critics had to concede the truth which they so frequently contained. He had prodigious energy and resilience; his alertness of mind was perhaps his greatest asset, and there seemed to be no place in his life for either inactivity or infirmity.

He is survived by his wife and a married daughter.—M. J. P.

J. P. writes: The passing of Hugh Garland has left an unbreachable gap, both in British neurology and in the Leeds General Infirmary. He was an outstanding teacher, and certainly the best lecturer that Leeds students were privileged to attend. His precision and clarity of thought and expression made him a most stimulating and exacting chief to work for. He did not suffer fools gladly, and was sometimes intolerant of those less gifted than himself. As a clinical diagnostician he was superb. With logical thought, scrupulous accuracy, and above all a flair of diagnostic inspiration, he was seldom wrong. He was never too proud to say, "I don't know," but at such times neither did anyone else. His flamboyant and endearing personality was felt beyond the confines of medicine, but he was happiest with a crowd of old associates around him retelling, in extraordinary detail, tales of earlier days. With his staff he was exceedingly generous, and was always at great pains to further their careers, a task in which he never failed. His academic achievements are legion, but he was especially proud to be the president of the neurological section of the Royal Society of Medicine, and to be the founder, father, and first president of the North of England Neurological Association—which he aptly christened N.E.N.A. A prolific writer, he made many outstanding contributions to clinical neurology; his papers on hypertrophic polyneuritis, endogenous hypoglycaemia, and diabetic amyotrophy are classical works of reference. In administration he was outstandingly successful, and was in constant demand as a chairman of numerous hospital committees as well as being the chairman of the research committee of the Multiple Sclerosis Society of Great Britain. In everything he laid his hands to, Hugh Garland showed himself to be a man of great intellectual powers, moral courage, and integrity.

P. T. HERRING, LL.D., M.D.
F.R.C.P.ED., F.R.S.ED.

Emeritus Professor T. P. Herring, of St. Andrews University, died on 24 October at his home at St. Andrews. He was 94. The death of Percy Herring has meant the loss of one of the distinguished physiologists who emanated from the illustrious and world-famous school of physiology which flourished under the guidance of the late Sir Edward Sharpey-Schafer.

Percy Theodore Herring was born in Yorkshire on 3 November 1872, but at an early age he emigrated with his parents to New Zealand, and it was while he was there that he received his school education in Christchurch and then proceeded to Otago University. Like many New Zealanders, in the latter part of the last century he came to Edinburgh to continue his course in medicine, and it was during this time that he

established the pattern of the academic brilliance which was to be a feature of his future work. He graduated M.B. in Edinburgh with first-class honours in 1896, after which he held resident posts in Edinburgh Royal Infirmary and at the Simpson Memorial Hospital. In 1897 he was awarded the Murchison Memorial Scholarship in clinical medicine, and one year later received the Crichton Research Scholarship in pathology. While



holding this scholarship he pursued investigations which led in 1899 to his being honoured with a gold medal for his M.D. thesis on "A Study of the Malpighian Bodies of the Kidneys." He took the M.R.C.P.Ed. in the same year. While in the pathology department he formed a close and lasting

friendship with the late Sir Robert Muir, and he frequently made reference to the stimulus and deep personal pleasure that he had obtained from this association with him. He was elected F.R.C.P.Ed. in 1903.

When Edward Sharpey-Schafer was appointed to the chair of physiology in Edinburgh in 1899, Herring joined his research staff as the holder of the Goodsir Memorial Fellowship in anatomy and physiology. During his early years with Schafer he became engaged on a histological study of the pituitary gland, and especially in regard to its posterior lobe. It was then that he described the granules in the neurohypophysis which are now customarily designated "Herring bodies," and whose functional significance has provoked so much investigative work; Schafer fully recognized the importance of Herring's work in the volume of *Quain's Anatomy* devoted to microscopic anatomy. He subsequently joined the staff of the physiology department, and it was during the first decade of this century that through his outstanding ability as a teacher he made such a stimulating impact on preclinical students in Edinburgh. Herring was a man of outstanding personality, and was punctilious in all he undertook. It was in keeping with

these attributes that he had been elected president of the Royal Medical Society in 1898, and it was likewise in keeping with his academic achievements that he was elected to the Chandos chair of physiology in the University of St. Andrews in 1908. This position he held until his retirement in 1948, and during his tenure of office he was Dean of the Faculty of Science from 1921 until 1939. St. Andrews University recognized its gratitude to him for all he had done for it by conferring upon him the degree of LL.D. He took a major part in the affairs of St. Leonard's and St. Katherine's School, of whose council he was chairman from 1930 to 1947, and it was due to his judicious and far-sighted policy in many matters that the school continues to prosper. A member of the British Medical Association, in 1910 he was vice-president of the section of physiology at the Annual Meeting, and in 1927

vice-president of the section of physiology and biochemistry.

Professor Herring was a pleasant and stimulating colleague who had a charm of manner and a warmth of personality which will never be forgotten by those who knew him. He celebrated his diamond wedding two years ago, and is survived by his wife and four daughters, three of whom are medical graduates of St. Andrews University.—R. W.

J. C. DICK, M.D., F.R.C.P.GLASG. F.C.PATH.

Dr. J. C. Dick, senior consultant pathologist to Glasgow Northern Hospitals, died on 21 October at the age of 56.

John Carson Dick, the son of a Glasgow schoolmaster, was born in Glasgow on 28 March 1911, and was educated at Hutchesons' Boys' Grammar School and at Glasgow University, where he graduated M.B., Ch.B. in 1933. He became interested in pathology, and joined the staff of the Glasgow Royal Infirmary under the late Professor Shaw Dunn. While there he proceeded M.D. in 1938, and was awarded honours and the Bellahouston gold medal for his thesis "Elastic Tissue of the Skin." During the second world war he served in the R.A.M.C. as a specialist pathologist with the rank of major, and was posted to the Canal Zone. Among his other duties he carried out research and original work on typhus and the Weil-Felix reaction. He was mentioned in dispatches. After demobilization he returned to the Glasgow Royal Infirmary, but on 1 July 1948 he was appointed senior pathologist to Glasgow Corporation Hospitals, and headed his department in Stobhill General Hospital. Later he was appointed senior lecturer in pathology to the University of Glasgow. In 1952 he was elected Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow, and in 1962 was admitted as a Fellow of the Royal College of Physicians of Glasgow. The following year he became a founder Fellow of the College of Pathology.

Dr. Dick contributed to many scientific journals, and was recognized as an international authority on the effects of drugs in the treatment of tuberculosis, particularly as it affected the urinary system. This original work he started in 1948, and by 1955 he had published many articles on the effects of streptomycin, P.A.S., and isoniazid on renal tuberculosis. Until his death he still maintained his interest in this subject, and his earlier findings still retain an important place in medical literature. He was a very skilful pathologist, a fine colleague and friend with whom it was a privilege to have been associated.

He leaves a widow, two sons, and a daughter, to whom the many friends of Dr. Dick extend their deep sympathy.—W. M. B.

R. R. W. writes: I did not join John Dick's staff until 1964, when he was already suffering from the illness which ended in his untimely death. It is not for me to speak about him as a pathologist, but I can and must show my respect for the man. Almost the first thing I learnt was that all

his staff thought well of him and were fond of him. I never heard an unkind word said of him, nor heard one from him either. He endured his ill-health with a combination of objectivity and quietness that would be hard to emulate. So it was that all his staff, medical and non-medical, did what they could to help him, as occasion indicated, out of their admiration, their affection, and their compassion. And now in corresponding degree our sympathy is offered to his family.

W. NAPIER, M.D.

Dr. W. Napier, consultant physician to the Paisley and Renfrewshire Infectious Diseases Hospitals until his retirement in 1961, died in Mearns Kirk Hospital on 8 October after a long illness borne with exemplary patience and fortitude. He was 71.

William Napier was born on 30 January 1896, and was educated at Ayr Academy and Glasgow University, where he graduated M.B., Ch.B. in 1918. During his university career he won the Asher-Asher gold medal among other prizes. After graduating he served in the R.A.M.C. in Mesopotamia for two years, and attained the rank of captain. After demobilization he held several junior posts in the Glasgow Western Infirmary, the Glasgow Royal Maternity Hospital, and Belvidere Fever Hospital, Glasgow. In 1923 he was appointed deputy superintendent of Belvidere Fever Hospital, and in 1925 he became superintendent of Shieldhall Fever Hospital, a post which he held until 1952, when he was appointed consultant physician to the Paisley and Renfrewshire Infectious Diseases Hospitals. A thesis on "Puerperal Fever—A Review of 500 Cases" gained for him an M.D. with commendation at Glasgow University in 1928. While his work covered every aspect of infectious diseases he was especially interested in diphtheria, and contributed a paper in 1937 advocating early tracheotomy in laryngeal diphtheria. Among other papers he published was one on "Febrile Reactions Among Smallpox Contacts" as the result of a study of smallpox contacts during the 1942 outbreak in Glasgow.

He was a man of a quiet, gentle disposition and simple tastes, with a great love of family life, classical music, and literature. He was fond of the open air and was never happier than when tramping over the moors of Renfrewshire and his native Ayrshire with his family. He was also a keen member of the Church of Scotland, and was an active supporter of his church, being an elder for 28 years.

In 1934 he married Miss Mary Ramsay Brotchie, whom he met while she was nursing in Belvidere Hospital. They had two daughters and one son, who is a general practitioner in Lerwick, Shetland. We extend the sincerest sympathy to his devoted wife and family.—J. B.

A memorial service for the late Sir Archibald Gray will be held at the University Church of Christ the King, Gordon Square, London W.C.1, at 12 noon on Tuesday, 14 November.

News and Notes

EPIDEMIOLOGY

Fireworks Injuries

Last year there was a slight decrease from the previous year's total of firework accidents in England and Wales round about Guy Fawkes Day, but the number of patients admitted to hospital increased. Comparative figures in the table below are from the report of *Her Majesty's Inspectors of Explosives for the Year ended 31 December 1966, 1967, H.M.S.O.*

Fireworks Injuries in England and Wales During 16 October-12 November 1966 and Comparable Periods in 1962-5

Year	Total Accidents	Admitted to Hospital
1962	2,832	483
1963	2,461	332
1964	2,220	241
1965	2,339	213
1966	2,302	259

England and Wales in Third Quarter

The birth rate for the third quarter was 17.0, being 0.9 below the rate for the corre-

sponding quarter of 1966. The stillbirth rate at 13.9 per 1,000 total births was 1.2 below the rate for the preceding third quarter. Infant deaths were 17 per 1,000 live births. The general death rate was 9.8 per 1,000 of the population and was 0.1 above the rate for the preceding September quarter.

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

Dysentery	Week Ending 13 Oct.	Week Ending 20 Oct.
Greater London ...	28	38
Kent ...	6	13
Sevenoaks R.D. ...	1	12
Lancashire ...	28	27
Denton U.D. ...	4	10
Lincolnshire ...	7	14
Scunthorpe M.B. ...	2	10
Surrey ...	12	25
Reigate M.B. ...	0	22

Dysentery (contd.)

	Week Ending 13 Oct.	Week Ending 20 Oct.
Warwickshire ...	22	20
Birmingham C.B. ...	6	19
Yorkshire West Riding ...	41	40
Leeds C.B. ...	18	26
Glasgow ...	52	42
Edinburgh ...	20	19
Angus County ...	4	10

Food-poisoning

	Week Ending 13 Oct.	Week Ending 20 Oct.
Derbyshire ...	0	39
Repton R.D. ...	0	39
Greater London ...	34	38
Havering ...	2	12
Lancashire ...	26	26
Liverpool C.B. ...	11	12
Sussex ...	12	21
Brighton C.B. ...	11	16
Yorkshire West Riding ...	6	14

Typhoid Fever

	Week Ending 13 Oct.	Week Ending 20 Oct.
Greater London ...	4	4
Bexley ...	0	1
Hackney ...	0	1
Hounslow ...	0	1
Richmond ...	1	1

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 14 October (No. 41) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire. A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	1	0	
Dysentery ..	205	28	112	4	2	384	42	86	14	6
Encephalitis, acute ..	1	0		0		3	3		0	
Enteric fever: Typhoid ..	8	4	0	0		2	0	0	0	
Paratyphoid ..	0	0	3B	0		6	2	1B	0	
Food-poisoning ..	177	34	25	0		306	20	9	6	
Infective enteritis or diarrhoea under 2 years ..				46	49				20	41
Measles* ..	1,101	72	5	21	29	6,087	694	209	115	89
Meningococcal infection ..	1	0	4	0		3	1	0	0	
Ophthalmia neonatorum ..	12	3	0	0		18	3	0	0	
Pneumonia† ..	85	11	65	2	1	94	10	88	2	1
Poliomyelitis, acute: Paralytic ..	0	0	0			0	0	0		
Non-paralytic ..	0	0	0			0	0	0		
Puerperal fever§ ..	65	27	4	0		94	39	13	0	
Scarlet fever ..	208	31	30	10	13	351	45	20	11	12
Tuberculosis: Respiratory ..	168	42	44	7		213	40	41	4	
Non-respiratory ..	46	10	1	2		48	6	12	0	
Whooping-cough ..	652	80	61	5	25	479	57	69	7	19

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0		0
Dysentery ..	1		0	0		0	0			
Encephalitis, acute ..				0						0
Enteric fever ..	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years ..	6	0	1	1	1	9	0	2	0	1
Influenza ..	3	0	0	0	0	8	0	1	1	0
Measles ..	0		0	0	0	0		0		0
Meningococcal infection ..				0				0		
Pneumonia ..	642	101	26	11	11	572	89	28	41	10
Poliomyelitis, acute ..	0	0		0	0	0	0			0
Scarlet fever ..	0		0	0	0	0		0		0
Tuberculosis: Respiratory ..	28	5	4	0	1	37	6	5	0	1
Non-respiratory ..				0	1				0	0
Whooping-cough ..	1	0	0	0	0	0	0	0	0	0
Deaths 0-1 year ..	290	57	26	10	13	251	39	20	5	8
Deaths (excluding stillbirths) ..	9,925	1619	562	132	188	9,781	1575	564	119	150
LIVE BIRTHS ..	16,267	2713	918	263	336	16,642	2852	973	288	329
STILLBIRTHS ..	222	32				237	35	17		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.

PARLIAMENT

Abortion Act will Become Effective Next April

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The Abortion Act is now law. It received the Royal Assent on 27 October, and will come into force six months from that date. The last comments in the Commons, who accepted the revised version which the Lords sent to them on 25 October, were to agree with this six-months interval so that the Ministry of Health can make the various regulations now necessary, and to adopt the changed title for the measure, which was introduced to them as the Medical Termination of Pregnancy Bill.

The Act includes the change, reported here in the House of Lords proceedings last week, and subsequently accepted by the Commons, enabling a doctor other than the two concurring in support of a termination, on the grounds stated, to perform the operation. There has also been added to the conscience clause a saving provision in respect of Scottish legal practice, which requires corroborative evidence of conscientious objection.

Balancing the Risks

One of the several subjects which has engaged members of both Houses during the protracted stages of this Bill has been the degree of risk involved in termination and the extent to which it should be taken into account as a factor in weighing the need for lawful abortion. It arose again during the concluding stages in the Lords on 23 October, and eventually resulted in a decision to reject qualifications such as "serious" and "substantial," and to adopt a formula proposed by the Lord Chief Justice, accepted by LORD SILKIN without consultation with or commitment to his co-promoters in the Commons, and ultimately endorsed in the House. This was to insert words in Clause 1 (1) (a) requiring the two doctors to be satisfied that the risks associated with a continued pregnancy would be "greater than if the pregnancy were terminated."

LORD PARKER OF WADDINGTON said of his amendment that he had been moved to suggest it when it became clear that what some people really wanted was to weigh the risks inherent in terminating a pregnancy against the risk of allowing it to continue. Only if the risk in continuation were greater than the risk in termination would a defence be created under the Bill. If that were the test it was unnecessary, and indeed would be wrong, to talk about risk as being "serious," "substantial," "real," or any words of that sort.

The doctors' decision, he added in a later intervention, was to be arrived at by comparing one risk with another.

Provisions of Act

The final form of the principal clauses of the Act is:

Medical Termination of Pregnancy

1.—(1) Subject to the provisions of this section, a person shall not be guilty of an offence under the law relating to abortion when a pregnancy is termi-

nated by a registered medical practitioner if two registered medical practitioners are of the opinion, formed in good faith—

(a) that the continuance of the pregnancy would involve risk to the life of the pregnant woman or of injury to the physical or mental health of the pregnant woman or any existing children of her family greater than if the pregnancy were terminated; or

(b) that there is a substantial risk that if the child were born it would suffer from such physical or mental abnormalities as to be seriously handicapped;

(c) in determining whether the continuance of a pregnancy would involve such risk of injury to health as is mentioned in paragraph (a) of subsection (1) of this section, account may be taken of the pregnant woman's actual or reasonably foreseeable environment.

(2) Except as provided by subsection (3) of this section, any treatment for the termination of pregnancy must be carried out in a hospital vested in the Minister of Health or the Secretary of State under the National Health Service Acts, or in a place for the time being approved for the purposes of this section by the said Minister or the Secretary of State.

(3) Subsection (2) of this section, and so much of subsection (1) as relates to the opinion of two registered medical practitioners, shall not apply to the termination of a pregnancy by a registered medical practitioner in a case where he is of the opinion, formed in good faith, that the termination is immediately necessary to save the life or to prevent grave permanent injury to the physical or mental health of the pregnant woman.

Conscientious Objection to Participation in Treatment

(1) Subject to subsection (2) of this section, no person shall be under any duty, whether by contract or by any statutory or other legal requirement, to participate in any treatment authorized by this Act to which he has a conscientious objection:

Provided that in any legal proceedings the burden of proof of conscientious objection shall rest on the person claiming to rely on it.

(2) Nothing in subsection (1) of this section shall affect any duty to participate in treatment which is necessary to save the life or to prevent grave permanent injury to the physical or mental health of a pregnant woman.

(3) In any proceedings before a court in Scotland, a statement on oath by any person to the effect that he has a conscientious objection to participating in any treatment authorized by this Act shall be sufficient evidence for the purpose of discharging the burden of proof imposed upon him by subsection (1) of this section.

[The Royal College of Obstetricians and Gynaecologists and the British Medical

Association were opposed to the section justifying abortion on the ground of risk to the physical or mental health of any existing children of the family—the so-called "social clause." They also considered that, of the two medical practitioners who must approve an abortion, one should be employed under the National Health Service as a consultant or be approved by the Minister of Health or the Secretary of State for Scotland.]

"Sans Everything" Inquiry

Mr. P. BESSELL (Lib., Bodmin) asked the Minister of Health on 27 October whether the name of the contributor to the book entitled *Sans Everything*, who made allegations of cruelty and neglect at St. Lawrence's Hospital, Bodmin, would be disclosed by the committee of inquiry to any person required to give evidence to the committee in respect of these allegations; whether the committee of inquiry would be empowered to disclose the nature of these allegations and their source to any members of the medical staff who may be required to give evidence during the course of the investigations; and to what extent he had verified the allegations before ordering an inquiry.

Mr. K. ROBINSON: I am not willing to confirm or refute assumptions about the identity of the hospitals which were the subject of allegations in *Sans Everything*, but where serious allegations of malpractice are made it is my duty to see that they are investigated. So far as *Sans Everything* inquiries are concerned, if a witness so indicates to one of the independent committees of inquiry his name will be revealed to no one except the members of the committee and its secretary, who will themselves observe complete confidentiality in the matter. Witnesses who wish to make allegations against named individuals must, however, be prepared to give evidence in the presence of the persons accused.

MEDICO-LEGAL

Agreed Reports

[FROM OUR LEGAL CORRESPONDENT]

The courts are continuing their efforts to reduce the time spent by professional men in giving evidence in court.

In a Practice Direction recently published¹ the President of the Divorce Division reminded lawyers of the desirability of disclosing to their opponents a copy of their expert's report in cases where expert evidence is to be called.

In the Divorce Division the expert will most usually be a doctor. Disclosure of the medical witness's report before trial will facilitate agreement that the report be read at the trial without calling oral evidence. Where the report cannot be agreed prior disclosure

will at least ensure that cross-examination is properly prepared and well-informed and directed at true points of issue.

The Practice Direction points out that where the expert evidence is that of a doctor it may frequently be expedient to incorporate or exhibit any relevant clinical notes, where necessary suitably explained. The exhibition of the material on which opinions are based should assist in the reaching of agreement on medical reports.

These considerations apply of course only to cases where a doctor is ethically free to disclose information before trial.

¹ *Weekly Law Reports*, 1967, 1240.

MEDICAL NEWS

Chair of Medical Statistics

Dr. DAVID JOHN NEWELL, Ph.D., has been appointed to a chair of medical statistics, personal to himself, at the University of Newcastle upon Tyne. Dr. Newell, who is 38,



went to Sidney Sussex College in 1949 after two years of National Service. He read Parts I and II of the Mathematics Tripos, graduating B.A. in 1952. The following year he was awarded the Cambridge diploma in mathematical statistics, with medical

statistics as a special subject. In 1961 he obtained the Ph.D. (Durham) after presenting a thesis "A Statistical Study of the Provision of Hospital Beds." From Cambridge he went to Newcastle in 1953 as medical statistician in the department of industrial health. He was promoted senior lecturer in biostatistics in 1962, and a year later was appointed to a personal readership. In 1959-60 he was visiting professor in the department of biostatistics at the University of North Carolina. A feature of his work has been his application of statistical methods to a range of medical problems that has included clinical research and administration.

Royal College of Surgeons of Edinburgh

At the annual meeting of the Royal College of Surgeons of Edinburgh, held on 18 October, the following office-bearers were elected: President, Mr. J. R. CAMERON; Secretary, Mr. J. A. ROSS; Treasurer, Mr. W. M. DRUMMOND.

Diploma in Aviation Medicine

The first examination for the diploma in aviation medicine (D.Av.Med.), which has been established by the Royal Colleges, will be conducted in July 1968. Copies of the regulations can be obtained free of charge from the Secretary, Examining Board in England, Examination Hall, 8-11 Queen Square, London W.C.1.

Romford Academic Medical Centre

Professor Sir JOHN MCMICHAEL, F.R.S., director of the British Postgraduate Medical Federation, opened the Romford Academic Medical Centre at Oldchurch Hospital, Romford, Essex, on 25 October. The centre provides for lectures, courses, clinical meetings, and formal and informal discussion. There is a conference and lecture room, laboratory, seminar and common rooms, and a library with space for study as well as for reference. In wishing the centre success Sir John predicted that practitioners in the area would continually turn to it for refreshment of knowledge and mutual education through the interchange of informed opinion and experience.

Commonwealth Foundation Awards

Grants totalling nearly £60,000 have been announced by the trustees of the Common-

wealth Foundation (see *B.M.J.*, 25 December 1965, p. 1556). The largest, £20,000, is to promote attendance of university representatives at the 10th Commonwealth Universities Congress in Australia in August next year. Other grants include £3,500 to the Commonwealth Society for the Deaf to meet the costs of a seminar in Nairobi on problems of deafness in Commonwealth Africa; £3,250 to the Uganda Medical Association in support of a project for refresher courses for up-country doctors; £2,500 to the Zambia Medical Association as a contribution to the costs of a regional Commonwealth meeting on aspects of tropical medicine; and £1,000 for an advisory visit to Africa by the secretary-general of the British Epilepsy Association.

Health Education Council

The Minister of Health has appointed BARONESS SEROTA to be chairman of the Health Education Council which the Government is setting up to organize the development of health education in England and Wales and Northern Ireland.

Nuffield Provincial Hospitals Trust

Over a million pounds has been spent by the Nuffield Provincial Hospitals Trust in the last three years on 181 projects covering almost every aspect of the health services in Great Britain. A special interest of the Trust has been the advancement of schemes for postgraduate medical education. By March this year, according to the Trust's triennial report, the investment in this field by way of grants amounted to £470,643, and a further £97,000 had been allocated by way of interest-free loans. Substantial sums have also been allocated to support projects relating to general practice, mental health, and the organization and operation of hospital and medical care services. An appendix to the report provides a list of projects, recipients of grants, and principals concerned.

Education in Psychology and Psychiatry

The need of general practice for doctors trained in psychology and psychiatry is described in a report by a working party appointed by the Royal College of General Practitioners (7s. 6d.). Having established the need, the report proceeds to consider in detail how it can be met, both before and after qualification, and to make recommendations. The present teaching of psychiatry in medical schools is analysed in an appendix. A leader on teaching the behavioural sciences was published in the *B.M.J.* of 21 October, p. 123.

Control of Drugs

Professor ARNOLD BECKETT, of the Chelsea College of Science and Technology, spoke on the subject "Drugs and Society" at the lunch given by the Royal Society of Health on 24 October. Professor Beckett commented on legislation proposed to control the safety, quality, and distribution of drugs, and warned that there was a danger of confusing the active principle and the drug preparation that is given to patients. The two were not synonymous. This had implications for the proposal to introduce generic names rather than brand names for new preparations. Despite careful quality control both within the industry and elsewhere there was no standard of biological availability of pharmaco-

logically active substances, said Professor Beckett. At the present time the responsibility for controlling availability rested with the pharmacological industry, but any measures to reduce the reward obtained by the manufacturers of a new preparation would at the same time discourage research into its properties that was not immediately profitable.

Research into Drug Addiction

A report on drug addiction published last week by the Office of Health Economics (2s. 6d. post free) observes that little large-scale co-ordinated research has been done in Britain. There is need, it says, for epidemiological studies to identify potential addicts with a view to prophylaxis. A key project would be to analyse the circumstances in which some cannabis users "progress" on to heroin addiction while others do not. Treatment and methods of rehabilitation are other subjects proposed for investigation, also the exact long-term effect of drugs on the human body. The report calls for more dependable statistics and for greater exchange of international research work. What may be needed, it suggests, is a Government-sponsored institute for the study of addiction to foster adequate research and facilities for the study and treatment of drug addiction.

Gift to British Heart Foundation

The British Heart Foundation has received £50,000 from Mr. HUGH SUMNER, former chairman of Typhoo Tea Ltd., of Droitwich, Worcestershire. It is one of the largest individual gifts made to the foundation.

Institute of Urology, London

Mr. HOWARD G. HANLEY has been appointed Dean of the Institute of Urology in succession to Mr. A. R. C. HIGHAM.

Experiment in Psychiatric Care

The Phoenix Group Homes, a voluntary organization in Colchester, Essex, provides care for ex-psychiatric patients who have nowhere suitable to live. In the houses that are rented or purchased the residents live independently except for a visit from a social worker every few days. There is no residential staff. The scheme is the product of co-operation between the hospital and local authority mental health services and is supported by the Gulbenkian Foundation. By the middle of next year some 36 to 40 people are expected to be accommodated. The chairman of the project is Dr. RICHARD FOX, Severalls Hospital, Colchester.

University Intake, 1967

In October this year the number of students entering undergraduate courses in universities in Great Britain through the Universities Central Council on Admissions was 49,000—about 5,000 more than in 1966. For universities in the United Kingdom the entry through U.C.C.A. was 50,500. In addition, there were between 6,500 and 7,000 students who gained university places outside the U.C.C.A. scheme, bringing the total number of new admissions to 56,000 for Great Britain and 57,500 for the United Kingdom as a whole.

People in the News

► LORD ADRIAN, O.M., F.R.S., has been nominated as Chancellor of Cambridge University in succession to LORD TEDDER.

► Major-General Sir NIGEL TAPP has been appointed Lieutenant-Governor and Secretary, Royal Hospital, Chelsea, London S.W.

► Professor JOHN W. DUNDEE, head of the department of anaesthetics at Queen's University, Belfast, is visiting South America this month under the auspices of the British Council.

► Professor J. H. MIDDLEMISS is visiting Jamaica as visitor to the University of the West Indies and as adviser in radiology to the Government of Jamaica.

► Mr. HAROLD EDWARDS, consulting surgeon to King's College Hospital, is giving a number of lectures in Pakistan under the auspices of the British Council.

► Mr. J. W. S. IRWIN has been appointed honorary consultant in surgery to the Army in Northern Ireland in succession to Sir IAN FRASER.

► Dr. J. A. ODDIE has been appointed senior administrative medical officer by the Oxford Regional Hospital Board. He succeeds Dr. J. O. F. DAVIES, now secretary of the Central Committee on Postgraduate Medical Education.

► Mr. DAVID A. SOLOMON has been appointed chairman of the Liverpool Regional Hospital Board from 1 April 1968.

News in Brief

Meldreth Training School, near Royston, Hertfordshire, was opened on 25 October by PRINCESS MARINA, DUCHESS OF KENT. It has been designed for spastics with multiple handicaps who cannot benefit from any other form of education. There are four houses, each accommodating up to 30 children. A central block provides treatment and educational facilities.

Christmas cards produced by various charitable organizations associated with hospital or health services are displayed at the Hospital Centre (24 Nutford Place, London W.1).

Grants and Awards

Dr. GEOFFREY CHAMBERLAIN was recently awarded the annual prize given by the American Association of Obstetricians and Gynecologists for research leading to a thesis entitled "An Artificial Placenta. The Development of an Extracorporeal System for Maintenance of Immature Infants with Respiratory Distress."

Coming Events

Medical Women's Federation.—Jubilee council meeting, 2-4 November, Manchester. Exhibition, "Women in Medicine," by Wellcome Historical Medical Museum and Library at the library, Manchester University. Admission without ticket.

Postgraduate Medicine, 1967 (T.V. Programme).—"Advances in Cardiology," Scottish Television, 6 November (11.50 p.m.), repeat 8 November (1.10 p.m.). "Growth in Childhood," Tyne Tees Television, 7 November (1.15 p.m.), repeat 12 November (10.15 a.m.).

Royal Medico-Psychological Association.—Autumn quarterly meeting, 16-17 November, in London. Programme includes seminars, papers, and section meetings. Details from General Secretary, R.M.P.A., Chandos House, 2 Queen Anne Street, London W.1.

National Association for the Welfare of Children in Hospital.—Conference, "The Child as a Long-stay Patient," 21 November, 10 a.m. to 12.30 p.m., Royal Commonwealth Society, Craven Street, London W.C.1. Opened by PRINCESS ALEXANDRA.

Society for Low Temperature Biology.—Symposium on blood preservation, 23 November, 2 p.m., Middlesex Hospital Medical School. Details from Secretary, Dr. DAVID E. PEGG, Clinical Research Centre Laboratories, National Institute for Medical Research, Mill Hill, London N.W.7.

King Edward's Hospital Fund for London.—Conference, "Making Better Use of Outpatient Departments and Accident and Emergency Units," 23 November, Hospital Centre, 24 Nutford Place, London W.1. Fee £1. Completed application forms by 13 November. This conference is the second of a series of three on making better use of hospital resources.

Royal College of Nursing and National Council of Nurses of the United Kingdom.—Conference, "Use and Abuse of Drugs," 23-24 November, Church House, Westminster. Sir GEORGE GODBER will give the opening address. Details from Conference Secretary, Royal College of Nursing, Henrietta Place, Cavendish Square, London W.1.

Institute for the Study and Treatment of Delinquency.—Week-end discussion course, "The Child, the Family, and the Institution," 24-26 November, Knuston Hall, near Wellingborough, Northants. Applications to General Secretary, I.S.T.D., 8 Bourdon Street, London W.1.

Societies and Lectures

For attending lectures marked ① a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 6 November

INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Dr J. Sutcliffe: Chest Radiology in Infants and Children.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Professor I. Friedmann, Dr. D. A. Osborn, Dr. M. I. Wright: clinicopathological conference.

INSTITUTE OF OBSTETRICS AND GYNACOBLOGY.—At Chelsea Hospital for Women, 3 p.m., discussion: Vaginal Hysterectomy. Speakers, Mr. J. Howkins, Professor J. Stallworthy.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. E. Dowsett: The Body's Response to Viral Infection; 6.30 p.m., Dr. G. Stirling: Thrombosis.

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University Medical School, 5 p.m., Dr. E. Boijesen (Lund): Selective Abdominal Arteriography.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Erasmus Wilson demonstration by Dr. W. D. Linsell: Granulomatous Lesions of the Myocardium.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. K. S. Holt: Present Thoughts on Assessment of Hearing Problems in Young Children.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. W. A. Lishman: Psychiatric Aspects of Pain.

SCOTTISH TELEVISION LTD.—11.45 p.m., Advances in Cardiology. (Sponsored by Glasgow Postgraduate Medical Board.)

SOCIETY FOR MEDICAL AND DENTAL HYPNOSIS.—At Royal Society of Medicine, 8 p.m., Dr. J. C. Barker: Precognition and Aberfan.

Tuesday, 7 November

B.B.C. 2 TELEVISION.—1.15 p.m., medicine today: Low Back Pain. (Sponsored by A.S.M.E.)
BOLTON AND DISTRICT MEDICAL SOCIETY.—At Gymnasium, Bolton Royal Infirmary, 8.15 p.m.,

Professor R. B. Hunter: Treatment of Hypertension.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Professor D. W. Smithers: Clinical Research in Hodgkin's Disease.

INSTITUTE OF OBSTETRICS AND GYNACOBLOGY.—At Hammersmith Hospital, 2 p.m., Professor P. Rhodes: Management of Antepartum Haemorrhage.

MENTAL HEALTH RESEARCH FUND.—At Edward Lewis Theatre, Middlesex Hospital Medical School, 5 p.m., Sir Geoffrey Vickers: The Promotion of Psychiatric Research.

NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., joint medical, surgical, and anaesthetic presentation of a case.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., SOCIETY FOR THE STUDY OF ADDICTION.—At West Hall, Royal Society of Medicine, 8 p.m., discussion on Legalization of Marijuana. Speakers will include Mr. S. Abrams.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. H. C. Grant: Examination of the Brain.

WESTMINSTER MEDICAL SCHOOL.—At Meyerstein Lecture Theatre, 5.15 p.m., Mr. K. P. Robinson: Tumour Dissemination and Surgical Treatment.

WEST SUFFOLK HOSPITALS POSTGRADUATE CENTRE.—At Bury St. Edmunds, 1.15 p.m., Mr. R. E. B. Taggart: The Prostate Gland.

Wednesday, 8 November

ANGLO-CONTINENTAL MEDICAL SOCIETY.—At Royal Society of Tropical Medicine and Hygiene, London W., 8.45 p.m., Dr. K. R. Capper: Side Effects of Drugs.

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—(1) At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting, (2) At Social Hall, St. John's Hospital, Wood Street, 12.30 p.m., obstetric conference, Mr. J. Moore: Spina Bifida and Allied Conditions of the Newborn.

INSTITUTE OF CHILD HEALTH.—At Kennedy Lecture Theatre, 5.30 p.m., Professor D. V. Hubble: Sex Problems in the Teenager.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. R. W. Riddell: Clinical Pathology of Ringworm Infections.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. D. C. Muir: Aerosol Deposition in the Respiratory Tract.

INSTITUTE OF UROLOGY.—5 p.m., Dr. R. C. B. Pugh: Pathology of Bladder Tumours.

MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University Medical School, 5 p.m., Mr. H. Varley: Clinical Biochemistry in Manchester since 1902.

NORTHAMPTON GENERAL HOSPITAL.—8 p.m., Professor C. D. Calnan: The Skin and Autoimmunity.

OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Professor R. R. Porter, F.R.S.: Very Recent Ideas on Structure and Origin of Antibodies.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. P. D. Marsden: Intestinal Parasites.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conference by Dr. E. J. M. Campbell: Respiratory Failure. (2) 2 p.m., Dr. W. D. Alexander: Thyroid Function Test.

SCOTTISH TELEVISION LTD.—1 p.m., Advances in Cardiology. (Sponsored by Glasgow Postgraduate Medical Board.)

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At West London Hospital, 8.30 p.m., clinical meeting: Addiction. Speakers: Dr. M. Glatt, Dr. V. Marks.

WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Sir Brian Windeyer: Medical Aspects of Radiotherapy.

Thursday, 9 November

ABERDEEN UNIVERSITY FACULTY OF MEDICINE.—At Large Lecture Theatre, University Medical Buildings, Foresterhill, 5 p.m., Dr. S. Browne: Leprosy—some outstanding problems and paradoxes.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. J. L. Turk: The Cell Mediated Immunological Response.

DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Professor A. Duncan: What Kind of Doctors Should We Train?

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Infections—Their Role in Otolaryngology.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 4 p.m., Mr. W. J. Dempster: Early and Long-term Changes in the Sectional Ureter. (2) 5 p.m., lecture on medical history by Dr. E. S. Clarke: History of Leprosy, Plague, and Syphilis.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Dr. F. P. Meehan: Caudal Analgesia in Obstetrics.

WESTMINSTER MEDICAL SCHOOL.—At Meyerstein Lecture Theatre, 5.15 p.m., surgical conference by Professor G. W. Taylor: Peripheral Vascular Disease.

Friday, 10 November

BROOK GENERAL HOSPITAL.—2 p.m., Dr. R. Hartley, Dr. M. Zoob: Cardiology—extended course.
KINGSTON-UPON-THAMES MEDICAL CENTRE.—3.30 p.m., obstetrics seminar by Dr. S. B. Kuğu: Lactation.
NORTHAMPTON MEDICAL SOCIETY.—8.30 p.m., Dr. Sheila Kenny: Problems of Intensive Care.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Mr D. M. Wallace: There is No Place for Surgery or Radiotherapy in the Treatment of Bladder Tumours. (2) 11.30 a.m., clinicopathological conference. (3) 4 p.m., Dr. J. D. N. Nabarro: Idiopathic Hirsutism.
ST. MATTHEW'S HOSPITAL, London.—2.30 p.m., Mr M. J. Notaras: Faecal Incontinence in Elderly People.
WEST KENT MEDICO-CHIRURGICAL SOCIETY.—At Miller General Hospital, Greenwich, 8.30 p.m., Mr W. Mitchell: Art in Architecture.
WEST MIDDLESEX HOSPITAL.—4 p.m., Mr. D. Morris: Resuscitation of the Newborn.

Saturday, 11 November

MANCHESTER MEDICAL SOCIETY.—At Small Anatomy Theatre, Manchester University Medical School, 10 a.m., medical research papers.

Universities and Colleges**ROYAL COLLEGE OF PHYSICIANS OF LONDON**

At the quarterly comitia of the College held on 26 October, with the president, Sir Max Rosenheim, in the chair, Dr. T. C. Hunt was elected second vice-president; Dr. L. C. Marun, Dr. E. G. L. Bywaters, Dr. H. J. Wallace, and

Dr. R. I. S. Bayliss were elected councillors of the College.

Dr. C. E. Newman was elected College representative on the Committee of Management of the Examining Board. The president, Dr. K. Robson, Dr. R. S. B. Pearson, Dr. A. G. W. Whitfield, and Dr. J. Badenoch were elected members of the Standing Joint Committee of the three Royal Colleges.

The appointment of Dr. K. S. Holt as Milroy lecturer for 1969 was announced. His subject will be "The Quality of Survival." The award of the Jenks memorial scholarship to Dr. J. S. Carmichael was announced. The appointments of Dr. J. Waterlow as Charles West lecturer for 1968 and Dr. F. D. Hart as Philip Elham lecturer for 1969 were announced.

Licences

Licences to practise were conferred upon the following candidates:

D. F. Abbott, Penelope J. Aeberhard, R. W. G. Allison, J. A. R. Anderson, C. I. Andrew, N. M. Bannerman, R. H. J. Begent, J. K. Bell, M. C. Bishop, W. D. Biset, Marie H. L. Blankert, M. M. Bowen, Jennifer W. Bradburn, D. W. Branton, P. W. Briggs, J. B. Broadfield, J. K. Brockbank, R. J. S. Browne, N. Buchanan, G. W. S. Burgess, Gillian Carrington, R. S. Carruthers, J. H. Casson, A. P. Chakravorty, H. R. Champion, J. O. Clarke, Jerra Chubwala, J. Collier, J. R. O. Collin, Delia M. Crawley, J. P. J. Curran, Gillian R. Darch, J. P. M. Davies, J. H. W. Davies, T. P. Davis, Mara Dunis, N. R. V. Edmonds, Jennifer M. Edwards, C. G. Ellis, M. St. J. Floyd, Priscilla M. Fogarty, R. C. Freedman, K. Gopinatha Rao, Diane P. L. Gorvette,

Angela M. W. Greig, R. H. B. Grey, R. J. N. Gribble, A. W. Grieve, M. J. Griffiths, Susan J. Hall, Janet M. I. Hamilton, T. B. Hargreave, N. E. M. Harker, P. C. Harland, Carolyn Haworth, Margaret E. Hodson, P. J. Holt, I. M. Hutton, Bridget A. Jack, Gwyllyd W. B. J. Johnson, Katherine R. H. Johnson, R. W. Johnson, M. P. Jones, R. D. Jones, J. P. Kennedy Scott, Ruth M. Lacey, B. A. Leatherdale, S. I. Lewis, G. W. Libby, E. W. McLarty, G. P. H. Mason, M. A. Martin, Barbara M. Mawer, M. H. Mehta, D. R. V. Mercer, S. B. Merrill, D. P. B. Miles, R. Miller, C. J. Mitchell, Judy Moulds, G. H. Mumford, M. J. Myers, D. J. O'bome, V. O'Sullivan, W. D. Owusu-Yianomah, J. C. Pappin, H. R. Patel, J. Pemberton, E. H. Penry, Suzanne E. Powrie, A. Prakash, E. A. Proctor, D. H. K. Ratsey, H. R. D. Rawlinson, D. L. P. Rees, P. Renton, B. F. Ribeiro, D. N. G. Ridgway, K. H. Riding, F. P. Roberts, S. C. Robinson, S. G. Rubin, R. J. Sergeant, Z. K. S. Sharaiha, R. J. G. Soper, M. Spira, Jennifer T. Spring, Monica H. Spring, E. F. C. Stamp, J. B. Stevens, E. W. Taylor, J. G. Thomas, Margaret E. Tompsett, J. A. Townsend, M. G. Tweeddale, M. E. Twite, P. R. Vassal-Adams, R. C. Volkers, J. S. Walker, P. T. Walling, J. H. Walton, Hazel M. Watson, J. L. Watts, P. E. Watts, M. Webley, C. H. West, T. Wheeler, R. W. Whittlesey, Melanie Williams, P. D. Wimberley, T. R. Wykes.

Diplomas

Diplomas were granted jointly with the Royal College of Surgeons of England as follows:

DIPLOMA IN CHILD HEALTH.—L. A. S. A. Al-Kindi, E. J. J. Almeida, M. Aman, M. R. Baral, S. G. Benady, J. F. Branton, Gail C. Bridgman, J. Tin-Sui Chan, C. H. Cheetham, M. L. Chiswick, Margaret A. Cochran, D. W. D. Collure, P. P. Dawson, Gillian M. Day, C. J. Ellis, N. A. P. Evans, P. S. L. Fernando, W. O. Gbajumobi, A. Ghani, C. M. Gwynn, S. A. Haider, G. R. Hamilton, Josephine C. R. Harris, Elizabeth A. Harrison, A. J. C. Hawks, G. B. Haycock, S. S. Herman, Mary A. Hickey, P. Hickman, Linda M. Holland, Judith F. Hornby, J. K. Howell, S. K. A. Jafri, S. Jan, Devika S. Jayasuriya, J. R. Jelly, M. D. Kaye, A. S. S. I. Khan, M. J. A. Khan, S. P. Liyanage, S. E. G. Lubulwa, Erica R. McLerie, R. L. Mitchell, C. D. Molteno, Sarda-Ul Mulk, Margaret A. Muller, J. E. Ogwo, G. D. Osho-Williams, Christine A. Parr, Margaret R. Pendray, R. Prasad, Z. A. Qureshi, Leila Raju, K. Ramanathan, K. W. Rassam, T. S. Ravikant, R. P. A. Rivers, Wendy M. Rostron, H. B. Sahay, Katherine E. U. Salter, W. A. Saunders, Anna V. Seager, J. H. B. Sheppard, Jennifer M. Shobbrook, B. A. Sijuwade, Mary A. M. Slaughter, Carol M. Starkie, Suha W. F. Tappoun, J. R. Telfer, I. T. Thomas, A. M. Tucker, Louie A. Udai, Yat-Kwong Wong, C. J. E. Wynne-Williams, Priscilla M. Wooldridge, Kaniz Z. Zaidi.

Deaths

Adams.—On 23 October 1967, in Carlin House Nursing Home, Camberley, John Andrew Adams, M.B., B.Ch., B.A.O., formerly of Sowerby Bridge, Yorkshire, aged 100.
Mackay.—On 26 October 1967, at 5 Ravelston Park, Edinburgh, Angus Cameron Mackay, L.R.C.P., L.R.C.S., L.R.F.P.S. Glasg., of Creag Dhu, Connel, Argyll.
Townsend.—On 3 October 1967, at Kingswinford, Staffordshire, late of Kirk Ella, East Yorkshire, Tom Snowden Townsend, M.A., B.M., B.Ch., D.P.H., aged 73.

Correction

Infectious Hepatitis in Leicester 1963-6.—The final sentence of the summary of this article by Dr. C. Burns (23 September, page 773) should have read, "Most of the cases had illness of mild or moderate severity but three (0.31%) died."

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY

Contents of the October issue are as follows:

Some Neuro-ophthalmological Observations. C. Miller Fisher.
 Median and Ulnar Neuropathy in the Guinea-pig. Pamela M. Fullerton and R. W. Gilliatt.
 Quantitative Electromyography Using Automatic Analysis: Studies in Healthy Subjects and Patients with Primary Muscle Disease. A. L. Rose and R. G. Willison.
 Enzymes of the Glycogen Cycle and Glycolysis in Various Human Neuromuscular Disorders. Salvatore Di Mauro, Corrado Angelini, and Claudia Catani.
 Studies of the Carrier State in the Duchenne Type of Muscular Dystrophy. Part I: Effect of Exercise on Serum Creatine Kinase Activity. Peter Hudgson, David Gardner-Medwin, R. J. T. Pennington, and John N. Walton.
 Phrenic Nerve Conduction in Man. J. Newsom Davis.
 Excitability of Motor Neurones in Spinal Shock in Man. E. Diamantopoulos and P. Zander Olsen.
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 Spinal Cord Embolism. Lionel Wolman and Peter Bradshaw.
 Hereditary Cataplexy. Jo-Ann M. Gelardi and Jason W. Brown.
 Longitudinal Movement of Radiolabelled Albumin Within Extravascular Spaces of Peripheral Nerves Following Three Systems of Experimental Trauma. Ross Mellick and J. B. Cavanagh.
 Combined Degeneration of the Spinal Cord Due to Deficiency of Alimentary Vitamin B₁₂. A. Verjaal and A. H. C. C. Timmermans-Van Den Bos.
 Tachistoscopic Number Estimation in Patients with Unilateral Cerebral Lesions. Elizabeth K. Warrington and Merle James.
 Book Reviews.

Volume 30, No. 5. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

GUT

Contents of the October issue are as follows:

Obituary: Henry A. Magnus, F. Avery Jones.
 Hepatic Scintigraphy. E. A. Jones.
 Pancreatic Scanning. Ian A. D. Bouchier.
 Rectal Biopsy as an Aid to Cancer Control in Ulcerative Colitis. B. C. Morson and Lillian S. C. Pang.
 Primary Sclerosing Cholangitis, the Biliary Tree, and Ulcerative Colitis. M. E. C. Thorpe, P. J. Scheuer, and Sheila Sherlock.
 Studies on the Familial Incidence and Clinical History of Patients with Chronic Unconjugated Hyperbilirubinaemia. Paul M. Smith, J. E. Middleton, and Roger Williams.
 Zinc and Manganese Levels in Serum and Liver after Alcohol Feeding and Development of Fatty Cirrhosis in Rats. Anthony J. Barak, Harriet C. Beckenhauer, and Felix J. Kerrigan.
 Observations on Oral Betamethasone-17-valerate in the Treatment of Idiopathic Steatorrhoea. A. T. Otaki, J. R. Daly, and A. Morton-Gill.
 Motor Responses of the Human Alimentary Tract to Near-maximal Infusions of Pentagastrin. J. J. Misiewicz, D. J. Holdstock, and Sheila L. Waller.
 Analysis of the Motor Effects of Gastrin and Pentagastrin on the Human Alimentary Tract in vitro. A. Bennett, J. J. Misiewicz, and Sheila L. Waller.
 Gastric Response to Subcutaneous Injection of a Gastrin-like Pentapeptide. K. G. Wormsley, M. P. Mahoney, and G. Kay.
 Serum Proteins in Ulcerative Colitis: Electrophoretic Patterns in the Inferior Mesenteric Artery and Vein. F. T. de Dombal.
 Changes in the Motility of the Small Intestine in Digestive Disorders. F. Pirik.
 Histochemistry of the Colonic Epithelial Mucins in Normal Subjects and in Patients with Ulcerative Colitis. V. Greco, G. Lauro, A. Fabbrini, and A. Torsoli.
 The Antrum in Patients with Duodenal and Gastric Ulcers. J. Schrager, R. Snink, and S. Mitra.
 Limitation of the Use of Inert Gases in the Measurement of Small Gut Mucosal Blood Flow. J. D. Hamilton, A. M. Dawson, and Joan Webb.
 Gastroenterological Society of Australia.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 11 NOVEMBER 1967

Pointers

Cross-infection: Predisposing factors, treatment, and prophylaxis against recurrence of respiratory infection due to *Ps. aeruginosa* in a cardiac surgery unit described (p. 313). Leader at p. 309.

Respiratory Tract Infection: Management in children, particularly by antibiotic and biochemical measures, and report of investigation into 22 fatal cases (p. 316). Leader this page.

Complications of Triple Vaccination: Survey in Sweden shows an apparent increase in number of neurological reactions, but severe reactions leading to permanent injury seem to have decreased (p. 320).

Burkitt's Lymphoma: Long-term survival rate in Mulago Hospital, Uganda, is markedly dependent on the anatomical involvement at presentation, although there may be a relation to drug used and its dosage (p. 323).

Hyperaldosteronism: Discussion of a fourth case of a syndrome characterized by hypokalaemia, glomerular abnormalities, normal blood pressure, and absence of oedema (p. 327).

Parathyroidectomy in Renal Failure: This may produce healing of bone lesions due to secondary renal hyperparathyroidism, and may avoid calculus formation in a transplanted kidney if surgery is performed at an early stage (p. 331).

"Acrosclerosis": Three cases of sclerodactyly, Raynaud's phenomenon, calcinosis, and telangiectasia (p. 334).

Case Reports: Incest and mental ability (p. 336); Unusual cause of tongue pain (p. 337); Diagnosis of bacterial endocarditis (p. 338).

Body Building: Hazards of self-medication with anabolic steroids (pp. 310 and 353).

Dyspepsia: Indications for surgery and type of operation in duodenal ulcer (p. 339).

Low Back Pain: Article complementing television programme shown on 7 November and to be repeated on 15 November (p. 341).

Alcoholism Information Centres: Discussion of use of these centres and the type of people visiting them (p. 346).

Epidemic Keratoconjunctivitis: Lanarkshire outbreak (pp. 353 and 366).

Administration of N.H.S.: Minister to study possibility of further integration (p. 367).

Pay-beds: Number reduced by 1,385 (p. 367).

G.M.S. Committee: Meeting report (*Supplement*, p. 43).

Universities and Armed Forces: Salaries to go to Prices and Incomes Board (*Supplement*, p. 48).

Respiratory Infection in Early Childhood

During the last 30 years mortality from respiratory disease in childhood has fallen considerably. But many problems remain. Some of them are discussed by Dr. P. S. Gardner and his colleagues at Newcastle upon Tyne in their article which appears at page 316 of this week's *B.M.J.* The authors hasten to point out that the 22 children whom they studied and who died as a result of acute respiratory diseases formed a selected group, not necessarily representative of this age as a whole. But this detracts little from the value of the article, since by a careful analysis of the histories and findings the authors are able to suggest possible ways of improving both diagnosis and treatment. With the approach of winter their warnings are timely.

Bacterial diseases were responsible for only six of the 22 deaths, and of the viral diseases bronchiolitis was much the most important. The infant with bronchiolitis is characteristically restless and distressed, with a repetitive, exhausting cough and rapid wheezy respirations, which, although accompanied by much effort, are ineffective. Obstruction of distal airways, with trapping of air, results in acute emphysema. This clinical picture differs considerably from that of the infant with pneumonia, nowadays often due to organisms highly resistant to antibiotics. Like bronchiolitis pneumonia is often preceded by brief upper respiratory symptoms, but wheezing is less marked, the rapid respirations are frequently accompanied by grunting and cyanosis, and tachypnoea and tachycardia are often out of proportion to the physical findings in the chest, especially in small infants. A high pyrexia is suggestive of a bacterial pneumonia. In both these conditions the infant may deteriorate suddenly, either from respiratory insufficiency or from a complication such as the pyopneumothorax which is commonly seen in children with staphylococcal pneumonia.

Another important condition which Dr. Gardner and his colleagues encountered was *Haemophilus influenzae* epiglottitis, and they rightly stress the importance of early diagnosis in this disease. It should be immediately suspected if a fiery red oedematous epiglottis is seen over the base of the tongue when examining the fauces of a child with croup. Prostration and collapse rapidly occur, either from inspiratory obstruction or from the septicaemia often present. Pertussis, though not included in the conditions reported, remains a danger to infants despite the reduction in mortality from this disease. In less severe cases the paroxysmal cough may resemble that of mucoviscidosis, but when more severe it may be accompanied by life-threatening periods of apnoea. Associated congenital abnormalities were found in 9 of the 22 children studied at Newcastle. Disproportionate degrees of tachycardia, cyanosis, or hepatomegaly should lead the physician to consider congenital heart

disease. Treatment today offers a much better prognosis in mucoviscidosis than formerly,¹ and the possibility of this condition should be borne in mind in all infants with bacterial pneumonia.

The most important requirement in the management of infants with severe respiratory infections is adequate oxygen therapy. This aspect is well discussed in the article by H. Simpson and D. C. Flenley,² to which Dr. Gardner and his colleagues refer. Simpson and Flenley stress the importance of cyanosis in assessing severity. They also point out that the risk of inducing carbon dioxide narcosis in young children requiring oxygen therapy is apparently negligible. Inspiratory oxygen concentrations will frequently need to be considerably in excess of 40%, a figure which in practice is often not achieved in oxygen tents now available.³ Severe hypoxia may result if the oxygen concentration falls suddenly,⁴ and care is therefore essential when attending to children who are being nursed at high concentrations of oxygen. As in the adult, repeated blood gas analyses must be undertaken for the correct management of severe degrees of respiratory insufficiency. Thus Simpson and Flenley suggest that a *pH* below 7.2 or *PCO*₂ above 65 mm. Hg might be suitable indications for giving parenteral bicarbonate or intermittent positive pressure respiration or both. Though the value of tracheostomy in bronchiolitis has been questioned,⁵ some children have been shown to benefit.⁶ Complications are common after this procedure, however,⁷ and nasotracheal intubation appears to be a preferable alternative.^{8,9} This too is not entirely without its problems, and it appears that it is preferably restricted to children with lower respiratory diseases.¹⁰ These aspects of management are highly specialized and will be possible only in hospitals with facilities for intensive care, the requirements for which were discussed by Drs. D. Campbell, J. M. Reid, A. B. M. Telfer, and W. Fitch in the *B.M.J.* last week.¹¹

The place of antibiotics in bronchiolitis was discussed in these columns two years ago.¹² As it is a viral infection, they will be of value only in preventing or treating the rare¹³ but disastrous secondary infection. The correct choice may be difficult, but it is necessary to recognize that infants who were born in hospital, and especially those who have already received broad-spectrum antibiotics, are likely to harbour organisms highly resistant to antibiotics. No time should therefore be lost in testing bacterial sensitivities in any infant thought to have pneumonia, and therapy should include a penicillinase-resistant antibiotic such as cloxacillin. Tetracycline or chloramphenicol are suitable antibiotics for use in *H. influenzae* epiglottitis, and chlortetracycline is a useful prophylactic for an unprotected infant who comes into contact with pertussis.

Other aspects of therapy which may play a part in these severe diseases of early childhood include attention to fluid

and electrolyte balance, mist therapy,¹⁴ and correct position for nursing. Cautious sedation with, for example, chloral hydrate is often indicated for the restless infant with bronchiolitis after hypoxaemia has been corrected. The value of corticosteroids in bronchiolitis is doubtful,¹⁵ but the occasional severely ill infant appears to derive benefit.

Cowpox and Paravaccinia

People whose daily work brings them into contact with farm animals are especially liable to develop bacterial infection such as brucellosis or rickettsial infection such as Q fever. It is less well known that they are also exposed to the risk of viral infections of the skin which may be acquired from cattle or sheep. The viruses concerned belong to the large group of poxviruses. The most important poxvirus in human disease is variola or smallpox virus, but this does not affect any animal species other than man. However, man is susceptible to other poxviruses whose natural hosts are cows and sheep.

Jenner's classic treatise in 1798¹ contained the first description of human cowpox, which at that time was not uncommon among dairymaids. Cowpox causes vesicles on the teats and udders of cows, and they progress to pustules, with the formation of scabs. It is a mild infection in that animal, and the disease is spread mainly by the process of milking. Cases of human cowpox are rarely reported, but A. W. Downie² found 10 outbreaks in cattle in England and Wales during 1944 to 1950, and in each instance attention was drawn to the disease by cases of infection in milkers. In 1909 R. J. Reece investigated an outbreak in Somerset which involved 23 out of 44 milkers and 214 out of 410 cows.³ More recently W. F. T. McMath and H. T. H. Wilson described a case in this journal⁴ of a young man who developed multiple lesions on the chin and lips from contact with an apparently healthy calf.

Human cowpox usually affects the hands—often between the thumb and forefinger—but lesions are sometimes seen on the forearm and face. The lesions are vesicular and closely resemble the reactions seen after successful vaccination against smallpox. Cowpox vesicles tend to be more haemorrhagic than vaccination reactions, and the vesicle fluid may be blood-stained. The lesions are painful and are usually associated with lymphangitis and lymphadenitis. There is often a mild constitutional upset, with some fever. The lesions are slow to heal and may take several weeks to resolve. The vaccinia virus used for vaccination against smallpox is very similar to cowpox virus and probably originally derived from it. Both have the brick-shaped particles on electron-microscopy which are seen with smallpox virus also. Cowpox and vaccinia have a similar range of susceptible hosts, and there have been outbreaks of cowpox in cattle due to infection introduced by a recently vaccinated person.⁵

In addition to cowpox, cattle are susceptible to other poxviruses that can infect human skin. These are members of the paravaccinia subgroup of poxviruses and include the virus of milker's nodules, bovine papular stomatitis virus, and the virus of orf or contagious pustular dermatitis in sheep.⁶ Paravaccinia viruses have oval particles on electron-microscopy with characteristic criss-cross surface banding, so that they resemble coiled skeins of wool.⁷ The virus of milker's nodules affects the teats and udders of cows, causing lesions

¹ Shwachman, H., Kulczycki, L. L., and Khaw, K.-T., *Pediatrics*, 1965, 36, 689.

² Simpson, H., and Flenley, D. C., *Lancet*, 1967, i, 7.

³ — and Russell, D. J., *Brit. med. J.*, 1967, 4, 201.

⁴ Campbell, E. J. M., *ibid.*, 1965, i, 1451.

⁵ Wright, F. H., and Beem, M. O., *Pediatrics*, 1965, 35, 334.

⁶ Canby, J. P., and Redd, H. J., *ibid.*, 1965, 36, 406.

⁷ McClelland, R. M. A., *Brit. med. J.*, 1965, 2, 567.

⁸ McDonald, I. H., and Stocks, J. G., *Brit. J. Anaesth.*, 1965, 37, 161.

⁹ Rees, G. J., and Owen-Thomas, J. B., *ibid.*, 1966, 38, 901.

¹⁰ Downes, J. J., Striker, T. W., and Stool, S., *New Engl. J. Med.*, 1966, 274, 226.

¹¹ Campbell, D., Reid, J. M., Telfer, A. B. M., and Fitch, W., *Brit. med. J.*, 1967, 4, 255.

¹² *Brit. med. J.*, 1965, 2, 714.

¹³ Disney, M. E., Sandiford, B. R., Cragg, J., and Wolff, J., *Brit. med. J.*, 1960, 1, 1407.

¹⁴ Avery, M. E., Galina, M., and Nachman, R., *Pediatrics*, 1967, 39, 160.

¹⁵ Dabbous, I. A., Tkachyk, J. S., and Stamm, S. J., *ibid.*, 1966, 37, 477.

which clinically bear some resemblance to those of cowpox. Orf produces lesions in the mouths of sheep and is mainly seen as an infection of lambs. The third paravaccinia virus—bovine papular stomatitis virus—is now thought to be the same virus as that causing milker's nodules.⁸ Bovine papular stomatitis has recently been reported in Britain⁹ and causes lesions which are clinically similar to milker's nodules on the hands and forearms of human handlers.^{8 10 11}

Human infection with the paravaccinia viruses of orf and milker's nodules is not uncommon in rural areas. Infection is seen in people who have contact with cows or sheep or with products derived from them. For example, orf is seen in shepherds, butchers, sheep shearers, and veterinary surgeons and has been described in housewives with a liking for sheep's heads.¹²⁻¹⁹ Milker's nodules are also seen in veterinary surgeons and in farm workers who tend dairy cattle—even if the animals are milked by machine.^{5 20 21} Both viruses cause similar disease in man, and the name ascribed to the infection depends on the animals which were the probable source of infection.²⁰ As a result, orf is diagnosed in shepherds and milker's nodules in cowmen. Clinically the lesions are usually single, but cases with two or with multiple lesions have been reported. The fingers and hands are the commonest sites for them, but lesions have been described on the arms, face, neck, and occasionally on the leg. Different types of lesion may be seen. Most start as bluish-red papules or nodules, which are sometimes surmounted by a small white blister. Ulceration is common. Lesions may also take the form of granulomas in which there is ulceration with proliferation of grey-coloured epidermal tissue. Many appear to be vesicular, but it is often difficult to extract fluid from them.²² The most striking feature is that the lesions are painless, though they look like acute inflammatory reactions. There is usually no constitutional disturbance. Lymphangitis and lymphadenitis have been described, but—in contrast to human cowpox—appear to be rare. The lesions persist for about five to eight weeks and resolve spontaneously without treatment. One attack appears to confer long-lasting immunity against reinfection, but, unlike cowpox, there is no cross-immunity with vaccinia.^{22 23}

The relationship between the three paravaccinia viruses is obscure, though it is clear that they are closely related. J. Nagington and his co-workers have shown that orf and

milker's nodules viruses are similar in their morphology and cultural characteristics.²⁰ In addition I. M. Lauder and his colleagues have shown that the bovine virus of milker's nodules can produce lesions in lambs after inoculation on to the gums and lips.²⁴

Neither cowpox nor paravaccinia is a serious infection in man. Diagnosis will present few problems to general practitioners in rural areas or to dermatologists, who also see these diseases from time to time. However, the infections might well puzzle a newly qualified casualty officer in a city, who may come across lesions on the hands of butchers, slaughtermen, or veterinary surgeons. When the infection has been diagnosed, the patient can be reassured—firstly as to the nature of the lesion, and secondly that it will resolve spontaneously and without complications within the following month or two.

Pseudomonas Infection in Hospital

In the last few years the problems of staphylococcal cross-infection seem to have become more manageable, thanks especially to the semisynthetic penicillins tolerant of penicillinase. Unfortunately the same cannot be said of infection with *Pseudomonas aeruginosa* (pyocyanea). Indeed, reports of such infections have become more frequent. This can be partly explained by the relative ineffectiveness of chemotherapy for pseudomonas infection. Successful treatment of infections with Gram-positive cocci has undoubtedly brought the less tractable infections with Gram-negative bacilli such as *Ps. aeruginosa* into prominence. A relative and absolute increase in the amount of infection by these opportunists appears to have occurred.¹⁻³

Epidemiological features of pseudomonas infection which have made it hard to eradicate⁴ include its tendency to grow or at least survive in moist environments and its relative insensitivity to certain disinfectants as well as to most antibiotics. Moreover, despite a low pathogenicity for healthy people, it tends to be more pathogenic and invasive than most other common bacteria in patients or in tissues with low humoral resistance—for example, in infants and in leukaemic patients, in the chambers of the eye, and on the meninges. Not surprisingly, *Ps. aeruginosa* is a special hazard to patients treated with corticosteroids and with immunosuppressive drugs.³⁻⁵ In burned patients two factors encourage pseudomonas infection—the presence of moist slough, which is easily colonized by *Ps. aeruginosa*, and (when the burns are extensive) reduced resistance to invasion.

The sources of these infections are varied and often elusive. Unlike *Escherichia coli* and *Staphylococcus aureus*, *Ps. aeruginosa* is usually not carried in large numbers by healthy people. Recent studies⁶ have shown a larger proportion (about 12%) of healthy people to be carrying *Ps. aeruginosa*, at least in small numbers, than most previous surveys had suggested, and in another recent report⁷ about 5% of healthy people were found to carry *Ps. aeruginosa* in the saliva. But, while sporadic self-infection with *Ps. aeruginosa* can undoubtedly occur, most endemic infection such as in burns and all outbreaks can be attributed to contamination from another human source or the inanimate environment. In many cases the source has been traced by typing of strains.⁸⁻¹⁰ Human sources are generally sites of heavy infection—wounds, burns, the urinary tract. Established inanimate

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² Downie, A. W., *Brit. med. J.*, 1951, 2, 251.

³ Reece, R. J., *Proc. roy. Soc. Med.*, 1922, 15, 13. Section of Epidemiology and State Medicine.

⁴ McMath, W. F. T., and Wilson, H. T. H., *Brit. med. J.*, 1965, 1, 1041.

⁵ Nomland, R., and McKee, A. P., *Arch. Derm. Syph. (Chic.)*, 1952, 62, 663.

⁶ Peters, D., Müller, G., and Büttner, D., *Virology*, 1964, 23, 609.

⁷ Nagington, J., Plowright, W., and Horne, R. W., *ibid.*, 1962, 17, 361.

⁸ ———, Lauder, I. M., and Smith, J. S., *Vet. Rec.*, 1967, 81, 306.

⁹ Williams, D. R., Plowright, W., and Burrows, R., *ibid.*, 1966, 78, 571.

¹⁰ Olson, C., and Palonis, T., *J. Amer. vet. med. Ass.*, 1953, 123, 419.

¹¹ Carson, V. M. D., and Kerr, K. M., *ibid.*, 1967, 151, 183.

¹² Peterkin, G. A. G., *Brit. J. Derm. Syph.*, 1937, 49, 492.

¹³ Blakemore, F., Abdussalam, M., and Goldsmith, W. N., *ibid.*, 1948, 60, 404.

¹⁴ Lyell, A., and Miles, J. A. R., *Brit. med. J.*, 1950, 2, 1119.

¹⁵ Rankin, A. K., *ibid.*, 1950, 2, 1279.

¹⁶ Kewish, O. K., *ibid.*, 1951, 1, 356.

¹⁷ Peterkin, G. A. G., *ibid.*, 1951, 1, 588.

¹⁸ Hodgson-Jones, I. S., *ibid.*, 1951, 1, 795.

¹⁹ Lloyd, G. M., *ibid.*, 1951, 1, 1144.

²⁰ Nagington, J., Tee, G. H., and Smith, J. S., *Nature (Lond.)*, 1965, 208, 505.

²¹ Neale, E. J. E., and Calvert, H. T., *Brit. J. Derm.*, 1967, 79, 318.

²² Blank, H., and Rake, G., *Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membranes of Man*, pp. 193-202, 1955. London.

²³ Nagington, J., and Whittle, C. H., *Brit. med. J.*, 1961, 2, 1324.

²⁴ Lauder, I. M., Martin, B., Martin, W. B., and Nagington, J., *Vet. Rec.*, 1966, 78, 926.

sources include saline,¹¹ soap and antiseptic solutions,¹² eyedrops,¹³ creams,¹⁴ jellies,¹⁵ and equipment which contains standing water or retains moisture (especially respirators and resuscitation equipment for premature infants),¹⁶⁻¹⁷ moist brushes (for example, shaving-brushes used for depilation of the scalp before craniotomy),¹⁸ and surgical instruments and catheters "sterilized" with an inadequate disinfectant.^{19 20} Dry sources (dust, air) are uncommon but may on occasion be important.²¹ The hands of nurses in wards where the infection occurs are often found to carry *Ps. aeruginosa* and are likely to contaminate uninfected patients if the nurses do not wear rubber or plastic gloves when attending to them.²² The importance of some sites which are commonly contaminated—for example, sinks and drains—has not been clearly established.

At page 313 of the *B.M.J.* this week Dr. J. E. Tinne, Dr. A. M. Gordon, Mr. W. H. Bain, and Mr. W. A. Mackey report an outbreak of infection of the respiratory tract with *Ps. aeruginosa* in a cardiac surgery unit. During two months, in which 30 operations were performed, five patients became infected with this organism and three of them died. These deaths occurred in the eight patients of the series who had open heart surgery followed by tracheostomy, hydrocortisone therapy, broad-spectrum antibiotics, and prolonged mechanical ventilation. All strains were of the infrequent pyocine type 10. A strain of the same type was found in the connecting tube of a respiratory ventilator and in a rebreathing bag. These findings strongly suggest that infection was acquired by the patient's respiratory tract from the ventilator. The authors subsequently found *Ps. aeruginosa* on various fittings and pieces of equipment in the operating-theatre suite, and introduced measures to prevent recurrences. These included the use of a new disinfectant, which appeared to be effective in removing *Ps. aeruginosa* from contaminated objects and sites.

Though outbreaks of *Ps. aeruginosa* infection continue to be reported, they are often due to some deficiency or error in technique (especially in sterilization or maintenance of sterility) which can be corrected. But outstanding difficulties still exist with types of equipment—for example, mechanical ventilators—that cannot be sterilized by heat, and also with the elaborate nursing procedures of intensive-care units. The design of some types of equipment needs improvement to facilitate cleaning and disinfection. In the treatment of burns the control of *Ps. aeruginosa* infection has been greatly helped by local application of 0.5% silver nitrate solution,^{23 24} and this can probably be enhanced by modern aseptic methods, notably the use of "isolators"^{25 26}—that is, special isolation chambers. Two new antibiotics, gentamicin^{25 28} and carbenicillin,²⁷⁻²⁹ give promise of providing better control of *Ps. aeruginosa* infection than has been obtained with the polymyxins, and immunological methods of protection have also shown promise.^{30 31} For the protection of high-risk patients it is desirable to use these and other methods in a system of multiple defences. But no set of rules can succeed without a high standard of aseptic discipline and understanding among the hospital staff under the guidance of an active infection-control officer.

Body Building by Drugs

The self-administration of anabolic steroids is becoming a problem in athletics. A letter from Dr. D. E. Pearsons at page 353 draws attention to the matter. Taking these artificial aids to athletic performance must surely be condemned as unethical. In addition, it is possibly hazardous to health, for this group of drugs have side-effects.

Those anabolic steroids that are active when taken by mouth commonly affect conventional liver-function tests and occasionally cause jaundice. These side-effects are probably caused by interference with the transport of conjugated compounds into the bile and usually disappear quickly on withdrawal of the drug. Serum enzyme levels of the transaminases S.G.O.T. and S.G.P.T. and lactic dehydrogenase are often raised, though this does not necessarily imply damage to liver cells. Only the compounds active by mouth cause liver damage, because of their particular chemical configuration. They may also raise the level of serum lipids, especially of cholesterol, with the possibility of causing serious harm in that way. This action has been specially noted in two groups of patients—those receiving glucocorticoids and obese diabetics not requiring insulin.¹ Some anabolic steroids may impair the hepatic degradation of cortisol, enhancing the action of this drug and necessitating a reduction in dosage.^{2 3}

All anabolic steroids so far investigated have proved to have some androgenic activity. In women this may lead to hirsuties, acne, and virilization of the voice.⁴ The patient feels her voice to be strange and is unsure about its use; in severe cases it wavers between the chest and falsetto registers. This effect is irreversible.

Increased muscular development and improved athletic performance are widely believed to result from use of anabolic

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- ³ — — — — — *ibid.*, 1964, **29**, 2.
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steroids,⁵ and there is good evidence that they do increase the muscle mass in castrates of both sexes and in most patients with a high rate of protein catabolism, but critical studies confirming these effects in normal men on an optimal protein and calorie intake are lacking. In a carefully controlled trial W. M. Fowler and colleagues⁶ failed to find any effect of an anabolic steroid on the physical performance of young healthy men, even in a group taking extra physical exercise along with the drug. It might be argued that the physical exercise used in this study was not severe enough to compare with that undertaken by athletes preparing for international competition. If that were so it is possible that anabolic steroids combined with a high-protein diet might have an anticatabolic effect under conditions of severe muscular exercise, and hence produce an increase in physical performance.

It is difficult to detect whether a patient is taking these preparations, because the doses used might be small, and in any case adequate methods for detecting these drugs and their metabolites in blood and urine have not been fully evaluated. Since any effect they may have on muscular development will be prolonged, athletes can stop taking the drugs several weeks before a competition, so that any chance of detection then would be negligible. Secondary effects of the anabolic steroids on serum enzyme levels or on the level of thyroxine-binding globulin,⁷ with lowering of the plasma protein-bound iodine, might be more prolonged, but further studies are required to clarify their duration. It is to be hoped that all the governing bodies of sports will take a stand against the use of such methods of training.

Mismanagement of Non-disease

Some two years ago C. K. Meador¹ wrote an amusing but important article entitled "The Art and Science of Non-disease," drawing attention to common errors of diagnosis in the endocrine field, with resulting treatment of nonexistent disease. Some of the mistakes were due to laboratory errors. "Laboratory error syndromes," he wrote, "are the delight of the alert non-disease clinician; one must add, however, only before therapy has been initiated. In this regard they are probably the most responsive to treatment of all entities. One merely has to repeat the test once to see astounding results; for example, in what other non-disease or disease can one see a rise in the haemoglobin level from 6 to 14 g./100 ml. in two hours with only one iron tablet?"

Recently A. B. Bergman and S. J. Stamm² have discussed morbidity of cardiac non-disease in schoolchildren. They studied 93 children who were said to have had rheumatic fever or to have "something wrong with the heart." Seventy-five (81%) had nothing wrong with them—and thirty of these had been subjected to severe restrictions on the instruction of their doctor. Eighteen had organic heart disease, and six of them had been put under severe but unnecessary restrictions. They wrote that "Restriction of children with innocent murmurs is only slightly more absurd than restriction of the vast majority of children with an organic heart defect"; and "The diagnosis of heart disease may cause profound changes in the functioning of a child and his family, far beyond the immediate physical effects." On the basis of their

study of these 93 children they concluded that "The amount of disability from cardiac non-disease in children is estimated to be greater than that due to actual heart disease." They rightly criticize the restrictions imposed on children with congenital or acquired heart disease, advocating that they should be left to find their own level of activity of which they are capable. Parents fear that their child will drop dead if allowed to cry or to exert himself in other ways. In fact, as the writers state, sudden death is rare except in children with aortic stenosis.

Functional murmurs are exceedingly common in children. R. W. Quinn and E. S. Campbell³ found them in 44% of 4,039 Nashville schoolchildren. Unfortunately it is not easy to describe in words the difference between a functional murmur and the murmur of organic disease. The distinction is a matter of experience. In general, the functional murmur is louder when the child is lying down, it is increased by exertion, and it has a musical, twanging nature, or is very soft. Murmurs in the newborn period frequently suggest serious congenital heart disease to the unwary, only to disappear in a few days. The venous hum, the to-and-fro murmur beneath the clavicle, can easily lead the doctor towards the diagnosis of a patent ductus arteriosus, while the true nature of the murmur could be readily established by causing its disappearance on rotating the head or by pressure on the vessels of the neck. The tachycardia of excitement or nervousness and the raised systolic blood pressure under the circumstances of the doctor's examination can likewise lead to the wrong diagnosis of cardiac disease.

Now R. S. Illingworth,⁴ of Sheffield, has tried to dispel "Fallacies in Four Fevers." Discussing measles, German measles, chicken-pox, and mumps, he questions the value of some of the time-honoured methods of managing children with these infections and quotes with approval N. L. Browse's remark that "the bed is often a sign of our therapeutic inadequacy."⁵ Certainly many doctors as well as parents would agree with Illingworth that too long confinement to bed of children with these fevers can do actual harm and give no benefit. He is likewise critical of the isolation and medication of these patients on principles that may be long accepted but have escaped careful scrutiny. When prescribing treatment, he says, one should always ask three questions: What good may it do? What harm may it do? What harm may be done by not giving this treatment?

Oesophageal Function in Diabetes

Among the better-known neurological complications of long-standing diabetes are peripheral neuropathy, impotence, diarrhoea, and postural hypotension. The exact nature of the neurogenic defect is still a matter of debate, and the effects are often complex and are not necessarily clinically apparent. In the gastrointestinal tract, for example,^{1,2} symptomless gastric atony can result in a radiological appearance similar to that produced by vagotomy,³ whereas diarrhoea in some patients may be associated with steatorrhoea or with changes in bowel flora.⁴

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² Bergman, A. B., and Stamm, S. J., *ibid.*, 1967, 276, 1008.

³ Quinn, R. W., and Campbell, E. S., *Yale J. Biol. Med.*, 1962, 34, 370.

⁴ Illingworth, R. S., *Brit. med. J.*, 1967, 3, 41.

⁵ Browse, N. L., *The Physiology and Pathology of Bed Rest*, 1965. Springfield, Ill.

¹ Ellenberg, M., *Adv. intern. Med.*, 1964, 12, 11.

² Katz, L. A., and Spiro, H. M., *New Engl. J. Med.*, 1966, 275, 1350.

³ Wooten, R. L., and Meriwether, T. W., *J. Amer. med. Ass.*, 1961, 176, 1082.

⁴ Malins, J. M., and French, J. M., *Quart. J. Med.*, 1957, 26, 467.

⁵ Rundles, W. R., *Medicine*, 1945, 24, 111.

⁶ Mandelstam, P., and Lieber, A., *J. Amer. med. Ass.*, 1967, 201, 582.

Rather surprisingly, little attention has been paid to the oesophagus. W. R. Rundles,⁵ in a classic review of diabetic neuropathy, mentioned the finding of degenerated nerve plexuses in the oesophagus of two patients, but there has been no detailed investigation of oesophageal function. A recent report⁶ shows that oesophageal abnormalities may in fact be fairly common. Fourteen patients with evidence of diabetic neuropathy were examined by cineradiography, and 12 had evidence of dysfunction. Peristalsis was reduced or absent, emptying was delayed, the oesophagus was dilated, and tertiary contractions were seen. Two patients had oesophageal reflux and hiatus hernia. No abnormalities were found in 14 matched control subjects. In spite of the frequency of radiological findings, only three patients had symptoms, consisting of heartburn in one and dysphagia in two.

These results are similar to previous investigations of other parts of the gastrointestinal tract, in which a high incidence of radiological abnormalities contrasts with the paucity of clinical symptoms. In addition, there was no correlation with the degree of diabetic control, with other evidence of visceral neuropathy, or with other complications of the disease. One patient with severe dysphagia died, but the oesophageal nerve plexuses appeared normal. The enigmatic nature of diabetic neuropathy, in which disorders of function may be found without either recognizable pathological changes or the production of symptoms, presents a challenge to the physician. In the case of the oesophagus further insight might be provided by the use of intraluminal manometry.

Ventricular Aneurysm

For the past quarter of a century radiologists have recognized that after myocardial infarction there are commonly abnormalities of ventricular contraction. These have been reported in as many as 70% of an unselected group of patients with both old and fresh myocardial infarcts,¹⁻³ and may take the form of paradoxical pulsation of a localized segment of the cardiac silhouette or of diminished or absent pulsation. Serial kymographic studies have shown that in some patients these abnormalities disappear or become less marked with healing of the infarct.

The advent of cineventriculography has made it easier to study disturbances of ventricular contraction. Using this technique R. Gorlin and his colleagues⁴ found abnormalities of contraction in about 20% to 25% of patients with coronary artery disease who were being assessed before the operation of implantation of an internal mammary pedicle. In Gorlin's study the term ventricular aneurysm was used to describe abnormalities of local movement of the ventricular wall, whether or not these were associated with thinning or fibrosis.

This definition of aneurysm is mechanical rather than anatomical and is probably too great an extension of the traditional meaning of the word. A more acceptable definition is that of J. Schlichter and his colleagues,⁵ who defined a cardiac aneurysm as a localized outpouching of the cavity of a cardiac chamber with or without outward bulging of the external surface—in either case a large transmural infarct leads to thinning of the left ventricular wall and consequent paradoxical pulsation. If Schlichter's definition of aneurysm is accepted a different term will be needed for the reversible abnormalities of ventricular contraction without a full thickness infarct described by Gorlin and his coworkers.

Abnormalities of ventricular contraction after myocardial infarction can usually be recognized at the bedside. Careful palpation of the cardiac impulse will detect the development of a sustained abnormal impulse appearing during the first week after acute cardiac infarction in about one-fifth of patients.⁶⁻⁸ Recognition of this simple physical sign can be made without the aid of graphic recording by simultaneous palpation and auscultation. If a sustained outward impulse is felt, lasting up to the time of the second heart sound, this is abnormal. Where this sign persists after acute cardiac infarction strong presumptive evidence of a ventricular aneurysm exists, provided there was not already left ventricular hypertrophy due to co-existing hypertension or aortic valve disease. The site of greatest excursion of the abnormal impulse varies with the site of the aneurysm. If it is anterior the impulse is usually greatest somewhere over the mid-praecordium. If, however, the aneurysm is postero-lateral then the abnormal impulse is usually confined to the apex. The surest evidence that the sustained impulse is related to the infarction rather than to previous left ventricular hypertrophy is observation of its development during the first week after acute infarction. Graphic records confirm the abnormally sustained nature of the impulse and usually show a double hump due to a large palpable preceding atrial beat. Apex cardiography is an unreliable method of recording late systolic events, as it is influenced by the pressure with which the pick-up head is applied to the moving chest wall; but absolute displacement techniques such as impulse cardiography⁹ and kinetocardiography¹⁰ give faithful records. When the diagnosis of cardiac aneurysm has been suggested by the presence of an abnormal cardiac impulse, it can be confirmed by fluoroscopy and electrocardiography. Angiocardiography is of value in detailed preoperative investigation.

D. L. Abrams and his colleagues¹¹ in a review of 65 consecutive cases of ventricular aneurysm at necropsy recommended a conservative approach to treatment. Their main indications for ventriculoplasty were progressive heart failure refractory to medical therapy, where coronary arteriography showed the blood supply to the rest of the ventricle was adequate; and repeated systemic embolization that could not be controlled by treatment with anticoagulants. The highest mortality from cardiac aneurysm is within the first year, and is caused by intractable heart failure. If patients survive this period the prognosis does not appear to be very different from that of ischaemic heart disease in general.

The next session of the General Medical Council will open on Tuesday, 28 November, at 2.15 p.m., when the president, the Rt. Hon. Lord Cohen of Birkenhead, will take the chair and will deliver an address.

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⁴ Gorlin, R., Klein, M. D., and Sullivan, J. M., *Amer. J. Med.*, 1967, 42, 512.

⁵ Schlichter, J., Hellerstein, H. K., and Katz, L. N., *Medicine (Baltimore)*, 1954, 33, 43.

⁶ Mourdjinis, A., Olsen, E., Taubman, J., and Mounsey, J. P. D., *Brit. Heart J.*, 1966, 28, 430.

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⁸ Mourdjinis, A., Olsen, E., Raphael, M. J., and Mounsey, J. P. D., *in press*.

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Papers and Originals

Cross-infection by *Pseudomonas aeruginosa* as a Hazard of Intensive Surgery

J. E. TINNE,* M.D., B.SC., D.P.H., M.C.PATH.; A. M. GORDON,* M.B., D.PATH., M.C.PATH.
W. H. BAIN,† M.D., F.R.C.S.ED.; W. A. MACKEY,† T.D., M.B., F.R.C.S.ED., F.R.C.S.GLASG., F.A.C.S.(HON.)

Brit. med. J., 1967, 4, 313-315

Although cross-infection has always presented serious problems, there has within recent years been an increased awareness of the growing prevalence of Gram-negative organisms, especially *Pseudomonas aeruginosa*, as causes of serious morbidity in the hospital environment (Finland *et al.*, 1959; Williams *et al.*, 1960; Barber, 1961). A variety of factors appear to have contributed to this changing pattern of hospital-acquired bacterial infections, but the extensive use of broad-spectrum antibiotics, corticosteroids, and cytotoxic and immunosuppressive drugs, and the increased susceptibility of individuals subjected to advanced and intensive surgery or medical techniques, have been of major significance. In this context, infections by *Ps. aeruginosa*, an organism of low pathogenicity to healthy individuals, are likely to be particularly serious and associated with a high mortality. This opportunist has an inherently high resistance to most currently available antibiotics, and many antiseptics are less active against *Ps. aeruginosa* than against other vegetative bacteria.

Recently a series of *Ps. aeruginosa* infections of the respiratory tract occurred in a cardiovascular surgical unit involving seven patients, three of whom died. The three fatal cases had been subjected to open-heart surgery followed by intensive care, including tracheostomies and prolonged postoperative mechanical ventilation. They had also received corticosteroids, while all the cases had had prophylactic broad-spectrum antibiotic cover.

This paper describes the clinical and bacteriological features of the outbreak together with the epidemiological investigations and control measures which were undertaken.

History of the Initial Outbreak

During the two months December 1966 to February 1967 30 operations were performed in the unit. Twenty-two were mitral valvotomies or other short closed-heart procedures, and none of these showed any evidence of respiratory or wound infection. On the other hand, of the eight patients who underwent open-heart surgery with extracorporeal circulation, five developed respiratory tract infections due to *Ps. aeruginosa* and three of these subsequently died. The following is a synopsis of the postoperative course of the first five cases in which *Ps. aeruginosa* was isolated.

Case 1.—This patient's operation was for closure of an atrial septal defect. He was breathing spontaneously immediately after the operation, and subsequently his course was uneventful apart from a respiratory infection. Culture of his sputum on the fourth day grew *Escherichia coli* (sensitive to ampicillin, streptomycin, and tetracycline) and *Ps. aeruginosa* (sensitive to colistin only). The patient made a good recovery.

Case 2.—An aortic valve (Starr) prosthesis was inserted in this man on 12 December, after which intermittent positive-pressure ventilation by Bennet's machine was required and a tracheostomy was performed two days later. *Ps. aeruginosa* was cultured from his bronchial aspirate during the subsequent 10 days, and he died of progressive respiratory insufficiency and septicaemia.

Case 3.—This boy had an operation for closure of an atrial septal defect on 19 January 1967 and required a tracheostomy for respiratory insufficiency on 21 January, and ventilation was assisted. Four days later *Ps. aeruginosa* was grown from specimens of tracheal aspiration and he died three weeks after operation.

Case 4.—Another operation for closure of an atrial septal defect took place on 2 February 1967. Though the postoperative course was uncomplicated by clinical evidence of infection, culture of sputum on the fifth day revealed *Ps. aeruginosa*. This was an isolated specimen, however, and subsequent cultures were negative. The patient made a good recovery.

Case 5.—An operation for replacement of the mitral valve was carried out on 6 February 1967. Tracheostomy was performed for respiratory insufficiency on 8 February and ventilation was assisted mechanically. Culture of tracheal secretions on each of the next three days showed a heavy growth of pseudomonads. Blood cultures on the fourth and fifth days also grew *Ps. aeruginosa*. The patient died on the sixth day after operation.

On reviewing the postoperative course of these cases, certain common factors emerge. It has been routine practice in this unit to administer ampicillin and methicillin by slow intravenous drip for seven days after open-heart surgery. Further, the three patients who died had received comparatively large doses of hydrocortisone (500 mg. six-hourly) throughout the first postoperative week in an effort to modify the "post-perfusion lung" syndrome. While the three patients who died were certainly the most ill from the point of view of their cardiovascular status, it might also be argued that the combination of the antibiotics used, together with continued large doses of hydrocortisone, rendered them unduly susceptible to an overwhelming infection by *Ps. aeruginosa*.

Bacteriological Investigations and Control

It will be noticed that all five cases had had tracheostomies. This operation is notorious for profoundly modifying respiration and so exposing the lung to pseudomonas infection (Dupont *et al.*, 1962), and this risk is much greater when the artificial airway has to be prolonged, as *Ps. aeruginosa* is about 10 times commoner in the secretions collected after a month than in those taken after a week (Tunevall, 1956). Moreover, all the cases had been given ampicillin and methicillin prophylactically, and *Ps. aeruginosa*, resistant to these antibiotics, was present in the sputa of all seven cases; it was also found in the tracheostomy wounds of two of the fatal ones (Cases 2 and 5) and in the throat, bronchi, and blood of one (Case 5) at necropsy.

* University Department of Bacteriology, Royal Infirmary, Glasgow C.4.
† University Department of Surgery, Royal Infirmary, Glasgow C.4.

These findings suggested a respiratory source for the infection, and this was confirmed when random swabbing of the equipment of the theatre suite and adjacent rooms showed that at this stage isolation of pseudomonads was limited to the anaesthetic equipment, and in fact to the connecting tube of the Bennet ventilator and the Ambu rebreathing bag.

Wahba (1965) showed that by identifying the specific pyocines produced by the pseudomonads it was possible to distinguish different strains, and, using 12 such indicators, he differentiated eight strains. Gillies and Govan (1966), using only eight pyocine indicators, identified 36 types, of which Nos. 1, 3, 5, 6, and 9 comprised over 70% of all *Pseudomonas* strains they tested. With this technique Dr. Gillies was able to confirm that the strain of *Ps. aeruginosa* found in the ventilator and the Ambu bag was the relatively rare type 10 identical to that also found in the three fatal cases.

The respiratory equipment had come under suspicion after the second case. The Ambu bag was destroyed and sterilization of the ventilator attempted by washing with chlorhexidine digluconate followed by exposure to ethylene oxide by running the gas through the machine. Solutions of chlorhexidine have recently been incriminated in the actual spread of pseudomonads in a hospital (*Brit. med. J.*, 1967; Burdon and Whitby, 1967). The last three of these five cases were infected by *Ps. aeruginosa* after the anaesthetic equipment had been treated by both methods before use in each case. Clearly these methods of disinfection were ineffective. Moreover, the organism had by now contaminated the distilled water in the nebulizer of the Bennet ventilator and also the alternative Barnett ventilator, the connecting tube being again implicated as well as the flowmeter, which was found to contain blood clotted on the vanes when dismantled.

Pseudomonas aeruginosa was recovered from the throat swabs of 6 of the 50 staff and patients, and it was suspected that the organism, which would not normally be a commensal in this site, had become widely disseminated.

For our earlier isolations of pseudomonads we had relied on the selective medium of Lowbury and Collins (1955) which employs 0.03% cetrinide; and to eliminate *Klebsiella* and *Proteus* spp., which also survive, we had depended on pseudomonal colonies giving a positive oxidase test, rather than the improved fluorescence of the organism which Brown and Lowbury (1965) achieved by modifying the medium. As it was intended to culture numerous swabs from the theatre and surroundings, the cetrinide plates were made even more selective by adding 5 µg. of nalidixic acid per ml. This was based on a clinical trial (Barlow, 1963) in which 24 out of 25 strains of *Pseudomonas* had resisted nalidixic acid inhibitory to *Klebsiella* and *Proteus* spp. in cultures of urine. Experiments showed that our *Ps. aeruginosa* type 10 could just survive these combined inhibitory agents, which together excluded other bacteria.

Several hundred moistened swabs were now used to sample the flora on the fittings and equipment of the theatre and adjoining rooms. *Ps. aeruginosa* was isolated from the following relatively inaccessible places even after the use of various disinfectants, which had included glutaraldehyde, and chlorhexidine with cetrinide: ventilator of ceiling light; ventilator louver on wall; panel of air-conditioning control on wall; trap and gauge of suction apparatus on wall; corrugated tubing of Boyle's anaesthetic apparatus; sampling tube and undersurface of chassis of Astrup blood-gas analysis trolley; grids on drains of floor and sink; a pair of clogs; and in adjacent rooms the x-ray camera, and the drains of the dark-room, ward, and sluice.

It was obvious that there was particularly widespread contamination with *Pseudomonas* sp., and it had to be assumed that nothing short of their complete eradication would ensure elimination of the risk from the epidemic of type 10. A solution of activated glutaraldehyde has been recommended by

Rittenbury and Hench (1965) for sterilizing anaesthetic equipment such as masks, suction catheters, and endotracheal tubes; but Ross (1966) found that at a concentration of 50% this compound required between 15 and 30 minutes to kill pseudomonads in broth, and that with added blood even this was insufficient. It is problematic whether any disinfectant can be relied on with gross contamination with blood, but the timely appearance of a new disinfectant Portex-DCR containing diphenidol which was reputedly active against pseudomonads enabled us to test this agent, using a broth culture of the type 10 organism and a similar broth culture with 10% blood added. The results showed that Portex-DCR killed the pseudomonads in two minutes at a dilution of 1/160 in broth, but that in the presence of blood 1/40 was the effective dilution. This agent offers two further advantages: it is non-irritant in effective dilutions; and it changes colour from green to blue when no longer active—this indicator is a useful guide under circumstances where the solution is being applied by lay staff such as cleaners.

The unit was closed and the six nurses with positive throat cultures were sent on a week's leave. Intricate equipment was dismantled, cleaned, and then sterilized by 24 hours' exposure to ethylene oxide in plastic bags; but all other appliances and the rooms themselves were disinfected by washing with 1/40 Portex-DCR. As this still left surviving pseudomonads, notably in the drains and the Astrup blood-gas analysis apparatus, this washing was repeated with 1/20 Portex-DCR, and lysol was poured down the drains. Pipes and ducts were flushed for 30 minutes with Trilene to remove oil deposits. It was found, however, that the organism survived 25 minutes' exposure to this detergent, and therefore the Trilene was followed by washing with Portex-DCR 1/20. Two months elapsed before complete clearance was reached for all equipment and personnel, some equipment having to be dismantled by the makers to dislodge an organism described as "notorious for its ability to survive in unlikely situations" (*Lancet*, 1961).

Reappearance of Infection—Cases 6 and 7

On 15 May 1967 a housewife (Case 6) who had been admitted for mitral valve replacement produced a purulent sputum infected with *Ps. aeruginosa* type 10, raising doubts whether disinfection had been effective. Inquiry showed, however, that she had been in the ward during the first half of December 1966, when she would have encountered the infection and might well have harboured it since. Colistin was added to her prophylactic methicillin and ampicillin, and the sputum was cleared of pseudomonads after a week, though not before a patient in the adjoining bed (Case 7) had shown transient cross-infection. Closure of an atrial septal defect on this man 10 days previously had necessitated a tracheostomy, and on 15 May 20 colonies of *Ps. aeruginosa* were isolated from his tracheal secretions on a single occasion. Colistin methanesulphonate 1.5 mega units eight-hourly was given for three days and there was no recurrence.

Discussion

The distinction between pathogenic bacteria and harmless saprophytes, traditional since the days of Koch, has become blurred in recent years, and a survey at Boston City Hospital (Finland *et al.*, 1959) showed that between 1935 and 1957 intestinal commensals had progressively replaced the pyogenic cocci isolated from cases of bacteraemia. Moreover, the analysis disclosed that before 1941 *E. coli* alone was responsible but that after that date *Klebsiella*, *Proteus*, and *Pseudomonas* spp. increased in frequency. Secondary infection of wounds by *Ps. aeruginosa* has long been recognized because it will often colour the pus, and as skin and nasal carriers are relatively rare in contrast to those bearing staphylococci (Barber, 1961;

Williams *et al.*, 1966) cross-infection from other cases had to be assumed. Indeed, Selwyn *et al.* (1964), investigating 1,231 cases of hospital infection in Edinburgh, found that no less than 70% were non-staphylococcal, and they concluded that there had been comparative neglect of the role of these other organisms and especially of "coliform bacilli," including *Ps. aeruginosa*.

Opportunists such as these, though normally less invasive than the pyogenic cocci, are also far less fastidious in growth, so that their destruction is a formidable challenge to both antiseptics and antibiotics. Two ecological hazards are inseparable from the use of antibiotics. One is the emergence of resistant mutants, which has already become a major problem with the hospital staphylococcus; the other is disturbance of the diversity of bacterial flora. With "broad-spectrum" antibiotics only the hardier organisms will survive, and *Pseudomonas* is perhaps the hardiest of all. Widespread and even autochthonous, this organism is essentially a saprophyte and its normal habitat in man is limited to the intestine, and even in this situation its presence is exceptional (Lowbury and Fox, 1954).

Although human susceptibility to *Ps. aeruginosa* has been shown by random serological tests (Jones and Lowbury, 1965) to be very variable, certain groups would seem to be gravely at risk. Ayliffe *et al.* (1965) attributed cases of meningitis and urinary and wound infections in a neurosurgical unit to pre-operative use of a shaving brush infected with *Ps. aeruginosa*, and similarly contaminated eye-drops accounted for pseudomonal infection of 15 out of 25 ophthalmic operations, in six of which there was loss of the eye (Ayliffe *et al.*, 1966).

Phillips and Spencer (1965), who described 10 medical cases of respiratory infection with *Ps. pyocyanea*, four of which were fatal, noted that, ordinarily, the organism is virtually absent from human sputum, not one of 347 routine samples containing pseudomonads. Eight of their cases were infected like ours by a ventilator, two being cross-infections in adjoining beds, and they noted the role of prophylactic antibiotics, tracheostomy, and corticosteroids also in predisposing to infection.

In the present series of eight cases one or other of these three factors (corticosteroids, broad-spectrum antibiotics, and tracheostomy) again played a part, and in the three fatal cases all were present.

Though *Pseudomonas* sp. were found distributed in inaccessible sites ranging from the ceiling light to the drains the infections were primarily respiratory, and the fortunate chance of a relatively uncommon pyocine type being involved clearly implicated the ventilator and the rebreathing bag.

That droplet and dust-borne infections may not in practice be a risk from other sources was confirmed by experiment. While the theatre was closed 18 settle-plates were exposed for an hour on the floor and fittings. For 10 minutes of this time a surgeon, anaesthetist, and four nurses wearing masks and gowns talked and moved about the theatre, being asked to locate the plates. Notwithstanding that two of the team had positive nose or throat swabs for *Ps. aeruginosa* and that these organisms still persisted on the floor grid to the drains, no pseudomonads settled on the plates. We believe that carriers play little part in an epidemic of pseudomonal infection, but that even a single major case, especially respiratory, may contaminate the entire environment to such a degree that eradication becomes very difficult indeed.

Cetrimide-nalidixic acid plates and pyocine typing were found to be valuable tools in tracing the source and mode of spread of pseudomonads, just as modern disinfectants were needed for the control. Portex-DCR 2% proved to be the disinfectant most effective against *Ps. aeruginosa*, acting even in the presence of blood, unlike its rivals, though up to 10% was necessary *in vitro* in the presence of gross contamination. This was supplemented by ethylene oxide fumigation of electrical

and other intricate equipment and by Trilene irrigation for ducts. No disinfectant is likely to succeed, however, in the eradication of pseudomonads that are being harboured in blood-clot and other protein debris; and, as Phillips and Spencer (1965) found, there is still need for a practical filter to protect anaesthetic equipment. Such a filter would need to have really easy access to disposable pads so that they could be replaced constantly as they became sodden. In the absence of such filters we raised the Barnet ventilator to a level above the patient's head to minimize the contamination of the apparatus by gravity. Expedients suggested by others have been to place a filter on the intake tube of the ventilator (Bishop *et al.*, 1963) or to put chlorhexidine in its humidifier unit (Phillips and Spencer, 1965); but none of these precautions deals with what is probably the prime source of infection, the patient himself who originally infected the machine.

There may be an additional argument here for adding colistin to the prophylactic antibiotics recommended for cases on intensive care, but its nephrotoxicity must be borne in mind. There are certainly good grounds for monitoring the sputum of all such cases on admission and before and after operation. By using cetrimide-nalidixic acid plates we were able to screen heavy inocula, and we felt well justified when this procedure detected *Ps. aeruginosa* in the respiratory tracts of the last two cases. It showed that it is possible to get early warning of what might have become recrudescence of infection by this most formidable organism.

Summary

An outbreak of respiratory infection in a cardiac surgery unit affected seven cases, with three deaths. *Pseudomonas aeruginosa*, type 10, the causative organism, was also isolated from the anaesthetic equipment.

Possible predisposing factors were tracheostomy, corticosteroids, and prophylactic antibiotics.

Measures taken to prevent a recurrence included screening of sputa on a selective medium and the use of an efficient new antiseptic containing dipenidam.

We wish to thank Dr. J. C. J. Ives for his advice, and Mr. W. Forbes for his help. Dr. R. R. Gillies and Mr. J. R. W. Govan kindly undertook the pyocine typing, and we are grateful to Mr. J. D. Campbell, Miss Robina Spence, and Miss June Harley for skilled technical assistance. Messrs. Portland Plastics provided urgent supplies of Portex-DCR containing dipenidam (Messrs. Alan Glasby).

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Deaths Associated with Respiratory Tract Infection in Childhood *

P. S. GARDNER, M.D., DIP.BACT.; D. C. TURK, D.M., M.R.C.P., M.C.PATH; W. A. AHERNE, M.D., M.C.PATH.
T. BIRD, M.D., M.C.PATH.; M. D. HOLDAWAY, M.B., M.R.C.P.; S. D. M. COURT, M.D., F.R.C.P.

Brit. med. J., 1967, 4, 316-320

The number of children who die from respiratory tract infections has decreased markedly during the period in which antibacterial drugs have become available. The figures given in Table I illustrate this point clearly, but they also show that such deaths have by no means been eliminated and that the extent of the improvement is much less among infants than among older children.

TABLE I.—Numbers of Children Who Died in Newcastle upon Tyne from Lower Respiratory Tract Infections

Age in Years	No. of Deaths During			Approximate Ratio of Deaths 1931-5 to 1961-5
	1931-5	1946-50	1961-5	
<1	416	206	73	6:1
1-4	294	24	6	50:1
5-14	52	6	5	10:1
Total	762	236	84	9:1

This table is based on figures for deaths from bronchitis or pneumonia given in the appropriate Annual Reports of the Medical Officer of Health for the City and County of Newcastle upon Tyne. Virtually all deaths from non-tuberculous lower respiratory tract infections were included under these two diagnoses.

In the course of an extensive survey of respiratory tract infection in children in the Newcastle area we have obtained information about 22 children with such infections who died during the period October 1964 to December 1966 and who fulfilled the following conditions: that they were admitted to hospital before they died; that they came to necropsy; and that bacteriological and virological investigations of their infections were carried out either before or after death, or both. We have analysed our data in an attempt to find out why these children died, and have paid particular attention to information on three subjects: the presence of conditions which might have made the children unduly liable to succumb to infection; the nature of the infecting organisms; and any features of the children's clinical conditions which might suggest the mechanisms of death and measures that might have prevented it. These children are admittedly a selected group; "cot deaths," for example, were excluded by our criteria. Our information is incomplete at many points, but it is sufficient to provide a valid, even though only a partial, picture of respiratory tract infection as a continuing threat to the lives of young children.

Methods of Investigation

In addition to clinical examination and assessment the children were investigated as follows:

Bacteriology.—Nasal and cough swabs for bacterial culture were collected from 13 children shortly after they were admitted to hospital. No such swabs were collected from the other nine, many of whom died within a few hours of admission, but blood cultures were set up from two of them before they died. Heart and lung punctures were carried out within 15 minutes after death in 11 cases; the resulting fluids were inoculated into Robertson's cooked meat medium, which was placed in a 37° C. incubator as soon as possible

and was subcultured to solid media when visible growth occurred. Necropsy tracheal or lung swabs were collected in 13 cases. In one case a small amount of broth was injected submucosally into the swollen epiglottis at necropsy and then withdrawn and used for inoculating cultures for *Haemophilus influenzae* (Jones and Camps, 1957).

Virology.—Nasal and cough swabs collected from 11 children shortly after admission were transported to the laboratory and examined there as previously described (Elderkin *et al.*, 1965). Lung tissue for virus culture was collected at necropsy, up to 48 hours after death, in 21 of the 22 cases. Such tissue was homogenized in 10 times its own volume of medium 199 and then lightly centrifuged, and the supernatant fluid was used for inoculating tissue cultures. The cell lines used for cultures of swabs and of lung tissue were HeLa, Hep II, rhesus monkey kidney, and human diploid cells (W.I.38).

Pathology.—Seven pathologists carried out necropsy examinations of children in this series, but two of us, who had carried out nine of the necropsies, each examined histological sections of lung from all 22 cases. Final pathological classification of respiratory tract conditions was based on the following combinations of findings: *epiglottitis*—oedema, hyperaemia, and neutrophil infiltration of the epiglottis; *bronchitis*—mucosal oedema, enhanced mucus formation, and neutrophil infiltration confined to the bronchi; *bronchiolitis*—inflammatory exudate in the intralobular air passages but little or none in the surrounding pulmonary alveoli, the inflammatory cells being in some cases mainly neutrophils within the lumina and in other cases mainly lymphocytes within the walls of the bronchioles; *pneumonia*—inflammatory exudate and infiltration involving the pulmonary alveoli. We hope to publish elsewhere further details of the pathological findings in the lungs.

Findings

Nine of the 22 children were boys and 13 were girls. Eighteen were 6 months old or less and only three were more than a year old. Most of the illnesses were short—three days or less in eight cases and four to seven days in seven cases. Eleven children died within 24 hours of admission to hospital, four of them within the first two hours.

Classification of the patients according to the findings shown in Table II. provides a satisfactory basis for a description of the main features of their illnesses. This is followed by a review of the treatment given and of certain additional aspects of their conditions to which we wish to draw attention.

Twenty-two Patients Classified According to Pathological and Microbiological Findings

The first six children (Cases 1-6) apparently died from bacterial infections. The first two had staphylococcal pneumonia with characteristic multiple lung abscesses. One of them (Case 1) had a pyopneumothorax when she reached hospital five days after the onset of her illness; she died two days later. The other (Case 2) did not receive any medical attention for nearly a week after he became ill; he died one hour after reaching hospital.

The child with epiglottitis (Case 3) was moribund when he reached hospital, having been treated for cardiac arrest during

* From the Departments of Virology, Microbiology, Pathology, and Child Health, the University and the Royal Victoria Infirmary, Newcastle upon Tyne, and the Institute of Pathology, Newcastle General Hospital.

the journey, and his breathing was maintained by positive-pressure ventilation from the time of his admission. He had had a mild coryzal illness for about a week but had been seriously ill for only a few hours—a common sequence of events in this often lethal disease (for references see Turk and May, 1967). *H. influenzae* type b, the expected causal agent, was isolated at necropsy from this child's grossly inflamed and swollen epiglottis, but an additional and unexpected finding was the isolation of respiratory syncytial virus (R.S.V.) from his upper respiratory tract before death and also from his necropsy lung specimen.

A 1-month-old infant with multiple congenital haemangiomas of her face and liver (Case 4) died within 12 hours of becoming seriously ill with streptococcal septicaemia and pneumonia, probably secondary to infection of her facial lesions.

Each of the two remaining children in this group (Cases 5 and 6) had for several weeks before death received continuous antibiotic treatment for bacterial superinfection of pulmonary mucoviscidosis; and in each case highly antibiotic-resistant bacilli, such as had been found in the upper respiratory tract during life, were isolated from tracheal swabs taken at necropsy and were thought to have been responsible for the terminal pneumonia. Details of the antibiotic treatment are given below.

One child (Case 7) was admitted to hospital two days after she became ill. She had pneumonia, with radiological appearances suggesting that it was staphylococcal. She seemed to make good progress on treatment with cloxacillin and ampicillin, but eight days after admission she suddenly collapsed and died. Necropsy revealed that as well as pneumonia, which was showing evidence of resolution, she had an unexplained area of myocardial necrosis, and this was thought to have been responsible for her death.

Four children (Cases 8 to 11) all had pneumonia for which no bacterial cause was found. All were ill for less than five days, and all died within a few hours of admission to hospital. R.S.V. was isolated from necropsy lung specimens in every case. Two of the children had congenital heart abnormalities—endocardial fibroelastosis (Case 10) and a large ventricular septal defect associated with mongolism (Case 11)—and one (Case 9) was found at necropsy to have acute myocarditis.

Nine children (Cases 12 to 20) had bronchiolitis. In seven the illness lasted only two to five days; one of these (Case 16) had previously undergone right upper lobectomy for congenital emphysema. One child (Case 13) had been treated with tetracycline for bronchitis three weeks before admission, following which she vomited blood and remained unwell, with diarrhoea. When she came into hospital with an exacerbation of her respiratory tract condition two days before she died she was markedly dehydrated, and at necropsy was found to have a sagittal sinus thrombosis as well as bronchiolitis. The

remaining child (Case 15) had a patent ductus arteriosus and an atrial septal defect and had been intermittently ill for six of his 12 weeks of life; he died two days after admission. R.S.V. was isolated from three of these nine children.

Two children (Cases 21 and 22) collapsed and died unexpectedly while under treatment for what appeared to be relatively mild respiratory tract infections, of 19 and 11 days' duration respectively. In each case the only respiratory tract abnormality found at necropsy was a mild bronchitis, not apparently sufficient to explain death; but one child, a mongol, was found to have a small atrial septal defect and the other to have endocardial fibroelastosis. R.S.V. was isolated from the upper respiratory tract of the first of these two children before he died.

Antibiotic Treatment

Only seven of the 22 children had been treated with antibiotics before coming to hospital. The two with mucoviscidosis had both received penicillins. One of them (Case 5), who had had phenoxymethylpenicillin for two days before admission, was treated with benzylpenicillin and cloxacillin throughout her three weeks in hospital and with polymyxin B (to which her *Pseudomonas* was sensitive *in vitro*) for the last four days. The other (Case 6) had been on ampicillin for several weeks before admission, and received benzylpenicillin, cloxacillin, and chloramphenicol during her five days in hospital; her *Proteus* was resistant to the penicillins but chloramphenicol-sensitive. Five children had been treated with tetracyclines before admission. These included one with staphylococcal pneumonia and pyopneumothorax (Case 1), who had been so treated for two days and who received cloxacillin (to which her staphylococcus was sensitive) and benzylpenicillin for the two days that she was in hospital; the child mentioned above as having had tetracycline three weeks before admission (Case 13), who received cloxacillin and chloramphenicol during her two days in hospital; and three others (Cases 11, 17, and 22) whose tetracycline treatment had lasted for one to three days and who died within 12 hours of reaching hospital.

Six of the 15 children who received no antibiotics before coming to hospital (Cases 2, 4, 8, 9, 14, and 20) died within 12 hours of admission, and the details of their treatment are thus of little importance. The child with haemophilus epiglottitis (Case 3) was treated with an appropriate antibiotic (ampicillin) but was moribund before this treatment began. It seems likely that one child (Case 7) was being successfully treated for staphylococcal pneumonia with cloxacillin, as already described, when she died from myocardial necrosis. The remaining seven children (Cases 10, 12, 15, 16, and 18–20), received benzylpenicillin, cloxacillin, ampicillin, tetracyclines, or combinations of these drugs for periods of between

TABLE II.—Pathological and Microbiological Findings

Case No.:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Age in months	1	36	21	1	4	5	1	1	1	4	6	1	2	3	3	4	5	6	9	22	2	4
Necropsy findings:																						
Epiglottitis			x																			
Bronchitis												x	x	x	x	x	x	x	x	x	x	x
Bronchiolitis																						
Pneumonia	x	x	m	x	x	x	x	x	x	x	x				m		m	m				
Congenital abnormalities																						
Heart																						
Other																						
Myocardial lesions																						
Potential pathogens isolated:																						
Bacteria ante mortem from	S				PS	Pr	S															
Blood culture				A																		
Bacteria post mortem	S		H																			
Epiglottis																						
Heart/lung punctures	S																					
Tracheal/lung swabs	S	S		A	P+	Pr			+	+	+	+	+	+	+	+	+	+	+	+	+	+
Viruses ante mortem from upper respiratory tract			R							R	R	R	R	R	R	R	R	R	R	R	R	R
Viruses post mortem from lung tissue			R							R	R	R	R	R	R	R	R	R	R	R	R	R

m=Pneumonia of minor degree, thought to have been less important than findings marked x. S=*Staphylococcus aureus* (all 3 isolates from Case 1 were of the same phage-type). P=*Pseudomonas pyocyanea*. Pr=*Proteus* sp. H=*Haemophilus influenzae* type b. A=*Streptococcus pyogenes*, Lancefield Group A. R=Respiratory syncytial virus. —=Cultures carried out but no relevant organisms isolated. +=Various intestinal-type Gram-negative bacilli, isolated only from necropsy lung swabs and therefore of doubtful significance.

16 hours and five days, but there is no evidence that they were suffering from bacterial infections.

Among the patients with no bacterial explanation for their infections (Cases 8–22) there were only four who had received antibiotics (tetracyclines in every case) before coming to hospital.

Other Forms of Treatment

All 22 children were treated with oxygen at some time, either in tents or by intermittent positive-pressure respiration. Intravenous fluids were given to five, including three who were hyperpyrexial on admission (rectal temperature 105° F. (40.6° C) or more). Ice-packs were used in treatment of one of these and of two other hyperpyrexial children. (In contrast to these, eight children had rectal temperatures of 100° F. (37.8° C.) or less on admission; we have found no correlation between temperature levels and pathological or microbiological findings.) Nine children were given digoxin for cardiac failure; these included four of the seven children with congenital or acquired heart lesions, but not the two whose cardiac abnormalities were unsuspected before necropsy (Cases 21 and 22) nor the child with a ventricular septal defect (Case 11) whose hopeless condition on arrival in hospital is described below. Eight children received hydrocortisone or prednisone; further information about six of these is given below.

Mode of Death

As indicated in our introduction, we have been concerned to discover not only why these children died—that is, the aetiology of their fatal illnesses—but also how they died, in the hope of seeing whether their lives could have been saved by measures other than those which were employed.

Cardiac Arrest.—This occurred in three cases. The heart of the child with a patent ductus arteriosus (Case 15) stopped suddenly while she was undergoing bronchoscopy for treatment of massive pulmonary collapse, having been successfully treated in this way twice in the preceding 24 hours; cardiac massage was ineffective. The heart of the child with epiglottitis (Case 3) also stopped suddenly, while he was on the way to hospital, but it responded to massage; however, he never breathed spontaneously after admission, and by the next day had ceased to show any evidence of cerebral function. One other child (Case 19) had a similar story except that his heart stopped and was started again by external massage on four occasions during his last three days.

Cardiac Failure.—One child (Case 10) suddenly became deeply cyanosed and showed signs of cardiac failure several hours after admission. He was treated with digoxin and hydrocortisone but died 10 hours later. Necropsy confirmed that he was in cardiac failure as well as having pneumonia, and also revealed that he had endocardial fibroelastosis. (As already stated, eight other children were treated for cardiac failure, but in none of these cases was it a principal cause of death.)

Sudden Collapse.—Thirteen children collapsed suddenly, becoming pale, hypotonic, and unresponsive to stimuli, with shallow irregular or gasping respirations but without cardiac arrest. These 13 included only one of the six children whose deaths were apparently due to bacterial infection. This child (Case 1) and six others (Cases 7, 8, 12, 16, 21, and 22) all died within minutes of collapsing. The remaining six children in this group (Cases 9, 13, 14, 17, 18, and 20) survived for periods ranging between one hour and two days; four of them were treated with hydrocortisone or prednisone after they collapsed, with little or no appreciable effect. One of those who died quickly had received prednisone for 36 hours before her terminal collapse. Four of the 13 children had convulsions—one as a prelude to terminal collapse and the others between collapse and death.

Gradual Deterioration.—Four children with bacterial pneumonia (Cases 2, 4, 5, and 6) became progressively more ill after admission and died without any notable terminal features to their illnesses. However, one of them (Case 4) was in a collapsed state when admitted six hours before she died, and may have been so as the result of a sudden episode. Finally, the child with mongolism and a large ventricular septal defect (Case 12) reached hospital moribund, with a rectal temperature of 108° F. (42.2° C.) and extensive bilateral pneumonia. He died two hours later.

Seasonal Incidence

Table III shows that most of the deaths occurred during the winter months, and that nearly all of those not attributable to bacteria occurred at times when bronchiolitis is commonest in this community (Elderkin *et al.*, 1965) and when R.S.V. was widely distributed, as judged by the frequency with which we isolated it from children with respiratory tract infections who were admitted to hospitals in this city.

Discussion

It is clearly necessary to be cautious when drawing conclusions from the findings presented here. As we have said, these 22 children are not representative of all who die while suffering from respiratory tract infections; and there are obvious limitations to a discussion of treatment which is based solely on data about fatal cases. However, despite these reservations a number of important facts and indications can be discerned among our findings.

Congenital Abnormalities

Nine of the 22 children had major congenital abnormalities, which probably helped to determine the fatal outcome in each case. Of the five children with congenital heart abnormalities, one (Case 10) died mainly as a result of congestive cardiac failure, one (Case 15) from cardiac arrest during bronchoscopy, and two (Cases 21 and 22) from sudden collapse for which their relatively mild respiratory tract infections did not provide sufficient explanation; the fifth child had extensive bilateral

TABLE III.—Comparison between Months of Death of the 22 Children and Monthly Totals of R.S.V. Isolations from Children Admitted to Newcastle Hospitals with Respiratory Tract Infections

	1964			1965												1966											
	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Time of deaths																											
Cases 1 to 7																											
" with R.S.V. isolations ..			1	2	1	1			1						1	1				2				1		1*	1
Other cases ..	1						1								1			1							2	2*	1
Numbers of R.S.V. isolations from children with respira- tory tract infections ..	2	6	21	17	8	12	6	4		4	2	2	1	3	7	7	6	2							5	23	9

* Case 3 (*H. influenzae* and R.S.V.) is recorded in both lines.

pneumonia, but his large ventricular septal defect must have added to his respiratory distress. Pulmonary mucoviscidosis commonly leads, as in two cases in this series, to a prolonged and ultimately unsuccessful fight against bacterial superinfection. Congenital facial haemangiomas were probably the portal of entry of the streptococci which killed one child. Lobectomy for congenital emphysema, even when carried out in infancy, leads to permanent impairment of vital capacity, and presumably also of ability to survive serious pulmonary infection (DeMuth and Sloan, 1966).

The frequent association of congenital abnormalities with death during respiratory tract infection in early childhood was noted in a previous report from Newcastle (Elderkin *et al.*, 1965) and has also been found by G. A. Neligan (personal communication, 1967) in follow-up studies of 13,430 single legitimate live births occurring in Newcastle during 1960–2. Of these children, 108 died between the ages of 1 month and 1 year, and of those who came to necropsy 18 were found to have had respiratory tract infections at the time of death, with associated major congenital abnormalities in five cases.

There is nothing original about the observation that children with congenital abnormalities, particularly those of heart or lungs, have a reduced chance of surviving respiratory tract infections; but the high proportion of children with such abnormalities in these series of fatal cases is noteworthy, and helps to explain why respiratory tract infections continue to have a relatively high mortality rate among young children.

Pathogenic Organisms

Only 6 of the 22 deaths in our series were demonstrably attributable to bacterial infections; one other child died from an unexplained complication of a pneumonia probably caused by staphylococci. The pneumococcus, principal agent of fatal respiratory tract infections in pre-antibiotic days, apparently played no part in our series. Our failure to find possible bacterial causes for the illnesses of 15 of the 22 children is all the more significant because only four of them had received antibiotics before coming to hospital. Furthermore, in many cases we were able to culture heart blood and lung aspirate collected a few minutes after death, and we think it unlikely that bacteria responsible for fatal pulmonary infections would commonly escape detection by such means.

R.S.V. was isolated from 3 of the 11 children from whom appropriate upper respiratory tract swabs were collected during life, and from necropsy lung tissue of 8 out of 21 children. The first of these findings can be compared with figures from a survey of our own, to be published in more detail elsewhere, in which we isolated R.S.V. from the upper respiratory tract swabs of only 4 out of 295 children admitted to hospital with no clinical respiratory tract infection; but we have no information about the frequency with which this virus can be isolated from the lungs of children who die from non-respiratory causes. The significance of our high rate of isolation of R.S.V. from the 22 fatal cases is enhanced by the fact that we isolated no other viruses from their respiratory tracts, despite the wide range of culture procedures used. It is of interest that we isolated R.S.V. from the lungs of all four children who died of non-bacterial pneumonia, but from the lungs of only three of the nine who died of bronchiolitis. The latter condition is known to be predominantly due to R.S.V., in Newcastle (Elderkin *et al.*, 1965) as elsewhere (Chanock *et al.*, 1961; Beem *et al.*, 1962), and though we do not know of conclusive evidence that it is also the predominant cause of fatal bronchiolitis, it seems likely that this is so. A possible explanation of our findings is that R.S.V. survives better in pneumonic lung than in bronchiolitic lung after the death of the patient, but there are many other possibilities.

R.S.V. infection was the presumptive cause of death in four cases of pneumonia and in three cases of bronchiolitis, and was

found in the upper respiratory tract of one other child who died with only minor pathological changes in his respiratory tract. The isolation of R.S.V. as well as *H. influenzae* type b from the respiratory tract of the child with epiglottitis may have been coincidental; but since pathogenic collaboration between viruses and this bacterial species has been postulated in various conditions and demonstrated in some (see Turk and May, 1967), the suggestion that R.S.V. plays a part in the aetiology of haemophilus epiglottitis cannot be dismissed out of hand.

Speed of Diagnosis and Treatment

Several of the children were desperately ill before they reached hospital, and in some cases before any medical help was sought. Of the two who died of staphylococcal pneumonia, one might have survived if she had received a more appropriate antibiotic than tetracycline during the early days of her illness, and the other if he had come under medical care before he had been ill for a week. Haemophilus epiglottitis is virtually always a necropsy diagnosis in Britain (Jones and Camps, 1957; Johnstone and Lawy, 1967), but in those parts of the U.S.A. where the condition is well known, promptly diagnosed, and treated by immediate tracheotomy and administration of appropriate antibiotics the recovery rate is high (Berenberg and Kevy, 1958). We suspect that more young children die of haemophilus epiglottitis in this country than the number of recognized and reported cases indicates, and that prompt recognition and treatment might save quite a number of lives. However, the one child with this condition in our series was moribund within about half an hour of being found in a state of severe respiratory distress, and his life could have been saved only by remarkably rapid and well-informed action. The fulminating course of the case of streptococcal septicaemia and pneumonia also left very little time for diagnosis and treatment, especially as there were no strong clinical indications of the nature of the infecting organism. It is impossible to assess the extent to which earlier diagnosis and treatment might have improved the prognosis of any of the children whose infections were apparently not bacterial.

Antibiotic Treatment

Apart from the suggestions made in the preceding paragraph it does not appear that better use of existing antimicrobial drugs would have prevented the deaths of any of the children in this series; but it seems likely that if effective antiviral agents become available there may be a further considerable fall in the mortality rate of respiratory tract infections in early childhood.

Other Forms of Management

Sudden and substantially irreversible collapse was a prominent clinical feature of the illnesses of many of these children, as it was in many of the cases of bronchiolitis reported by Hubble and Osborn (1941) and by Disney *et al.* (1960). The mechanisms underlying such collapse are obscure, and we do not know what parts dehydration and hypoxia play in its production. Some of the children in our series were given intravenous fluids and all received oxygen, but hardly any biochemical investigations were carried out to determine the extent of their need for such treatments and the adequacy of the measures employed. Morrison (1955) showed that oxygen tents, as commonly used, may fail to supply enough oxygen to children with acute respiratory tract infections. Simpson and Flenley (1967) confirmed that administration of 40% oxygen cannot be relied upon to produce normal levels of arterial oxygen tension in such cases; they also showed that clinical signs of respiratory distress are not to be trusted as indices of blood-gas levels, and that uncorrected respiratory acidosis in such

children carries a poor prognosis. Their work thus suggests that repeated direct measurements of arterial blood-gas and pH levels might do much to improve the management of children with severe respiratory tract infections; we would add that repeated electrolyte determinations might also be of value. The use of modern microtechniques greatly reduces the extent to which such investigations disturb a sick child. The mortality rate associated with respiratory tract infections in childhood seems more likely to be reducible by such an approach than by any other at present available to us.

Summary

Of 22 children with respiratory tract infections who died in Newcastle and Durham hospitals during a 27-month period, 19 were less than 1 year old. Nine had major congenital abnormalities. Bacterial infections were apparently responsible for only 6 of the 22 deaths. Respiratory syncytial virus was the only potential pathogen isolated from eight of the children; it was isolated from necropsy lung specimens in seven of these cases, including all four cases of pneumonia with no apparent bacterial cause; and it was also isolated from the upper respiratory tract and the lung of a child with haemophilus epiglottitis. No other viruses were incriminated in any of the 22 cases. Sudden and substantially irreversible collapse was a common feature, especially in the cases not apparently caused by bacteria. Investigation of the blood-gas levels and

biochemical changes in such children is suggested as the most promising approach to improved management.

We gratefully acknowledge the use of clinical notes and reports by numerous colleagues at the Royal Victoria Infirmary (11 cases), Newcastle General Hospital and Dryburn Hospital, Durham (five cases each), and Walker Gate Hospital, Newcastle (one case); also of necropsy reports on the five Dryburn Hospital patients by Dr. J. E. Ennis and on eight of the infirmary patients by Drs. T. Ashcroft, C. Ashton, A. R. Morley, and A. Talerman; and of histological sections of the lungs from all these patients. We are indebted to many of our laboratory colleagues for technical assistance, and also to the Scientific and Research Subcommittee of the United Newcastle upon Tyne Hospitals for their continued support. During this work one of us (M. D. H.) held a research grant from the Medical Research Council.

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Further Experience of Reactions, Especially of a Cerebral Nature, in Conjunction with Triple Vaccination: A Study Based on Vaccinations in Sweden 1959-65

JUSTUS STRÖM,* M.D.

Brit. med. J., 1967, **4**, 320-323

The previous report concerning reactions in conjunction with triple vaccination in Sweden during the period 1954-8 (Ström, 1960) aroused considerable attention and also criticism (Malmgren *et al.*, 1960; Hellström, 1962). To question the propriety of recommending universal vaccination against whooping-cough in all circumstances and in all countries was naturally a serious matter. Even if the predominant view is still that pertussis vaccination is of such value that it should be universally recommended, certain authorities (Wilson and Miles, 1964; Herrlich, 1965; Ehrengut, 1966) express some doubt on the point.

However, one absolute requirement must be that the complications occurring in connexion with vaccination are carefully observed and recorded. It is also important to note whether in due course the incidence or the severity of the side-effects is reduced. A further requirement is to ascertain whether the complications that may occur are likely to affect the incidence and fulfilment of vaccination.

Material.—A study was made of children under the control of child welfare clinics. Every vaccination clinic was sent an annual questionnaire for notification of reactions that had occurred. All children's hospitals in the country were asked to report annually concerning treated cases of postvaccinal complications. For the years 1962-4, furthermore, special reports were requested from the welfare clinics on whether vaccination had been carried out.

Results

Table I shows the various types of cerebral reactions observed. Of the 167 cases 81 were admitted to hospital.

TABLE I.—Cerebral Reactions in Conjunction with Triple Vaccinations 1959-65

Year	Cerebral Injury	Convulsions	Hypsarrhythmia	Shock	Irritability + Abnormal Spinal Fluid	Abnormal Screaming	Total
1959	1	7	1	3		4	16
1960		5	1	7		3	16
1961		12		3		1	16
1962	1	12		5		1	19
1963		9	2	9		1	21
1964	1	11		11		4	27
1965		24		16	2	10	52
	3	80	4	54	2	24	167

Cerebral injury was thus reported in three cases, which are described in some detail.

Case 1.—The child was said to have developed normally. The first injection was given at the age of 5 months. The patient was febrile for two to three days, and for one week was very drowsy. The second injection, given six weeks later, produced the same reaction, but the child then became extremely listless, "did not react to anything," and convulsive attacks started one week after the injection. The attacks increased in frequency and duration and were followed by rapid mental regression. E.E.G. showed great paroxysmal activity. While the child was in hospital, at 7 months

* Hospital for Infectious Diseases, Stockholm, Sweden

of age, decerebrate, rigidity was diagnosed, and encephalography revealed cerebral atrophy. Toxoplasmosis and Wassermann reactions were negative.

Case 2.—This child was healthy and of normal development. There was no reaction after the first injection. The patient had a convulsive attack, and a temperature of 39.5° C. on the ninth day after the second injection at the age of 7 months. Next day there was a new attack—clonic on the right side—followed by paralysis. Lumbar puncture revealed albumin 34 mg./100 ml. and 2 cells. On the following day there were similar convulsions and paralysis, and complete loss of contact. E.E.G. showed incessant paroxysmal activity over the entire left hemisphere. Increasingly severe convulsions occurred. The child was afebrile after three weeks, when a stage of complete decerebration developed. A special examination showed a heavy transient rise of total protein in the cerebrospinal fluid and a rise of the gammaglobulin fraction in blood and fluid. Culture for bacteria was negative. No virus was found in nasopharyngeal secretion, cerebrospinal fluid, or faeces. The senior physician expressed his suspicion of a direct relation to triple vaccination, and the National Bacteriological Laboratory declared that "vaccination as an aetiological factor could not be excluded."

Case 3.—This child, birth weight 2,840 g., had a normal birth and normal psychomotor development. The second injection was given at 4½ months of age. Four hours after the injection the child had a convulsive attack lasting a few seconds in the left half of the face and arms, followed by flaccidity in the left arm and leg, and slightly, too, in the right arm; was not unconscious, and was taken to hospital with a temperature of 38.2° C., but otherwise unaffected. Convulsions returned six weeks later, starting in the right half of the face and in the right arm and leg. After half an hour convulsions followed in the left side. A similar attack occurred on two other occasions. After a severe attack at 11 months of age the child was admitted to hospital. Wassermann reaction and toxoplasmosis were negative. E.E.G. showed grave abnormality. Encephalography revealed cortical and central atrophy on the right side. Later there was considerable regression in development.

Convulsions and Shock.—Clonic convulsions alone occurred in 80 cases. Certain remarkable states of persistent tonic cramp also seem to occur at times. The shock (54 cases) is characterized chiefly by a sudden loss of consciousness lasting for a few minutes up to half an hour, accompanied by flaccidity and pallor or cyanosis, or both.

Reaction and Ordinal Number of Injection.—Convulsions occurred in 42 cases after the first injection, in 28 after the second, and in 9 after the third (in one case after a fourth), and shock in 34 cases after the first, 19 after the second, and 1 after the third. Thus most cases occurred after the first injection.

Time interval between injection and reaction is shown in Table II (data are lacking in 20 cases of convulsions and two of shock). The reaction usually came on during the first day, and in most cases in the first six hours. Two cases of convulsions, however, occurred on the second day, one case on the sixth, and one on the seventh. As regards the two latter, it may be mentioned that one child had a temperature of 39° C. for a whole week, which was followed by convulsions, at first seven or eight a day, then diminishing in frequency and ceasing after a month. The second child had a convulsive attack without fever on the sixth day after the first injection. The convulsions returned five hours after the second injection, with a temperature of 38.1° C. Convulsions were observed on two other occasions later in the year. In two of the cases of cerebral injury the convulsions also came late. Repeated convulsive attacks were described in some other children. An example was a child who had convulsions six hours after the injection. An hour later they returned, accompanied by a temperature of 38.1° C. Three days later there were renewed attacks, the temperature being 37.4° C. Another child had convulsions

TABLE II.—Time Interval Between Injection and Reaction

Type of Reaction	Hours after Injection				Day after Injection		
	0-3	4-6	7-12	13-24	2nd	6th	7th
Convulsions	17	18	9	12	2	1	1
Shock	34	14	2	2	0		

one hour after the vaccination, again after seven hours, four times during the following night, and seven times on the next day.

Temperature at Time of Reaction.—The temperature was reported in only 26 cases of convulsions and 11 of shock (Table III). Fever was not always present. In 9 out of 26 cases of convulsions and in 6 out of 11 cases of shock the temperature was not above 38° C.

TABLE III.—Body Temperature at Onset of the Reaction

Type of Reaction	Temperature (°C.)						
	-37.4	37.5-38	38.1-38.5	38.6-39	39.1-39.5	39.6-40	> 40
Convulsions	5	4	3	8	2	3	1
Shock	3	3	2	3			

Hypsarhythmia was reported in two children two to three days after the vaccination and in two others after a week.

Persistent uncontrollable screaming was included only if the state lasted for more than 12 hours or necessitated admission to hospital.

Meningeal Involvement.—Lumbar puncture was performed in nine children who had convulsions: in six the findings were normal and in three abnormal. The latter cases were also clinically more severe. Twenty-four hours after the injection one child had a general attack, which recurred several times during the following week. The cerebrospinal fluid showed 9 cells. The second child was very irritable on the day of injection, had diarrhoea on the second day and a temperature of 37.8° C., and on the third day had convulsions and a temperature of 39.4° C. These symptoms recurred on the fourth day and for a time the child was in a moribund state (tachycardia, bigeminy, enlarged heart). Cerebrospinal fluid showed: P+, N+, 12 cells. The third child had fever on the day after the vaccination, thereafter vomiting for several days, and again fever, 38-39° C. with convulsions. Lumbar puncture showed 28 cells. Lumbar punctures were performed in four of the shock cases. In two the findings were normal, one had a borderline cell content (5 cells/cu. mm.), and one had a high protein level (81 mg./100 ml.) In the latter case the shock condition recurred once. Of special interest are two patients who clinically showed only very moderate irritability but nevertheless a distinct meningeal involvement. In one case the child was whiny and irritable on the day of injection and had a temperature of 39° C. The next day the temperature was 40.1° C. and the fontanelle was bulging. Lumbar puncture showed 30 cells. The other child was also moderately irritable and the lumbar puncture showed 57 cells. In all, therefore, six children on whom lumbar puncture was performed showed signs of meningeal involvement.

The incidence of cerebral reactions is shown in Table IV. Reaction in the form of convulsions, shock, and meningeal involvement occurred in 1:3,600 vaccinated children (convulsions 1:6,500, shock 1:9,500). Including abnormal screaming the incidence is 1:3,100.

Other Reactions

High temperature has been reported annually in 50 to 150 cases. A temperature above 40° C. is not unusual, the record being 42° C.

TABLE IV.—Incidence of Cerebral Reactions After Triple Vaccination 1959-65. (Cases of Abnormal Screaming Not Included)

Year	No. of Vaccinees	Cerebral Reactions	Incidence
1959	63,141	12	1:5,300
1960	55,042	13	1:4,200
1961	64,226	15	1:4,300
1962	68,225	18	1:3,800
1963	76,361	20	1:3,800
1964	90,697	23	1:3,900
1965	98,584	42	1:2,300
	516,276	143	1:3,600

One child had a temperature of 40° C. for three days, and the next injection, with only one-tenth of the previous dose, produced the same reaction.

In recent years rashes have been reported in 15 to 20 cases annually. *Exanthema* of a morbilliform character or *erythema* appears to be most common. The same kind of morbilliform exanthema of 48 hours' duration appeared in two children after both the first and the second injection. *Oedema* of the face, hands, and feet, accompanied or unaccompanied by erythema, has been observed. In 29 cases on which detailed reports were made the exanthema occurred in 15 cases after the first injection, in 11 after the second, and in three after the third; and in respect of time, in 19 of 27 cases on the first day, in six on the second, and in one case each on the third and fourth days.

Local skin reactions, particularly in the form of sterile abscesses, were very common up to 1963, but have since become rare, as aluminium has been eliminated from the vaccine.

Gastrointestinal symptoms were occasionally reported. Vomiting and diarrhoea occurred after a day or so, lasting for a couple of days to roughly a week. Repeated injections produced the same effect.

Incidence and Fulfilment of Triple Vaccination

Special reports were requested for children born in 1962-4. Figures were obtained concerning 208,186 children (out of a total of 235,283—that is, 88.4%). Of this number 156,802 (75.3%) had been completely vaccinated, 17,342 (8.3%) incompletely, and 34,042 (16.4%) not at all.

The reasons for non-vaccination or incomplete vaccination are given in Table V. The reason for non-vaccination in over half of the cases was the parents' refusal. This corresponds to 8.6% of the total number of children. Medical reasons were reported in only 5.2%—that is, about 1%. Incomplete vaccination would seem to be due chiefly to a reaction to earlier injection. Medical reasons and parents' refusal were the cause of interrupted vaccination in roughly equal numbers of cases—1.4 and 1.5% respectively, together representing about 3%. This figure is naturally a minimum, as the "unknown" group undoubtedly contains some cases attributable to these two causes. The "other cause" group includes mostly children who had moved or were no longer brought in for control, etc.

TABLE V.—Reasons for Non-vaccination and Incomplete Vaccination

Vaccination	Medical Cause	Parents' Refusal	Other Cause	Unknown Cause	Diphtheria-Tetanus Vaccination Instead
Not done (%) ..	5.2	52.7	10.9	27.5	3.7
Incomplete (%) ..	17.1	18.3	33.4	30.7	0.5

Discussion

The first question on which the material presented throws some light is the classification of the cerebral reactions as serious or negligible. As a rule, naturally the main emphasis was on encephalopathies, which caused serious injury; while convulsions, for example, were regarded as a simple febrile reaction. This may be so in some cases, but the present study shows that in nine out of 26 cases the temperature was normal or at most 38° C. Furthermore, pleocytosis was found in the cerebrospinal fluid of three out of nine children on whom lumbar puncture was performed. In several cases, too, there was a marked tendency towards repeated convulsive attacks, contrary to the usual situation in febrile convulsions.

Provocation of hypsarrhythmia was observed in four cases. Similar observations have been made by others (Baird and Borofsky, 1957; Chao *et al.*, 1957; Bower and Jeavons, 1960; Kringelbach and Sensius, 1965).

Shock appears to be still less dependent on the temperature. In six out of 11 cases this was normal or at most 38° C. In one of the four cases in which lumbar puncture was performed the protein content of the cerebrospinal fluid was raised; another case was on the borderline of pleocytosis.

In two children with relatively mild irritability the cerebrospinal fluid findings were distinctly abnormal. It would be of value to know the situation as regards abnormal screaming, which is not so unusual, and which, because of its intensity and difficulty of appeasement, gives the impression of being of cerebral origin (Hopper, 1961).

With these facts in mind it may be asserted that the convulsions, shock, and abnormal irritability observed after triple vaccination cannot always be regarded as commonplace general symptoms but reflect an objectively demonstrable cerebral reaction. The provocation of hypsarrhythmia supports this view. This is a rather more serious aspect of the problem, and the dividing line between what should and should not be regarded as a severe reaction becomes more fluid. Happily, in the short-term view at least, these reactions appear to have a favourable prognosis.

Pathogenetically the endotoxin of the pertussis bacteria—a well-known neurotoxic agent—must be the factor responsible for the cerebral reactions. The fact that most reactions occur after the first injection is against an allergic origin. Certain observations, however, show a quicker and more severe effect of subsequent injections.

Other observed reactions, such as erythema, exanthema, oedema, and gastrointestinal symptoms, also have a rapid onset, usually after the first injection. But there must be an individual predisposition as well, as it was repeatedly found that the same symptoms recurred after subsequent injections.

To sum up, the vaccination reactions may be regarded chiefly as manifestations of a toxic effect, an individual predisposition being of some significance. The allergic element, on the other hand, appears to fall into the background.

As regards the incidence of different reactions to vaccination, the study shows, for children born during 1962-4, that in at least 3% the side-effects were so serious that further vaccinations were not given. In respect of neurological symptoms there seems to be a tendency to an increase compared with my previous report, in which the incidence was 1:6,000 as against the present 1:3,600—uncontrollable screaming excepted. This is probably only an apparent increase due to keener observation on the part of the medical staff. Only three cases of destructive encephalopathy have occurred in these seven years (1:170,000) as against the figure of 1:50,000-60,000 established by the Board of Health (Malmgren *et al.*, 1960) after the earlier study.

If one further differentiates the present material another group with rather more marked symptoms is distinguishable—that is, the cases in which there was serous meningitis and/or a pronounced tendency to repeated attacks of convulsions, or provocation of hypsarrhythmia, altogether 15 cases. The incidence of these reactions is 1:34,000 vaccinees; the remaining cases—that is, the milder, quickly passing reactions—number 125 (1:4,000).

Finally, a general reflection. It may be seen that reactions following triple vaccination are unusually numerous in Sweden compared with other countries. But it must be remembered that our figures are based on very thorough centralized supervision, to which there is hardly any counterpart in other countries. Only by means of annual reports from all vaccinating bodies in a standardized form can a reasonably clear picture be gained. Experience shows that a general recording duty for physicians in fact results in reports of only a few reactions. This it is extremely important to note in times when vaccinations are increasing every day, and, through the action of our health authorities, tend to become a routine and to be virtually compulsory. The more this happens the more necessary it is to maintain a check on the side-effects, especially in combating

diseases which, with rising standards of hygiene and public services, are in themselves assuming milder forms (Ström, 1960, 1967).

Summary

Among 516,276 triple-vaccinated children in Sweden from 1959 to 1965 neurological reactions to the vaccination occurred in 167 cases—destructive encephalopathy 3, convulsions 80, hypsarrhythmia 4, shock 54, uncontrollable screaming 24, serous meningitis 2. Serous meningitis was also found in three out of nine examined cases of convulsions, and elevated protein in cerebrospinal fluid in one out of four examined cases of shock. Apart from these objective signs of meningeal involvement in certain cases, the study shows that in conjunction with both convulsions and shock there may be no or very little rise of temperature. The convulsive symptoms therefore cannot be classified as a matter of course as simple febrile convulsions.

The incidence of neurological reactions was 1:3,600 vaccinated children (1:3,100 if cases of persistent uncontrollable screaming are included), a rise in relation to the figure of 1:6,000 reported in a study from the years 1954 to 1958. The rise is probably merely apparent, however, owing to the more watchful eye that is kept on these conditions. The more severe reactions leading to permanent injury seem to have decreased.

Analysis of the vaccinations of 208,186 children showed that 75.3% had been completely vaccinated. The figure for the non-vaccinated was 16.4%, rather more than half of them due

to the parents' refusal. Vaccination had not been completed in 8.3%; in at least 3% the reason was probably the severe reaction to a preceding vaccination.

Apart from neurological reactions, erythema, exanthema, oedema, and gastrointestinal symptoms have also been reported. The great majority of reactions occurred after the first injection. Repeated injection appeared to produce the same reaction.

All forms of reaction can be explained as being of toxic origin. An allergic mechanism would appear to be of relatively limited significance; a certain individual predisposition, however, seems to be a factor to reckon with.

Finally, it is emphasized that when nation-wide vaccination is recommended detailed information should be required concerning postvaccinal reactions, as is done in Sweden in conjunction with triple vaccination.

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Survival of Burkitt's Lymphoma Patients in Mulago Hospital, Uganda

R. H. MORROW,* M.D.; M. C. PIKE,† PH.D.; A. KISUULE‡

Brit. med. J., 1967, **4**, 323–327

Although much work has been done on clinical aspects of Burkitt's lymphoma, and intense interest has been shown in the relatively high rate of remissions and even "cures" among patients with this disease, there has been little analysis of long-term survival. The major reason for this has been the apparently enormous and seemingly insurmountable problems of keeping track of patients in the developing countries of Africa.

Clifford, working in Kenyatta National Hospital, Nairobi, Kenya, has been able to circumvent this problem to a very large extent by keeping patients in hospital for extended periods, and to date his series (Clifford, 1966; Pike, 1966) is the only major one in which complete survival information on the vast majority of patients is available.

Ideas on survival of patients attending Mulago Hospital, Kampala, Uganda, have been based on those known to have died plus those who continued to return to the follow-up clinic, but the fate of upwards of 50% of the patients leaving the hospital has not been known (Burkitt *et al.*, 1965; Burkitt, 1966). However, by combining the data gathered by Mr. D. Burkitt and Mr. A. Lubega (the Kampala Cancer Registry

social worker) with the data we have ourselves collected since November 1966 it has been possible to obtain survival information on 74 of the 80¹ patients in a defined subpopulation of cases attending Mulago Hospital. This paper reports our findings in this group.

Clinical Material

The present study comprises the 80 patients diagnosed (microscopically, clinically, or at necropsy) as having Burkitt's lymphoma, who presented for the first time at Mulago Hospital between 1 January 1961 and 31 December 1965, and whose place of residence at onset date was in East or West Mengo Districts of Uganda (as demarcated on the last Ugandan Census in 1959²).

The East and West Mengo Districts, with a population of approximately 1½ million, comprise an area around Kampala with a radius of about 110 km. (70 miles). To have extended the follow-up to include further districts of Uganda would have provided rapidly diminishing returns for the extra effort and expense involved.

* W.H.O. Senior Lecturer in Epidemiology, Department of Preventive Medicine, Makerere Medical School, P.O. Box 2072, Kampala, Uganda.

† Member of the M.R.C. Statistical Research Unit, 115 Gower Street, London W.C.1, on secondment to the Department of Pathology, Makerere Medical School.

‡ Medical Assistant. Employed by Dr. Morrow under the U.S. National Cancer Institute (N.I.H.) Contract No. PH-43-67-47.

An early draft of this paper was read at the East African Medical Research Council's Conference on "Cancer in Africa" which took place in Nairobi, Kenya, from 11–14 January 1967.

¹ A table may be obtained from the authors giving for each of the 80 patients: reference number, age, sex, date of presentation at Mulago Hospital, length of history at that date, tumour involvement at presentation, staging of the disease, if and when microscopically proved, if and when treatment started and what it was (though not the dose, as this was too often unknowable from the notes), date last seen, and condition, length of survival, dates of discharge "improved," dates of recurrences after discharge improved, sites of recurrences, and therapy given.

² East African Statistical Department, Nairobi/Entebbe, 1960.

We considered only patients presenting on or after 1 January 1961. It was about this time that "adequate" chemotherapy became available, and the criteria for diagnosis of the tumour had become relatively clear. The difficulties of tracing patients (and finding their notes) increase greatly with time after discharge, and though restricting ourselves in this way we still had a sufficient number of cases to make analysis instructive, while standing a good chance of finding the necessary high proportion of patients to make analysis valid. We did not consider patients presenting after 31 December 1965, because there had not been a sufficient lapse of time to make analysis of their survival very meaningful.

Of the 80 patients in the defined population at the beginning of this study (early November 1966) 36 had died in the hospital and another three were reliably reported to have died at home, while seven were known to be alive. Of the remaining 34, 11 had been unimproved by treatment and were thought to be dying on discharge, and 22 had been "successfully" treated but had not been seen since discharge. We were unable to find the hospital notes of the remaining patient, Case K229, though we were able to ascertain that she had been discharged. Thus of the 44 patients discharged from the hospital, the fate of 34 was in doubt. One of us (A.K.) devoted three months to tracing these patients. Four were found alive and free from tumour,³ the deaths of 22 patients were confirmed, and indirect evidence of the deaths of two was obtained. No information was forthcoming on the remaining six: three of these had been discharged improved, two had been discharged dying, and one was Case K229 mentioned above (this patient was not considered further here). The position is summarized in Table I.

TABLE I.—Information on Survival Status

	At Start of Study, 1 Nov., 1966	At Analysis, 1 April, 1967
Died in Mulago	36	36
" at home	3	27
Alive	7	11
Lost	34	6
Total	80	80

The diagnosis in 10 patients was made on clinical grounds alone: in two a clinical diagnosis was later confirmed at necropsy. Thus there was microscopical proof of diagnosis in 69 of the 79 patients. In all but one of these 10 not microscopically proved cases the patients are known to be dead. The other patient was improved by therapy but had extensive disease at discharge, and we have not been able to trace him. All "long-term" survivors had Burkitt's lymphoma diagnosed microscopically.

Of the 79 patients, 24 received no specific anticancer therapy. Seven of them were first diagnosed at necropsy; 10 died before diagnosis was confirmed or treatment started; five died during an operative or diagnostic procedure; and two refused treatment—one with far-advanced disease was removed by his parents before biopsy or treatment and died at home the same day; the other (Case J152), a 9-year-old boy with all four quadrants of the jaw involved, was taken home by his parents after biopsy but before treatment. His parents stated that they then took him to the local traditional medical practitioner, after which he had a full remission, but the disease later recurred and he died 385 days after his initial presentation at Mulago. The remaining 55 patients had specific treatment for their disease.

All of these treated patients received some form of chemotherapy. The most frequently used first drug was cyclo-

phosphamide, usually given intravenously but quite often orally and under varying dose schedules—most commonly a single dose, and the vast majority no more than two doses, of 40 mg./kg. body weight intravenously. Other drugs used were mercaptopurine, nitrogen mustard, methotrexate, and vincristine. These drugs were often given in combination, and for recurrences the drugs were usually given in turn if no response was being obtained. Seven patients had fairly extensive surgical excision of their tumour—five bilateral ovariectomies, one bilateral orchiectomy, and one abdominal mass removed.

Survival Time

We have counted survival time from the date of presentation at Mulago Hospital. This date was always easy to establish, and for the purpose of this paper may be regarded as that on which treatment began, a date that was not always completely clear from the hospital notes we managed to find.

For the purpose of the survival curve analysis the three "lost" patients who were discharged to die are assumed to have died on the day they left hospital, but for the two lost patients discharged improved we assume nothing further than that they were alive when they left hospital.

Staging of the Extent of the Tumour

Burkitt *et al.* (1965) have pointed out that the initial response of lymphoma cases in Mulago Hospital to chemotherapy was in part determined by the size of the tumour mass, and from a preliminary look at the survival data it was evident that the extent of tumour involvement was a critical factor in long-term prognosis. In our analysis we finally settled on the following crude division of cases into three categories, similar to those used in the staging of Hodgkin's disease:

Stage 1: Lymphoma limited to one anatomic region or to two contiguous anatomic regions on the same side of the diaphragm.

Stage 2: Lymphoma in two or more non-contiguous or more than two contiguous regions on the same side of the diaphragm.

Stage 3: Lymphoma involving any intrathoracic, intra-abdominal, or intracranial areas, or bone marrow, or more extensive involvement than stage 1 or stage 2.

For example, involvement of both mandible and maxilla on one side of the face is classified as stage 2, whereas involvement of the maxilla and orbit on one side is classified as stage 1.

The major classification problem was whether liver or spleen enlargement constitutes tumour involvement in the absence of a laparotomy or needle biopsy—for this paper involvement was assumed only when there was a positive statement in the notes to this effect.

Results

Table II gives the survival times of the patients who received specific anticancer therapy. Fig. 1 shows the actuarially calculated survival curve for all these 55 cases. This curve

TABLE II.—Survival Times of Treated Patients in Days

Age at Presentation in Years	Stage of Disease at Presentation		
	1	2	3
0-4	1505†	80, 212, 503†, 943†, 1500†	169*, 1606†
5-9	13, 1379†, 1389†, 1581†, 1929†	119, 404*	20*‡, 21§, 22, 38, 39‡, 42§, 47, 50, 80, 107, 123, 145, 171, 266, 320*, 320, 384*, 479, 804†
10-14		31‡, 72	8, 17, 20*, 87*, 96, 102, 147, 159, 263*, 408, 440
15-19		227	139, 371, 1848†
20+		21	44, 67, 228

* Clinical diagnosis only. † Alive and clinically free of disease when last seen.
‡ Discharged "improved," not traced. § Discharged unimproved, not traced.

³ One of these patients (Case K76) was not actually seen, but the patient's father and the local chief stated that he was alive and well. The area near his home was particularly disturbed during the "troubles" of 1966 and the patient was alleged to have been afraid to show himself owing to misgivings concerning the reasons for our visits (we attempted to see him on four different occasions). We have no reason to doubt the truth of these statements, and we have accepted them at their face value.

has the same general shape as the graph that was constructed from Clifford's data (Pike, 1966), with the characteristic, striking, long right-hand tail. Patients falling into this tail we regard as "long-term" survivors; all of them have been clinically free from disease for at least 496 days, while the longest remission in a patient who has subsequently died is 382 days—this is the patient who died 479 days after admission. The point on the "% survivors" axis at which the curve becomes horizontal we call "estimated long-term survival rate," and for the treated cases as a whole it is 21%.

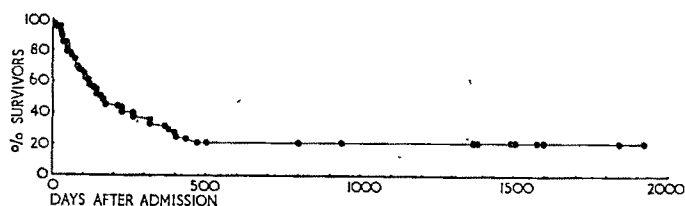


FIG. 1.—Survival curve for all 55 treated cases.

The most important determinant of survival in this series appears to be the extent of the disease on first admission (see Fig. 2 and Table III). The single stage 1 treated patient who has not survived was a 9-year-old girl who presented with a large tumour of the left thigh. This child died in the hospital two weeks after admission with an apparently fast-extending tumour, but it is not clear from the hospital notes why she died so soon and why necropsy was not performed. There is a suggestion on the histology request form that she might have had more extensive tumour involvement, and hence might not have been a stage 1 case.

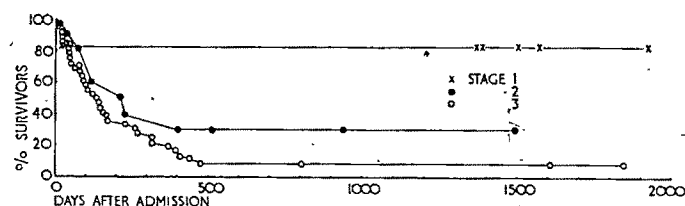


FIG. 2.—Survival times in Stages 1-3.

TABLE III.—"Long-term" Survival and Stage of Disease at Presentation

Stage	No. of at Risk Patients*	No. of Long-term Survivors	Estimated % Long-term Survivors†
1	6	5	83
2	10	3	28
3	34	3	8
All patients	50	11	21

* Excludes "lost" patients.

† Actuarially calculated (see Figs. 1 and 2).

Younger patients did better than older patients (see Fig. 3). However, the age of the patient and the extent of his disease at presentation are highly interrelated (see Table II), and it is not possible with this limited number of cases to separate them completely satisfactorily. Fig. 4 shows that among stage 3 cases age is apparently irrelevant, though there is a hint of better prognosis for the younger patients with stage 2 disease. If attention is restricted to patients under 10 years of age it is clear from Table II that the stage of the disease remains of paramount importance.

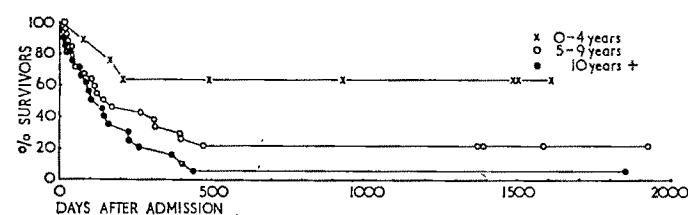


FIG. 3.—Survival times of patients according to age.

No relation exists—within a staging division—between length of history and prognosis.

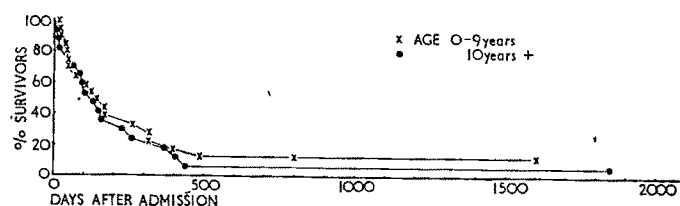


FIG. 4.—Survival times in stage 3 patients according to age.

It would clearly be extremely useful if on the basis of this series we could make some assessment of the relative efficacy of different chemotherapeutic regimens. However, as the extent of the disease at presentation appears to have a critical prognostic value, we need to compare different drugs (and different drug schedules) *within a single staging category*. Table IV shows that this is possible only with stage 3 cases; and Fig. 5 shows, within this staging division, the comparison of initial treatment with cyclophosphamide against all other drugs. For the first few months the patients receiving cyclophosphamide do better, but this advantage is not maintained.

TABLE IV.—Initial Chemotherapy

Stage of Disease at Presentation	Drug		
	Cyclophosphamide	Other	Total
1	5	1	6
2	10	1	11
3	25	13	38
All patients	40	15	55

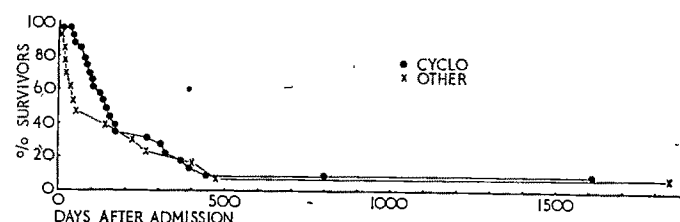


FIG. 5.—Survival times in stage 3 patients according to treatment.

Long-term Survivors

Ten of the 11 long-term survivors were under the age of 7 at presentation; while their sex ratio (seven males, four females) is identical to that of all treated cases.

Two important points arise from a study of the treatment of these 11 patients. The first is the apparent value of surgery in some cases. All three survivors with stage 3 disease had extensive surgical excision of their tumour—two had bilateral ovariectomies and one had a tumour mass that involved the bladder, right ureter, and ileum removed. Though there was possibly abdominal tumour remaining in all three patients, the bulk of it is excised. Two of these patients also had jaw or orbit involvement, but surgical excision was never attempted at these sites. An orchidectomy, first of the right testis and two and a half years later of the left, was performed on one stage 1 survivor (Case K99). Altogether seven patients had surgery with removal of most of the tumour mass, and four of these are long-term survivors.

The second point is that four of the survivors (all stage 1 cases) had recurrences. One of these patients was the testicular tumour case referred to in the previous paragraph. All of the remaining recurrences were in a site clearly different from the original one. These four patients all had complete clinical remissions followed by recurrences from 22 to 80 weeks later. Their recurrences were all still classifiable as stage 1.

Discharged "Improved"

To decide whether a patient has had a full or partial remission, or neither, is difficult in the best of circumstances. It is particularly so when these decisions have to be made retrospectively on the basis of case notes alone. We have nevertheless attempted this, and a certain amount of useful information was obtained.

Mulago Hospital notes invariably stated for each discharged patient whether "improved" or "not improved," and we have accepted this dichotomous definition of remission as the best we could manage—we have thus taken "improved" to mean "in remission" except when the notes also showed that the patient still had "significant" residual tumour (this was not always easy to decide).

Table V shows the discharged improved rate related to the extent of the disease at presentation—this relationship has been reported in a slightly different manner and in further detail as regards extent of remission by Burkitt *et al.* (1965).

TABLE V.—Discharged "Improved" and Stage of Disease at Presentation

Stage	No. of Patients	No. Discharged "Improved"	% Discharged Improved
1	6	5	83
2	11	8	73
3	38	21	55
All patients	55	34	62

Of the 24 patients discharged improved who subsequently had recurrences 10 did not bother to return to Mulago Hospital—two of these were stage 2 and the others stage 3 cases. The length of time between the discharge of these patients and death are (in days): 51, 63, 88, 124, 133, 162, 240, 285, 307, and 391. It is surprising that these patients did not think it worth their while to return, in particular those with lengthy remissions.

Discussion

In this series the stage of the disease at presentation was of critical prognostic importance. However, as is well known to anyone working with this tumour, the disease does not invariably progress from stage 1 through stage 2 to stage 3. In fact, many stage 3 patients present with abdominal lesions alone, and by our definition these cases have been stage 3 throughout the course of their disease. From the histories of the vast majority of the stage 3 cases with both abdominal and jaw lesions it was simply not possible to tell the time sequence of symptoms; and in the few instances where the jaw tumour appeared to have preceded the abdominal involvement one was always doubtful of the true significance of this, since the jaw lesions were so much more obvious. Similarly, though a number of stage 2 patients who later died had progressed to stage 3 before death, so that this sequence seems at least to be possible, we have to bear in mind that the first physical examination might well have missed a small abdominal mass. There are a number of cases in which the abdominal tumour appears to have preceded the jaw lesion.

Surgical reduction of abdominal tumour masses produced our only stage 3 survivors. This result, we feel, lends support to the finding that the critical factor in prognosis is the extent of disease at presentation. The risks attendant on abdominal surgery would therefore appear to be worth taking. This is in accordance with the results obtained in Ibadan, Nigeria (Ngu, 1964), where the only long-term survivors with stage 3 disease had excisions of their abdominal tumours.

Four of the five stage 1 long-term survivors had recurrences. Treatment of recurrences is thus distinctly worth while. In two of the stage 2 deaths the patients had had long remissions before dying at home without returning to Mulago Hospital,

and it is possible that they might have survived if they had returned for further treatment at recurrence.

The results obtained from this series do *not* agree in all respects with the results found by Clifford (1966).

We divided Clifford's patients into our three staging categories on the basis of the details given in his paper, but both the "remission" rate (about 80%) and the long-term survival rate (about 17%) were independent of this division. A possible explanation of this discrepancy is to be found in the different drug dosages used in Nairobi and Kampala.

On average Clifford gives about two to three times the initial dose of drug given at Mulago Hospital. This appears to have resulted in a number of important differences in what we might term secondary response. A number of Clifford's stage 3 patients are long-term survivors on chemotherapy *alone*, a phenomenon not observed in our series. But the recurrence times for tumours of small extent are on the whole much shorter than those observed in Kampala.

There is some evidence, both clinical and experimental (Burchenal and Burkitt, 1967), that host defences may play an important role in survival in Burkitt's lymphoma. Regressions (one in this series, see above) and "cures" have been noted after little or no specific chemotherapy; while Klein and his co-workers have obtained results interpreted as showing a tumour specific component in the sera of Burkitt's lymphoma patients in complete remission. If one adopts this proposition then one may argue that the chemotherapeutic agents used might not only affect tumour tissue but also affect the patients' immune response, and the balance between these two results of therapy might be critical. Clifford is giving a quantity of drug which will destroy the greater percentage of tumours (at least of large ones), but this results in a greater reduction in the patients' own defences—some of his cases die of leukaemia, and the initial drop in the Nairobi survival curve is very steep, so that the end-result is a similar "success" rate in Nairobi and Kampala, but with marked differences in effect of initial tumour location—these arguments in a slightly different form have been previously suggested by Burkitt *et al.* (1965).

This, however, is all very speculative, and the major problems of which drug to give, the best total dose (of a particular drug) to give, and whether this should depend on the "extent" of the disease, remain unresolved. It is our belief that these problems will not be resolved without strictly controlled clinical trials. Joint trials conducted simultaneously in a number of centres, with each of these centres drawing patients from an area as wide as possible, and the maintenance of a complete follow-up, would be of enormous value in getting sufficient numbers of cases together in a short time, and it is hoped that this can be arranged.

This study has shown that successful follow-up of a limited group of young patients, even retrospectively, is possible in Uganda. We attribute our success to having a non-hurried approach, in particular to being willing to spend considerable time explaining what we were doing to people encountered in our searches. After this explanation information was often forthcoming that the informant either denied knowing beforehand or did not bother to remember.

NOTE.—Mr. Clifford has now reviewed his data, employing a system of staging similar to that used here, and reports that he has found some relationship between this method of staging and prognosis. The relationship was not nearly as striking as that found in our series, and we still feel that the factors discussed above are those most likely to account for the difference.

Summary

Follow-up of 80 cases of Burkitt's lymphoma treated in Mulago Hospital, Uganda, has shown that the "long-term"

survival rate is approximately 1 in 5. This rate is markedly dependent on the extent of anatomical involvement of the lymphoma at presentation in this series, but in the previously reported series of Clifford (1966) this is not so. A possible reason for this discrepancy is sought in the different dosages of drugs used in the two centres.

This investigation represents a continuation and extension of the work initiated by Mr. D. Burkitt. We are grateful to Mr. Burkitt and Mr. S. Kyalwazi, who between them treated nearly all the cases reported in this series, for permission to follow up their patients. Special acknowledgement is due to both the past and the present pathologists at Makerere Medical School, and in particular to Dr. D. H. Wright, for carrying out the microscopy of the cases considered in this paper. We would like to thank Mrs.

Barbara Wright (registrar, B.E.C.C.-financed Kampala Cancer Registry) for the assistance she gave us in collecting details of the patients. We gratefully acknowledge the financial support of the U.S. National Cancer Institute (N.I.H.) under their Contract No. PH-43-67-47, and of the British Empire Cancer Campaign for Research.

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Hypokalaemic Alkalosis and Hyperplasia of the Juxtaglomerular Apparatus without Hypertension or Oedema*

L. J. BEILIN,† M.D., M.R.C.P.; N. SCHIFFMAN,‡ M.D.; M. CRANE,§ M.D.; D. H. NELSON,||

Brit. med. J., 1967, **4**, 327-331

Hyperaldosteronism is commonly associated with either hypertension and hypokalaemic alkalosis as in renal vascular hypertension, malignant hypertension, and primary aldosteronism, or with oedema as in cirrhosis with ascites, the nephrotic syndrome, and chronic congestive heart failure. A dissociation between the hypertensive, potassium-losing, and continued sodium-retaining effects of aldosterone has previously been noted (Nelson and August, 1959) in patients who become oedematous. Three patients have been described with hypokalaemia, hyperaldosteronism, and hyperplasia of the juxtaglomerular apparatus but without hypertension or oedema (Bartter *et al.*, 1962; Boucher *et al.*, 1964; Ames *et al.*, 1965). The present case, like the other similar cases, apparently represents another instance in which aldosterone in excess has not resulted in hypertension. The cause of the syndrome described in these cases is unknown, but it has been suggested that it represents an important aberration from the normal relations between the renin-angiotensin-aldosterone system and blood pressure control.

Case Report

The patient was an 18-year-old negro male whose illness dates from infancy. He was delivered after a seven-month pregnancy and was well until 4 months of age, when he stopped growing. At 7 months he was admitted to the Children's Medical Center in Dallas, Texas, after two weeks' incessant vomiting. He was found to be grossly dehydrated, wasted, and drowsy. He was in opisthotonos, but Trousseau and Chvostek signs were negative. The testes were undescended and he had a first-degree hypospadias. Investigations at that time revealed a serum bicarbonate of 46 mEq/l., serum chloride 74.6 mEq/l., serum sodium 123 mEq/l., serum potassium 4.8 mEq/l., and a blood pH of 7.65. Idiopathic alkalosis was diagnosed, and he was initially treated with ammonium

chloride, sodium chloride, and deoxycortisone without effect. He eventually recovered after subcutaneous fluids and oral feeding, and was discharged clinically well but with persistent hypochlorhaemic alkalosis.

He grew slowly, walked at 15 months, but at 4 years was noted to have polyuria and polydipsia. He was then reinvestigated and found to have one testis in the scrotum and a bone age of 3½ years. Hypochlorhaemic alkalosis was present with serum chloride of 87 mEq/l., serum bicarbonate 41 mEq/l., a blood pH of 7.59, and a creatinine clearance of 116.6 ml./min. He was given no further treatment at that time.

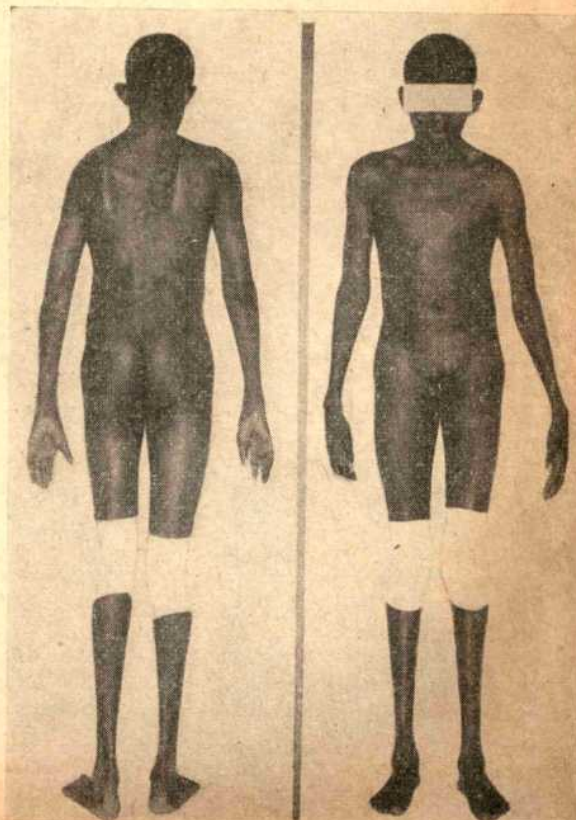


Fig. 1.—Patient aged 18, with prepubertal genitalia.

* From the University of Southern California School of Medicine and the Los Angeles County General Hospital, Los Angeles, California. This work was supported in part by a grant from the USPH Service, General Clinical Research Centre Grant FR-43.

† Holder of Sir Henry Wellcome Travelling Fellowship. Present address: Hammersmith Hospital, London W.12.

‡ Instructor in Medicine, University of Southern California School of Medicine, Los Angeles.

§ National Institutes of Health, Career Development Awardee—9-K3-HE-7627, and Research Professor of Medicine, Loma Linda University, Loma Linda, California.

|| Investigator, Howard Hughes Medical Institute. Present address: University of Utah College of Medicine, Salt Lake City, Utah.

He attended school, requiring special classes, and received no further medical treatment until the age of 17, when he suffered from recurrent dislocation of the patella. At 18 he presented to the endocrine clinic at the Los Angeles County General Hospital complaining of delayed puberty. His only other symptoms were constipation and diminished energy. He denied ingestion of drugs or having diarrhoea, and had no attacks of paralysis or tetany.

Physical examination showed him to be alert, with a eunuchoid build and prepubertal genitalia (Fig. 1). The right testis was in the inguinal canal and was 2 cm. long; the left was in the scrotum and was 3 cm. in length. His height was 159 cm. in the 10–25th percentile and exceeded his span by 2 cm. His weight was 34 kg., which was below the third percentile for his age and height. Blood pressure ranged from 108/60 to 90/50 with no significant postural changes.

Preliminary investigations revealed a serum potassium of 2.6 mEq/l., serum bicarbonate 29 mEq/l., serum chloride 85 mEq/l., serum sodium 134 mEq/l., and blood urea 10 mg./100 ml.; alkaline phosphatase 6.5 and 6 Bodanski units/ml.; and serum magnesium 1.6 mg./100 ml. Serum cholesterol was raised on two occasions to 301 and 256 mg./100 ml. Serum bilirubin was 0.7 mg./100 ml. and bromsulphalein retention less than 5% in 45 minutes. Haemoglobin was 11–13.5 g./100 ml., with a normal film and a W.B.C. of 7,100, and normal differential. Bone age estimated by skeletal x-rays was 15–17 years. Skull and chest x-ray examination showed nothing abnormal. E.E.G. was normal. Buccal smear was negative for Barr bodies. E.C.G. showed changes of hypokalaemia with inverted and biphasic T waves and a prolonged Q–U interval. Urinalysis showed a normal sediment with less than 100 mg. protein per 24 hours and no glucose (tested with Clinistix). Urine cultures were sterile. Creatinine clearance was 98 ml./min. Urine concentrating ability was impaired as shown by urine osmolality of 378 mOsm/l. after four hours' intravenous infusion of pitressin at a rate of 4 microunits/min. Urinary acidification was slightly impaired, the urine reaching a minimum pH of 5.9 after an oral ammonium chloride load of 0.5 g./kg. body weight (Wrong and Davies, 1959). Twenty-four-hour urine amino-acids totalled 179 and 490 mg./100 ml. with no distinctive pattern. An intravenous pyelogram suggested some irregularity of the calices of the right kidney but was otherwise normal. Renal aortogram and ¹³¹I hippuran renal scan were normal. Twenty-four-hour urine 17-ketogenic steroids and 17-ketosteroids were normal and there was a

normal response to intravenous A.C.T.H. and metyrapone. Urinary gonadotropins were less than 6 units and 6–16 units/24 hours on two occasions. P.B.I. was 6.8 µg./100 ml. and a ¹³¹I uptake was 14% in 24 hours, rising to 40% after thyroid-stimulating hormone.

Balance Studies

Metabolic balance studies carried out in the metabolic unit of the Los Angeles County General Hospital were designed to determine the site and cause of potassium loss. Results are shown in Fig. 2. On a potassium intake of 60 mEq/day excretion of urinary potassium exceeded intake, and this urinary potassium loss persisted when dietary potassium was reduced to 20 mEq/day. Total exchangeable potassium at this time was 1,172 mEq compared with an expected normal of 2,000 mEq for a person of his size. When dietary sodium was reduced to 10 mEq/day, urinary potassium excretion fell below intake. Increasing the dietary sodium to 120–150 mEq/day then caused an immediate rise in urine sodium and return of negative potassium balance. These results were interpreted as evidence that the hypokalaemia resulted from renal potassium loss due to hyperaldosteronism, the potassium retention induced by the low sodium diet being due to insufficient sodium reaching the distal tubule to exchange with potassium under the influence of aldosterone. When spironolactone, 200 mg. daily, was administered, urine sodium increased to 140 to 230 mEq/day, potassium was retained, and for the first time the serum potassium rose toward normal (Fig. 2).

Twenty-four-hour urine aldosterone excretion was measured on several different occasions. Table I shows that there was only one elevated value during the initial hospital admission, but that two weeks after cessation of two months' spironolactone therapy values were raised. Aldosterone secretion rate was 231 µg./100 ml., which was a high normal value for adults on 100 mEq sodium diet and is probably high for a prepubertal individual weighing 34 kg.

TABLE I.—24-Hour Urinary Aldosterone Levels

Diet	Lab. A (N 3–32 mg.)	Lab. B (N 5–19 mg.)
60 mEq K	22	—
80 mEq Na	11	—
20 mEq K	6	17.4
	7	14.1
58 mEq Na	57	27.7
	2	—
2 weeks after 2 months of spironolactone	—	44
	—	45

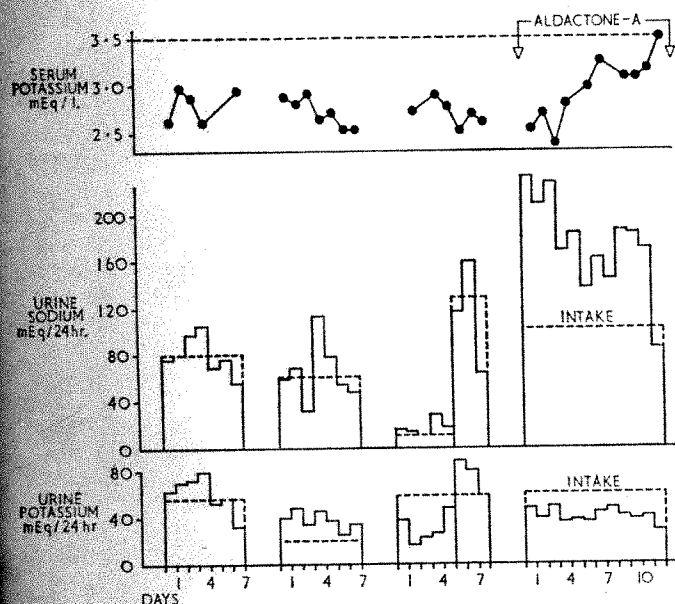


FIG. 2.—Upper graph: Solid line represents serum potassium; the horizontal dotted line indicates the lower limit of normal serum potassium. Middle graph: Solid blocks represent 24-hour urine sodium excretion; the horizontal dotted lines indicate daily sodium intake. Lower graph: Solid blocks represent 24-hour urine potassium excretion; the horizontal dotted lines indicate daily potassium intake. Four main balance periods are shown from left to right. The first two demonstrate a tendency to renal potassium loss in the presence of hypokalaemia. The third period shows potassium retention on a low sodium intake and increased potassium loss when the sodium intake was increased. The fourth period shows potassium retention and natriuresis induced by Aldactone-A (spironolactone) and a rise in serum potassium towards normal.

Plasma Renin Activity

Plasma renin activity was measured¹ by a modified method of Boucher. The patient was studied initially while taking a low-sodium diet, a high-sodium diet, and after a period of spironolactone therapy. Samples were withdrawn after the patient was supine, after an overnight sleep, and again after four hours' standing. Table II shows that the values obtained in the patient were

TABLE II.—Plasma Renin Activity (Dr. M. Crane). (mµg. Angiotensin II per 100 ml. Plasma)

		Patient	Normals	Hypertensives
Low sodium diet	Supine	9,120	150–705 (9)	176–904 (19)
	Standing	12,200	574–1240	258–3440
High sodium diet	Supine	6,000	36–236 (11)	46–1120 (19)
	Standing	6,400	237–825	
Normal diet and spironolactone	Supine	5,400		
	Standing	4,310		

¹ Values for the normals and hypertensives are ranges. The numbers of subjects are indicated in parentheses.

extremely high compared with normal subjects or patients with essential hypertension, renal hypertension, or primary aldosteronism. (Values given were ranges for each group.) Values for the patient were significantly higher on a low-sodium diet but showed no change after the period on aldactone.

¹ Measured in the laboratory of Dr. Milton Crane.

Renal Biopsy

A percutaneous renal biopsy of the right kidney was examined by light microscopy.² Haematoxylin and eosin stains revealed cellular proliferation in a few glomerular loops in a small number of the glomeruli. The juxtaglomerular cells that make up the walls of the preglomerular portion of the afferent arteriole were greatly increased in number, causing a distinct cellularity of the vascular pole of many of the glomeruli.

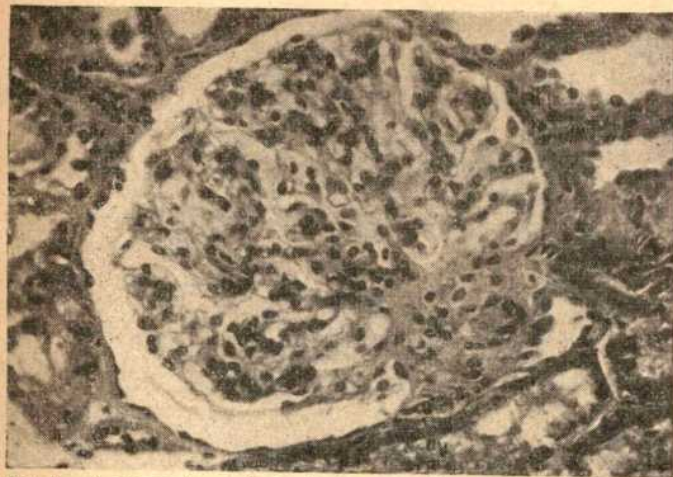


FIG. 3.—A glomerulus stained with haematoxylin and eosin showing increased cellularity of the vascular pole and cellular proliferation in a few capillary loops.

Periodic acid Schiff stained sections revealed P.A.S.-positive granules in the cytoplasm of the granular juxtaglomerular cells. The average number of granular juxtaglomerular cells per vascular pole was between 17 and 20, compared with four to six in normal individuals. Hence there was unquestioned hyperplasia of the granular juxtaglomerular cells. The granularity of each cell was more difficult to quantitate since human kidneys lack significant numbers of granules even in situations where the cells are known to have increased secretory activity.

Angiotensin Infusion Test

Synthetic angiotensin II amide was infused intravenously in a solution of 0.9% saline by means of an infusion pump to deliver

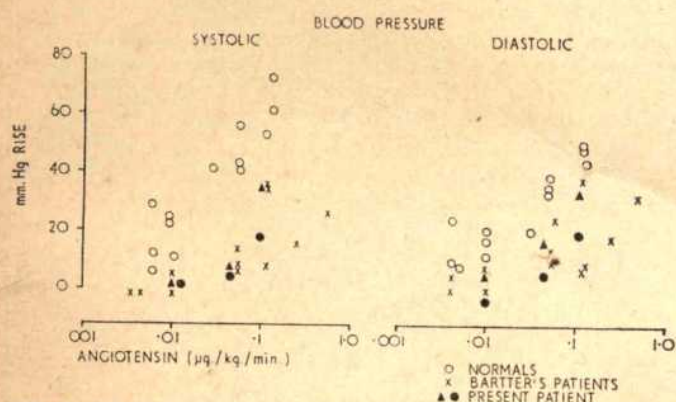


FIG. 4.—Effect of infusion of angiotensin II amide on blood pressure. Results in present case are superimposed on the data of Bartter *et al.* (1962). The latter are reproduced by kind permission of the *American Journal of Medicine*.

doses of 0.01, 0.05, and 0.2 $\mu\text{g./kg. body weight/minute}$. Blood pressures were recorded by sphygmomanometry during a basal period of 30 minutes and then at 60-second intervals for 8 to 10 minutes during each dose rate of angiotensin infusion. The mean systolic and diastolic blood pressures for each infusion rate were calculated and the increments in blood pressure above baseline levels

were estimated. The experiment was performed on two occasions when the serum potassium was below 3 mEq/l. Fig. 4 shows these results superimposed on data obtained from the patients studied by Bartter *et al.* (1962). It can be seen that our patient shows grossly diminished pressor sensitivity to angiotensin compared with the normal subjects and similar sensitivity to that seen in the other two patients. Expressed according to the criteria of Kaplan and Silah (1964), our patient required 70–100 $\mu\text{g.}$ of angiotensin per kg. body weight per minute to obtain a 20 mm. Hg rise in diastolic blood pressure. This compared with 2.6–7.6 mg. for normal subjects (Hocken and Kark, 1965). The normal pressor activity of the angiotensin used in our patient was confirmed in normal subjects.

The pressor response to noradrenaline was also studied by infusing noradrenaline at rates of 0.6, 1.2, and 3.0 $\mu\text{g./kg. body weight/minute}$. Average increments of 1.5, 7.2, and 24 mm. Hg in diastolic pressures were obtained for the respective doses of noradrenaline.

Discussion

The patient showed several features which suggested that he suffered from the same disease as the patients described by Pronove *et al.* (1960), Bartter *et al.* (1962), and Bryan *et al.* (1966)—namely, hypokalaemic alkalosis, evidence of hyperaldosteronism, hyperplasia of the juxtaglomerular apparatus, increased renin secretion, and presumably increased angiotensin formation, normal blood pressure, absence of oedema, and relative insensitivity to pressor effects of exogenous angiotensin.

The variably elevated urinary aldosterone levels in our patient were thought to be due to the inhibiting effect that hypokalaemia itself has on aldosterone secretion (Cannon *et al.*, 1964; Gann *et al.*, 1964). The balance studies appear to provide good evidence that the hypokalaemia was due to an aldosterone effect and values were raised after a period of potassium repletion. It is noted that preliminary values of aldosterone excretion reported by Bryan *et al.* (1966) were also normal in their patient.

Plasma renin activity was grossly raised in our patient (Table II). Despite the high levels on the sodium intake of 120 mEq/day, it appeared that the kidneys were still capable of producing more renin in response to a low sodium intake.

The increased granularity of the juxtaglomerular apparatus (Fig. 3) demonstrated by light microscopy was similar to that seen in the other patients (Bartter *et al.*, 1962; Bryan *et al.*, 1966) and provided further evidence of increased renin production.

If it is reasonable to assume that the increased renin production resulted in increased angiotensin formation and consequently hyperaldosteronism and hypokalaemia in these patients, then two outstanding questions are posed. Firstly, what is the fundamental cause of the increased activity of the juxtaglomerular apparatus? Secondly, why is the blood pressure normal in the presence of increased angiotensin and aldosterone production? It has been suggested (Bartter *et al.*, 1962; Bryan *et al.*, 1966) that the prime abnormality is a decreased vascular sensitivity to angiotensin as demonstrated by the infusion of exogenous angiotensin—the implication being that renin production is increased to produce angiotensin, which directly maintains vasomotor tone. The hyperaldosteronism would then be an unwanted side-effect of this compensatory mechanism. This theory assumes that angiotensin is of physiological importance as a peripheral vasoconstrictor. The situation is not clear in this respect, but it is apparent that any physiological pressor effect is modified and mediated at least in part by electrolyte changes and aldosterone (Peart, 1965).

Ames *et al.* (1965) showed that prolonged angiotensin infusions in normal subjects were associated with increasing pressor sensitivity coincident with increased aldosterone production and sodium retention. On the other hand, a diminished

² Kindly reported by Dr. H. Demopoulos.

pressor response to angiotensin has been described in both normotensive and hypertensive states where increased endogenous angiotensin circulates. For example, in the secondary hyperaldosteronism of cirrhotics (Ames *et al.*, 1965) and in some cases of malignant and renal hypertension (Kaplan and Silah, 1964), it has been suggested that the diminished pressor response to exogenous angiotensin in those conditions may be due to tachyphylaxis to the prolonged high levels of circulating angiotensin. Such tachyphylaxis might account for the pressor insensitivity seen in our patient. The absence of a simple alternative explanation for the increased renin production and decreased pressor response to angiotensin in these patients is presumably due to lack of knowledge of the precise mode of activation and functions of the renin-angiotensin system. It is therefore pertinent to examine two situations in which the renin-angiotensin-aldosterone system is known to be stimulated—namely, local abnormalities of renal blood flow and sodium depletion. Stemming from the experiments of Goldblatt *et al.* (1934), it has been shown that local disorders of renal blood flow may give rise to increased renin production and hypertension. A local abnormality of renal blood flow seems unlikely in our patient since hypertension was absent and the renal vasculature was grossly normal on aortography.

Sodium depletion also causes increased renin (Genest *et al.*, 1964; Brown *et al.*, 1964), angiotensin (Veyrat *et al.*, 1964), and aldosterone (Luetscher, 1956) production but without the development of either hypertension or oedema. It is therefore tempting to speculate that there is a tendency towards sodium depletion and thus extracellular fluid volume depletion in these patients. Abnormalities in extracellular fluid volume are not easy to establish, but if such a deficit were the stimulus to excess renin production then expansion of extracellular fluid or plasma volume should depress plasma renin activity, whereas if some other overriding stimulus were responsible then volume expansion would be less likely to affect renin output materially.

This theory was examined by measuring plasma renin levels before and after infusions of 0.9% saline and 6% dextran in 0.9% saline. The studies were carried out while the patient was on a constant sodium intake of 100 mEq/day. The two infusions were given four days apart and were each for four hours between 10 a.m. and 2 p.m. with the patient supine and fasted but without prior fluid restriction. Urine output and body weight were recorded every 20 to 30 minutes during the infusions. Plasma renin activity was measured immediately before and after each infusion. Plasma volume was estimated before and after the dextran infusion, using radioiodinated human serum albumin. Table III shows these results along with the volumes of fluid infused, the maximum weight increase during infusion, and the change in plasma volume after dextran. It can be seen that even when allowance was made for haemodilution plasma renin levels fell markedly with both saline and dextran infusions. The fact that at the end of the infusions renin activity, though drastically reduced, was still higher than normal may be due to the relatively short periods of volume

compared with the observed values of 918 and 654 units. If the infusions had been continued longer renin activity might well have fallen more.

It seems likely that the inhibition of renin activity with both infusions was mediated by changes in plasma volume rather than changes in extravascular volume. A total of 700 ml. of 6% dextran in saline caused plasma renin activity to fall to a similar extent to 3,700 ml. of saline, and whereas a rise in plasma volume is anticipated with both infusions, and a rise in interstitial fluid volume is expected with the saline alone, the observation that 550 of the 700 ml. of 6% dextran in saline could be accounted for by the rise in plasma volume (Table III) suggests that this infusion caused little interstitial volume expansion.

The demonstration that excess renin production could be inhibited by plasma volume expansion is compatible with the suggestion of an abnormality of fluid volume control in these patients, the increase in renin, angiotensin, and aldosterone acting in concert to retain sodium and to restore extracellular fluid volume to normal. Neither hypertension nor oedema would be expected in such a situation, and if fluid volume correction were inadequate blood pressure would tend to be low, as in these patients. A mechanism leading to subnormal extracellular or plasma volume still requires explanation. Impaired proximal tubular sodium reabsorption seems possible, as suggested by Laragh and Kelly (1964), in which case increased delivery of sodium to the distal tubule and exchange there of sodium for potassium would lead to the hypokalaemia observed.

Other features of this disorder which remain unexplained are the growth retardation and the glomerular damage. Growth retardation has been attributed to chronic hypokalaemia (Bryan *et al.*, 1966), and no better explanation is offered. Glomerular damage was widespread in the renal biopsies obtained in three of the patients. Light microscopy of the kidney in our patient showed capillary basement membrane thickening similar to that seen in many forms of glomerulonephritis. Despite this, there was no significant proteinuria. It is not clear whether these glomerular changes are related causally to the disease process or result from it. However, it has been shown that renin injections cause glomerular damage and proteinuria (Pickering and Prinzmetal, 1940), and it is possible that prolonged excessive release of endogenous renin might have a similar though less marked effect.

Management of our patient has been on the basis of spironolactone therapy to increase the serum potassium with attempts to administer up to 400 mg. a day, and though the drug is taken irregularly the serum potassium remains at 3.2–3.5 mEq/l., which is higher than the levels originally observed (Bartter *et al.*, 1962). The blood pressure has not changed significantly despite the initial saluresis caused by spironolactone. The patient appears to be more alert and active but he is receiving testosterone injections, which may influence this impression. No surgery is contemplated, since two of the three other patients had subtotal bilateral adrenalectomy with no immediate or long-term effect on their hypokalaemia and no symptomatic improvement.

Summary

A disorder characterized by hypokalaemia, evidence of hyperaldosteronism, increased plasma renin activity, increased granularity of the juxtaglomerular apparatus, glomerular abnormalities, normal blood pressure, and decreased pressor response to exogenous angiotensin is described in a non-oedematous 18-year-old prepubertal negro youth and is compared with a similar condition described in three other patients (Pronove *et al.*, 1960; Bartter *et al.*, 1962; Bryan *et al.*, 1966).

TABLE III.—Effect of Fluid Volume Expansion of Plasma Renin Activity

Infusion:	0.9% Saline	6% Dextran in 0.9% Saline
Plasma renin activity { Before ..	10,700 units	4,870 units
{ After ..	918	654
Volume infused ..	3,400 ml.	700 ml.
Maximum weight increase during infusion ..	1.2 kg.	0.5 kg.
Plasma volume { Before ..		1.81 l.
{ After ..		2.36 "

expansion compared with the biological half-life of renin. Data on the latter are scanty. In the dog it has been estimated as 15 minutes (Fasciolo *et al.*, 1964) and is probably longer in man. With a half-life for renin of say 30 minutes and volume expansion for three of the four hours of infusion, initial values of 10,700 and 4,870 units should fall to 446 and 203 units,

The pathogenesis of the syndrome is discussed and evidence for an abnormality of extracellular fluid volume control is presented.

We wish to acknowledge the invaluable assistance of the Metabolic Unit Staff at the Los Angeles County General Hospital in studies of this patient.

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Total Parathyroidectomy in Treatment of Secondary (Renal) Hyperparathyroidism

C. S. OGG,* M.B., B.SC., M.R.C.P.

Brit. med. J., 1967, **4**, 331-334

Recent improvements in the care of patients with chronic renal failure have revealed that symptoms attributable to renal glomerular (uraemic) osteodystrophy develop in a considerable number of cases.

The various components of this bone disease include rickets or osteomalacia, osteitis fibrosa, and osteosclerosis. These may occur in almost pure forms but more commonly appear in varying combinations in different patients.

Treatment with large doses of vitamin D (Liu and Chu, 1943; Dent *et al.*, 1961; Stanbury and Lumb, 1962) is often successful in promoting healing of the skeleton, but is dangerous because of the ease with which it is possible to produce hypercalcaemia and metastatic calcification. This danger is greatest in those patients who have osteitis fibrosa as the dominant skeletal lesion, and who, unlike the majority of patients with renal failure who have low plasma calcium levels (de Wesselow, 1923), have plasma calcium levels that are either within the normal range (Stanbury and Lumb, 1966) or even frankly raised (Hubbard and Wentworth, 1921; Smyth and Goldman, 1934; Shelling and Remsen, 1935).

Stanbury *et al.* (1960) were the first to embark deliberately on a policy of subtotal parathyroidectomy in a patient with severe secondary hyperparathyroidism, and they were subsequently able to heal the bone lesions with vitamin D without producing hypercalcaemia. Since then further reports have appeared in this country (Findley *et al.*, 1961), in South Africa (Stables *et al.*, 1964), and in the United States of America (Anderson *et al.*, 1963; Fordham and Williams, 1963; Golden *et al.*, 1965; Felts *et al.*, 1965; Wilson *et al.*, 1965). These reports include a total of only 12 cases, and it is considered worth while to report four more.

Case 1

A 43-year-old man presented in 1961 with severe chronic renal failure (plasma urea 210 mg./100 ml.). No cause for this was found, and he was treated with a high fluid intake, a low protein diet, and sodium bicarbonate 2 g. daily.

During the following year he developed radiological changes of hyperparathyroidism in his hands, but this caused no symptoms until 1964, when he felt severe pain in both shoulders. His plasma calcium had risen to 10.5 mg./100 ml. (Fig. 1), with an ionized fraction of 5.0 mg./100 ml. and a complexed fraction of 1.3 mg./100 ml. (normal range 4.9-5.8 and 0.0-0.7 mg./100 ml. respectively (L. Watson, personal communication, 1967). X-ray films showed progression of the subperiosteal erosions of the phalanges and the appearance of erosions of the lateral ends of both clavicles.

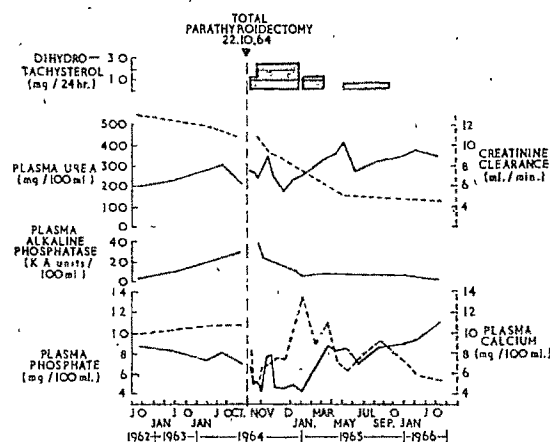


FIG. 1.—Case 1. Biochemical progress. Note changing time scale.

It was also noted that there was a considerable amount of calcification in the internal iliac arteries. Because of the metastatic calcification total parathyroidectomy was recommended, and four hyperplastic glands were removed. Preoperative and postoperative findings are shown in Tables I and II.

The plasma calcium fell to a minimum of 4.9 mg./100 ml. on the fifth postoperative day, and symptoms of tetany were controlled with intravenous calcium gluconate and oral dihydrotachysterol. Within a month he had lost his bone pain and was discharged.

* Medical Registrar, St. Peter's, St. Paul's, and St. Philip's Hospitals, London W.C.2. Present address: Renal Unit, Guy's Hospital, London S.E.1.

TABLE I.—Status of Patients Immediately before Surgery

Case No.	Renal Lesion	B.P.	Years of		Previous Vitamin D	Creatinine Clearance (ml./min.)	Plasma					Urine Calcium (mg./24 hr.)
			Renal Lesion	Bone Lesion			Urea (mg./100 ml.)	Calcium (mg./100 ml.)		Phosphate (mg./100 ml.)	Alkaline Phosphatase (K.A. Units/100 ml.)	
								Total	Ionized			
1	Unknown	130/80	> 3	2	No	10.0	205	10.5	5.0	6.8	22	152
2	Bladder neck obstruction	120/80	14	> 3	Yes	5.0	210	11.3	5.7	7.8	28	123
3	Chronic glomerulonephritis	165/100	29	?	No	8.4	125	11.1	6.0	5.9	40	110
4	? Dysplasia	140/90	> 2	> 1.5	"	3.0	280	10.2	5.6	10.0	42	72

from hospital taking oral dihydrotachysterol and calcium supplements. The doses of these were reduced until they were stopped in September 1965.

His renal disease continued to progress, but at the time of writing he was still working full time.

Case 2

In 1961 an 11-year-old boy had a urinary tract infection. Investigation revealed moderate renal failure (blood urea 91 mg./100 ml.) and bladder-neck obstruction with ureteric dilatation. Despite relief of the obstruction his blood urea remained raised, and he continued to have episodes of infection.

Two years later he first had pains in his legs, and in 1964 he was referred for further investigation. The presence of severe renal failure (blood urea 237 mg./100 ml.), together with a urinary infection, was confirmed. Plasma calcium was 10.3 mg./100 ml.,

and there was gross elevation of the plasma alkaline phosphatase (84 K.A. units/100 ml.) (Fig. 2). A radiological skeletal survey showed epiphyseal changes suggestive of rickets, together with subperiosteal erosions on the phalanges, resorption of the phalangeal tufts (Figs. 3 and 6), erosion of the lateral ends of the clavicles, and a "rugger jersey" spine. Dietary protein restriction, antibiotics, and a high fluid intake led to a fall in blood urea but did not affect his skeletal symptoms. The addition of calciferol resulted in clinical and radiological improvement, but was associated with hypercalcaemia (11.6 mg./100 ml.), which persisted despite

TABLE II.—Summary of Operative Findings and Postoperative Course

Case No.	Date of Operation	No. of Glands	Weight of Glands (g.)	Postoperative Therapy	Survival (Months)
1	22/10/64	4	1.46	10% Ca gluconate 40 ml. Dihydrotachysterol 5 mg.	> 32
2	20/1/66	4	2.53	10% Ca gluconate 40 ml. Dihydrotachysterol 8 mg. Parathyroid hormone 4 ml.	"
3	30/5/63	2	2.68	Calciferol 1.25 mg. alt. die	9
4	20/6/63	4	2.15	Dihydrotachysterol 5 mg.	0.1

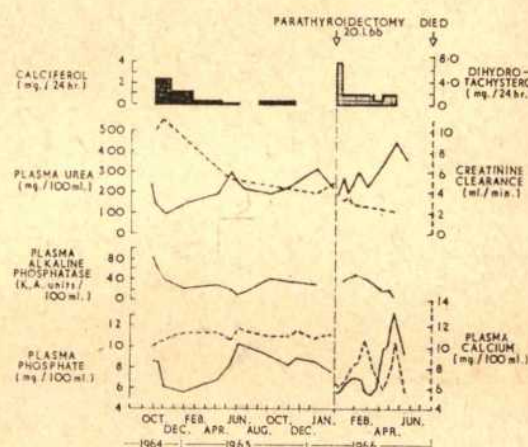


FIG. 2.—Case 2. Biochemical progress. Note changing time scale.



FIG. 3



FIG. 4



FIG. 5

FIG. 3.—Case 2. X-ray film of right hand, 2 October 1964. FIG. 4.—Case 2. X-ray film of right hand, 6 January 1966. FIG. 5.—Case 2. X-ray film of right hand, 30 March 1966.

reduction of dosage and eventual cessation of treatment in November 1965. By this stage his symptoms had returned, and when reassessed in January 1966 he was incapacitated by pain in his legs and had developed a waddling gait. His renal function had deteriorated, and x-ray films showed that the changes of secondary hyperparathyroidism had become more pronounced, while the changes suggesting rickets had if anything regressed (Figs. 4 and 6). Plasma calcium fractionation showed an ionized fraction of 5.7 mg./100 ml. (Table I) and a complexed fraction of 1.4 mg./100 ml. Total parathyroidectomy was advised, and four hyperplastic glands were removed.

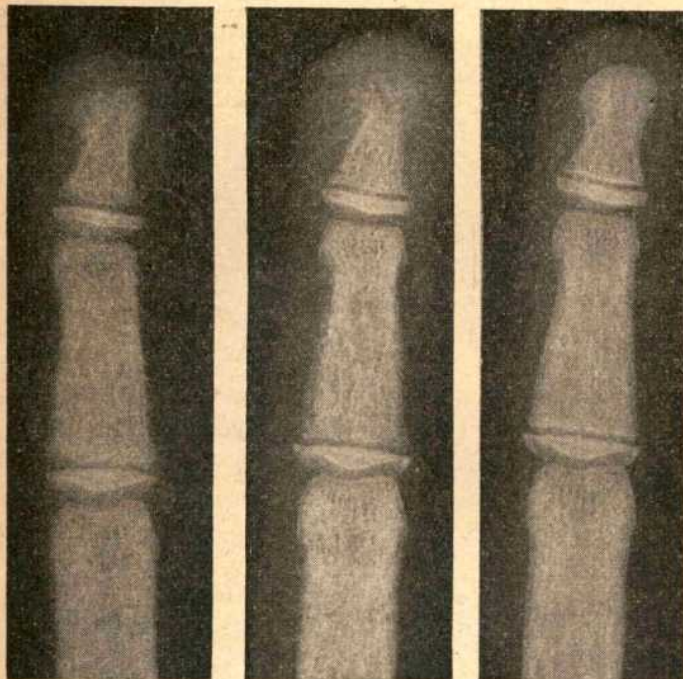


FIG. 6.—Case 2. X-ray films of right middle finger. Left, 2 October 1964. Centre, 6 January 1966. Right, 30 March 1966.

Postoperatively he developed severe hyperkalaemia (8.7 mEq/l.) but responded to conservative treatment for this. Within 24 hours the plasma calcium fell to 6.2 mg./100 ml.; subsequently it was maintained at this level, with intravenous calcium gluconate, intramuscular parathyroid hormone, and oral dihydrotachysterol (Table II). Four days later treatment was reduced to oral dihydrotachysterol with a calcium supplement. His bone pain disappeared within three weeks, and two weeks later there was obvious radiological improvement (Figs. 5 and 6). The dose of dihydrotachysterol was reduced, being finally stopped in April.

Unfortunately his renal function continued to deteriorate, but he remained free of bone pain until his death in July 1966. Necropsy was not performed.

Case 3

A 42-year-old woman had had acute nephritis at the age of 13, and in 1953 she was seen with proteinuria and a raised blood urea (70 mg./100 ml.). Ten years later she was referred because of progressive deterioration in renal function (blood urea 125 mg./100 ml.). Routine skeletal survey revealed changes of hyperparathyroidism with erosion of the borders of the phalanges and of the phalangeal tufts. Her plasma calcium was 11.1 mg./100 ml. (ionized fraction 6.0 mg./100 ml., complexed fraction 1.3 mg./100 ml.) with a plasma alkaline phosphatase of 40 K.A. units/100 ml. (Table I). At parathyroid exploration only two glands could be identified (Table II). Both were enlarged, but one (2.51 g.) was much larger than the other (0.17 g.). Despite this the histological appearances were thought to favour a diagnosis of secondary hyperplasia rather than of adenoma. Within 24 hours the plasma calcium and phosphate fell to 7.0 and 3.9 mg./100 ml. respectively. Calciferol 1.25 mg. on alternate days was started, and two weeks later she was discharged from hospital.

Subsequently, though there was radiological evidence of improvement of the bone lesions, her renal function continued to deteriorate

until her death nine months later. Necropsy revealed granular contracted kidneys compatible with the diagnosis of chronic glomerulonephritis.

Case 4

A 14-year-old girl presented in February 1962 with chronic renal failure (plasma urea 170 mg./100 ml.). Investigations revealed a solitary contracted right kidney and radiological evidence of hyperparathyroidism with erosion of the borders of the phalanges. She was treated with a high fluid intake, moderate protein restriction, and sodium bicarbonate 3 g. daily.

Fifteen months later she first complained of pain in the shoulders and legs. Further x-ray films revealed progression of the bone disease with severe changes in the hands, clavicles, and skull. There was extensive arterial calcification with metastatic deposits of calcium adjacent to several interphalangeal joints. Her renal function had deteriorated further, and the plasma calcium had risen to 10.2 mg./100 ml. (ionized fraction 5.6 mg./100 ml., complexed fraction 0.8 mg./100 ml.), with a plasma alkaline phosphatase of 42 K.A. units/100 ml. (Table I). Parathyroidectomy was advised, and four hyperplastic glands were removed (Table II). Postoperatively, continued haemorrhage necessitated re-exploration and drainage of the wound. Her plasma calcium and phosphate fell to 5.6 and 6.3 mg./100 ml. respectively on the third day. That evening she died unexpectedly, and subsequently her plasma potassium was found to have risen to 7.9 mEq/l.

Discussion

It is apparent that parathyroidectomy and subsequent treatment with large doses of vitamin D may allow healing of the bone lesions of secondary (renal) hyperparathyroidism without inducing hypercalcaemia. Once the bone lesions have healed the amount of vitamin D required to keep the patients free of symptoms attributable to hypocalcaemia may diminish, and in two of the cases it was possible to withdraw vitamin D altogether.

The operations did not influence the progress of the primary renal disease. In Cases 2 and 3 they were clearly performed too late to be of any great value to the patients. Case 1, however, experienced considerable benefit, and in retrospect it would seem that earlier operation in Case 2 might have saved the patient months of invalidism.

The progress (Figs. 3, 4, and 6) of the bone disease in Case 2 during the initial phase of treatment with vitamin D seems to contradict the view that hyperparathyroidism develops secondarily to the calcification defect of renal glomerular osteodystrophy. In these circumstances one might have expected the osteitis fibrosa to heal when the rickets was treated. However, the hyperparathyroidism which is commonly associated with osteomalacia of dietary origin, and which usually remits when the latter is treated, may occasionally become autonomous (Davies *et al.*, 1956). There is evidence that this may happen in patients with secondary (renal) hyperparathyroidism, for at least six patients have been subjected to parathyroidectomy only after successful renal transplantation had revealed the classical biochemical findings usually associated with primary hyperparathyroidism (McPhaul *et al.*, 1964; Wilson *et al.*, 1965; McIntosh *et al.*, 1966). In each case four enlarged glands were found.

Most patients with renal failure have low plasma ionized calcium levels (Fanconi and Rose, 1958; Walser, 1962), and the finding of a raised (Case 3) or high normal (Cases 2 and 4) level suggests that parathyroid autonomy has developed and is a strong indication for parathyroidectomy. Less definite indications include the presence of metastatic calcification and the failure of treatment with vitamin D to heal the skeleton without inducing hypercalcaemia.

In order to avoid the possibility of recurrence of the hyperparathyroidism, total rather than subtotal parathyroidectomy was advised. In consequence the fall observed in the plasma

calcium level was profound. This might be expected to sensitize the myocardium (Meroney and Herndon, 1954) to the rise in plasma potassium that may occur in any patient with renal failure who has had a major operation. This combination of events was presumably responsible for the death of Case 4. The postoperative fall in plasma phosphate is the opposite to what is seen in patients who have had a parathyroidectomy for primary hyperparathyroidism. This was found also by Stanbury *et al.* (1960), who pointed out that, as the normal phosphaturic effect of exogenous parathyroid hormone does not occur in the presence of a reduction in creatinine clearance to less than 10 ml./minute (Goldman and Bassett, 1954), parathyroidectomy would not be expected to change the renal phosphate clearance. Though the urinary excretion of phosphate fell postoperatively in all the patients, the fall was no greater than would be expected from that in the plasma level, and presumably the fall in the plasma level is due to the deposition of phosphate with calcium in bone.

The practical problems imposed by the appearance of autonomous hyperparathyroidism after successful renal transplantation are considerable. At least one transplanted kidney has been affected by calculi associated with autonomous (secondary) hyperparathyroidism (Hume *et al.*, 1966), and in any case the dangers of parathyroidectomy must be increased considerably by the immunosuppressive and steroid therapy that these patients receive. Thus if the presence of hyperparathyroidism is recognized it is probably advisable to deal with it before embarking upon transplantation.

Summary

Previous experience of the use of parathyroidectomy in the treatment of secondary (renal) hyperparathyroidism has been reviewed briefly. Four further cases are reported, and it is suggested that, with increasing interest in the management of chronic renal failure, the operation may be performed more

often in the future than it has been in the past. The indications for and the timing of surgery are discussed.

I wish to thank Dr. A. M. Joeckes and Dr. A. R. Harrison for permission to report these cases. Mr. J. D. Fergusson performed all the operations and Dr. L. Watson carried out the plasma calcium fractionations.

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Syndrome of Sclerodactyly, Calcinosis, Raynaud's Phenomenon, and Telangiectasia

A. W. DELLIPIANI,* M.B., M.R.C.P.ED.; M. GEORGE,† M.B., B.S.C., M.R.C.P., M.R.C.P.ED.

Brit. med. J., 1967, **4**, 334–335

Since Thibierge and Weissenbach (1911) described the association between scleroderma and calcinosis the Thibierge-Weissenbach syndrome has come to mean anything from progressive systemic sclerosis with calcinosis (Durham, 1928) to a much more benign syndrome in which sclerodactyly, calcinosis, and Raynaud's phenomenon are associated with telangiectasia (Prosser Thomas, 1942). In the 10 years preceding 1964 only 18 cases with this clearly defined syndrome had been reported, and to these Winterbauer (1964) added another seven. The present report describes three further cases and reviews the prognosis in this syndrome.

Case 1

A 66-year-old woman gave a history of Raynaud's phenomenon in the hands since the age of 20, which had been more of an inconvenience than a disability. The most recent admission was caused by an exacerbation of dyspnoea, which had been present for

two to three years. There was no family history of telangiectasia or of recurrent haemorrhagic episodes to suggest this.

Some rheumatoid deformity was present in the hands, there was also sclerodactyly and a thickened subcutaneous plaque in the left forearm. Telangiectatic spots were present on the lips, the buccal mucosa, and the hands. Other abnormal findings were a raised jugular venous pressure and a cardiac apex in the sixth space outside the midclavicular line, the impulse being left ventricular in type. A mitral grade III regurgitant systolic murmur was audible at the apex with a third heart sound. Marked dorsal kyphosis was present, and the liver was enlarged one fingerbreadth and was soft.

The abnormal findings on investigation were that the chest x-ray film showed left ventricular enlargement with pulmonary congestion. Radiographs of the hands showed contractures of the thumbs and fifth fingers of both hands with soft-tissue calcification in the fingers (see Fig.). Respiratory function tests demonstrated impaired vital capacity (1,350 ml.; predicted 1,900 ml.) with increased residual volume (2,460 ml.; predicted 1,800 ml.). There was evidence of obstructive airway disease, the ratio F.E.V.₁/F.V.C. being 56%. O₂ saturation was 86%; Pco₂ 38 mm. Hg; pH 7.40. The findings were thought to be compatible with the presence of pulmonary congestion and kyphoscoliosis.

* Department of Therapeutics, the Royal Infirmary, Edinburgh 3.
 † Department of Cardiology, the Royal Infirmary, Edinburgh 3.

Case 2

A 51-year-old woman gave a 30-year history of Raynaud's phenomenon. At times she had developed white lumps in the fingers, which were incised and took months to heal. In 1942 she had a right-sided cervical sympathectomy and 20 years later a right-sided lumbar sympathectomy for ischaemic symptoms in the feet. In addition, she had had the right index and middle fingers amputated, and in 1959 a local excision of a palatal angiomatous lesion because of recurrent bleeding. The most recent admission was caused by an exacerbation of ischaemic symptoms in the hands. There was no history of telangiectasia or of recurrent epistaxes, haemoptyses, or haematemesis in the family.

She was a thin woman, and had sclerodactyly with marked soft-tissue calcification. Telangiectatic spots were noted on the lips and the buccal mucosa. The blood pressure was 180/100 mm. Hg.



Radiograph of hands in Case 1.

The abnormal findings on investigation were that x-ray films of the hands showed marked calcification of the soft tissues. X-ray film of the chest showed slight cardiomegaly and the changes of chronic bronchitis and emphysema, while barium swallow showed slight oesophageal atony and dilatation.

Two of the patient's siblings examined by us were normal.

Case 3

A 35-year-old woman gave a 15-year history of Raynaud's phenomenon in both hands. In the previous three months this had become worse, and she had developed ulcers on the third digits of both hands. She had had varicose veins since the birth of the first of her three children nine years previously, and the immediate cause for admission was the development of a superficial thrombosis of the long saphenous vein in the left leg. There was no previous history of jaundice and no history to suggest telangiectasia in the family, which included four brothers and one sister.

Sclerodactyly was present with ulceration of the skin of both third digits. Telangiectatic spots were present on the lips and the surrounding skin, on the buccal mucosa, and on the hands.

The abnormal results of investigation were as follows: Serum alkaline phosphatase 76 and 63 K.A. units; S.G.P.T. 44 S.F. units; S.G.O.T. 54 S.F. units; 5-nucleotidase 181 and 141 i.u./l. The total serum proteins were 6.4 g./100 ml. (albumin 3.7 g.), and the electrophoretic pattern: α_1 -globulin 0.2 g./100 ml.; α_2 -globulin 0.9 g./100 ml.; β -globulin 0.9 g./100 ml.; and γ -globulin 0.7 g./100 ml. X-ray films of the hands showed decalcification and erosion of the heads of the middle phalanges on both sides and of the proximal phalanx of each middle finger. Calcification was present in the soft tissues of the middle fingers and the right index finger, mainly related to the interphalangeal joints.

None of the siblings lived in the area, and were therefore not examined. The patient's three children, aged 6 to 9 years, were examined and no telangiectatic lesions were noted.

Discussion

There is nothing to distinguish the telangiectasia in this condition, either in appearance or distribution, from the lesions in patients with hereditary telangiectasia. It has been suggested, however, that the lesions appear later than in the hereditary condition, where they usually occur in the second to the fourth decade—though they may be present in childhood (de Gruchy, 1964). It is also said that there is less tendency to haemorrhagic episodes, and that the telangiectatic lesions are not hereditary in this syndrome, where there is also a predominance of affected females (Winterbauer, 1964). None of our three patients gave any family history suggesting telangiectasia. Only Cases 1 and 3 could recall roughly when their lesions appeared, the former when well into her fifties and the latter just after the age of 20. Only Case 2 had been troubled by bleeding, which originated from a palatal lesion.

The occurrence of signs of systemic scleroderma in the syndrome of sclerodactyly, calcinosis, Raynaud's phenomenon, and telangiectasia is well recorded. Case 2 had oesophageal involvement, while Case 3 had abnormal liver-function tests. Though the latter was initially treated with phenindione, the abnormal findings persisted a year after stopping this drug. Sclerodermatous hepatic involvement is said to be extremely rare (Tuffanelli and Winkelmann, 1961). Calvert *et al.* (1958) described two cases of severe portal hypertension associated with hepatic fibrosis in two patients with systemic fibrosis, and Batsakis and Johnson (1960) reported systemic scleroderma in a patient with a pulmonary adenocarcinoma who had hepatic fibrosis. We feel that the abnormalities in our patient are most likely to be due to sclerodermatous involvement of the liver. Because of the possibility of visceral telangiectasia hepatic biopsy was not attempted.

It has been emphasized that the progress of the disease in patients with this syndrome is slow even in the presence of systemic involvement (Winterbauer, 1964). Though rare, the syndrome appears to come under the general heading of "acrosclerosis" (Sellei, 1934). In contrast, diffuse scleroderma (progressive systemic sclerosis) is a rare condition (Tuffanelli and Winkelmann, 1961) with a poor prognosis, the five-year survival being of the order of 50% (Farmer *et al.*, 1960).

Summary

Three cases of sclerodactyly, Raynaud's phenomenon, calcinosis, and telangiectasia are described. The syndrome appears to be a rare variant of the most common form of presentation of scleroderma "acrosclerosis." The occurrence of systemic manifestations is noted, but the fact that this type of scleroderma tends to run a relatively benign course is emphasized.

We would like to express our thanks to Dr. C. Burt, Mr. R. J. M. McCormack, and Professor R. H. Girdwood for permission to describe these cases.

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Medical Memoranda

Incest, Inbreeding, and Mental Abilities

Brit. med. J., 1967, 4, 336-337

Two recent communications have intimated the extent of the disadvantages from which children of incestuous unions may suffer. Adams and Neel (1967) reported that of 18 offspring from unions between first-degree relatives only seven were normal, one died at 6 hours and one at 15 hours, one died at 2 months from glycogen storage disease, one had a bilateral cleft lip, and two were severely mentally retarded with seizure disorder and spastic cerebral palsy, and five mildly so (I.Q.s 50 to 70 on repeated testing); thus seven were of subnormal mental standard. Carter (1967) reported the conditions seen in 13 children of similar unions; only five were normal, three failed to reach the age of 9 years (dying at 13 months from cystic fibrosis, at 21 months from progressive cerebral degeneration with blindness, and at 8 years from a congenital heart defect respectively), and one is severely mentally retarded and four mildly so (I.Q.s 50 to 76); thus five are of subnormal mental standard, making a total in the two series of 12 out of 31.

Since incest as defined in Western society is merely the extreme and socially designated form of consanguineous union, mating between related individuals, evidence of association between less close degrees of parental consanguinity and mental abilities of offspring is of relevance to the interpretation of these findings. The results of a preliminary analysis of consanguinity and mental ability in a small closed population are presented here.

CONSANGUINITY

The most extreme form of consanguineous union that can occur in man, and which gives rise to the most highly inbred offspring, is mating between two first-degree relatives (father/daughter, brother/sister, son/mother). A child is said to be inbred if he is born of a mating between two individuals who can both trace descent from a common ancestor, so that both the genes that the child possesses at a given locus may be replicates of a single gene that was present in the common ancestor and so may be identical.

The probability that both the genes an individual possesses at a given autosomal locus are identical is measured in terms of Wright's inbreeding coefficient (F), which therefore also indicates the proportion of autosomal loci at which the individual is expected to be an identical homozygote. By this measure inbreeding can be quantified. Offspring of incestuous unions between brother and sister or between father and daughter have an inbreeding coefficient of 0.25; offspring of a marriage between two first cousins have an inbreeding coefficient of 0.0625; both of these figures will be increased if any common ancestor was himself inbred. Mating of two completely unrelated individuals produces offspring with an inbreeding coefficient of zero. It is this likelihood of increased homozygosity in inbred individuals that is responsible for the increased frequency of manifestation expected in them of simple recessive characters, and for the increased frequency of those extreme conditions which represent the tails of the distribution curves of continuously varying quantitative attributes brought about by polygenic action.

ANALYSIS OF RECORDS FROM TRISTAN DA CUNHA

From the extensive records that are available for the population of Tristan da Cunha, based largely on those collected by

Dr. L. Woolley when resident on the island in 1942, supplemented by those obtained by Dr. P. Munch during an expedition to the island in 1938 and more recently by Dr. J. Loudon, it is possible to trace the descent of every individual from the founders of the population, and so calculate his inbreeding coefficient. This has been done for every present and past member of the Tristan population (Roberts, 1967). Dr. Woolley at the same period also recorded conditions of clinical interest, among which was his assessment of the mental capabilities of each member of the then population. These he classified, by clinical appraisal over long periods, into six broad categories from normal to low-grade mental defective. The association of these assessments with the inbreeding coefficients has been examined.

Table I sets out the mean inbreeding coefficient found in each intelligence category. There seems to be a tendency for the mean inbreeding coefficient to be higher in the lower intelligence categories (column 2). That this is almost but not entirely due to there being a greater proportion of non-inbred individuals in the higher categories (column 5) is shown by comparison with the mean inbreeding coefficient calculated for the inbred alone in each category (column 6). From Table II, setting out

TABLE I.—Inbreeding and Intelligence

Intelligence Category	Mean F	Total No. of Individuals	Individuals Not Inbred		Mean F in those Inbred
			No.	%	
1. Normal ..	0.0188	35	17	48.6	0.0366
2. Slow cerebration ..	0.0391	53	11	20.8	0.0505
3. Very slow cerebration ..	0.0379	60	16	26.7	0.0517
4. Definitely inferior mental capacity ..	0.0480	45	6	13.3	0.0554
5. High-grade mental defective ..	0.0457	8	1	12.5	0.0522
6. Low-grade mental defective ..	(0.0313)	1	0	0	(0.0313)

TABLE II.—Number of Individuals by Mental Category and Inbreeding Coefficient

F	Intelligence Category						Total No. of Individuals
	1	2	3	4	5	6	
0	17	11	16	6	1	—	51
<0.03	9	18	13	12	2	—	54
<0.06	5	10	12	5	2	1	35
<0.10	3	11	16	19	2	—	51
>0.10	1	3	3	3	1	—	11

the number of individuals by intelligence category and inbreeding coefficient, the association can be seen to be highly significant at the 1% level ($\chi^2=22.85$, 9 degrees of freedom).

COMMENT

Full allowance has to be made for the subjective nature of the classification of mental ability in interpreting these preliminary findings, which are being followed up by Dr. Keir, using the results of objective tests of intelligence. This association could mean that some of the worse mental conditions in this population are due to inbreeding so far; but the alternative explanation is also reasonable—that those of poor mental capacity tend to breed more closely if opportunity offers. Of these two explanations the second is supported in Adams and Neel's (1967) series by some of their father/daughter, but not by their 12 brother/sister, incestuous unions. In all except one of the latter the matings were between sibs of normal intelligence (I.Q.s 90 to 120, with mean values 110 in males and 103 in females), and the occurrence of mental retardation in four of

their offspring suggests an inbreeding effect. There is further supporting evidence from Japan, where Schull and Neel (1965) examined seven various indicators of school attainment—for example, performance in language or science—in relation to inbreeding, taking into account age, school grade, and socio-economic status. They observed a consistent and significant depression in performance in all seven indicators with inbreeding; by comparison with the outbred mean there was a reduction of 1% in performance per increase of 1% in F. It seems that, like physical dimensions, performance in neuromuscular tests, and other quantitative characters, mental capabilities may well be particularly susceptible to the effects of inbreeding.

The view was long since expressed that intelligence is under polygenic control, and there is much evidence to support it. On the other hand, Morton's (1960) analysis of Penrose's data suggested to him the influence of major autosomal recessive genes in an appreciable proportion of cases of severe mental defect. The present findings, which relate to less severe conditions, also suggest that some of the genes tending to lower

mental capabilities are recessive. It seems more reasonable, however, to interpret the results as indicating not control by major recessive genes but polygenic control with directional dominance, a suggestion which carries wide implications. But since the highest category here employed was "normal" and exceptionally able individuals were not distinguished, the data do not establish it. For this purpose information on the relative numbers of offspring of consanguineous unions who are above as well as below average in ability is required.

D. F. ROBERTS, M.A., D.PHIL.,

Laboratory of Human Genetics, University of Newcastle upon Tyne.

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Tongue Pain with Giant Cell Arteritis

Brit. med. J., 1967, 4, 337

Local effort pain of the tongue is described as a feature of giant cell arteritis in this case report.

CASE REPORT

A previously fit 78-year-old man woke with severe neck pain which radiated over his head and was attributed to cervical spondylosis. Two weeks later he began to experience increasing malaise and pain in the tongue. This was felt diffusely at the back of his tongue and was described as a tired ache; on one occasion it followed a prolonged period of talking, but otherwise occurred only on eating, and had prevented him from taking solid food for four weeks when he was referred to hospital on 8 March 1967. It was found that eating solid food was limited after two minutes by onset of the pain, which then after a further half-minute gradually faded over the next five minutes. The pain could also be reproduced by rapid repeated protrusion of the tongue, but not by drinking or by repeated jaw movements alone.

The tongue and the temporal and occipital arteries appeared clinically normal and there were no bruits over the carotid arteries. Neck movements were limited by cervical spondylosis. There were no other abnormal findings on physical examination.

Biopsy of the right temporal artery was performed. The histological features were those of giant cell arteritis, with thrombosis, and recanalization of the lumen. Haemoglobin was 14.8 g./100 ml., white blood cell count 13,000/cu. mm. with a normal differential count, and erythrocyte sedimentation rate 34 mm. in one hour (Wintrobe).

Corticosteroid therapy was started. One week later the malaise and tongue pain had resolved.

COMMENT

Giant cell arteritis is a widespread vascular disorder (Meadows, 1966). Pain in the jaw muscles on chewing has been regarded as a typical feature of the disease (Robertson, 1952; Meadows, 1954; Ross Russell, 1959), and Meadows (1966) has noted that pain may radiate to the tongue.

Missen (1961) found histological evidence of lingual arteritis in all of five patients whose tongues had appeared normal. However,

clinical evidence of tongue ischaemia is uncommon. Gangrene of the anterior part of the tongue has been reported in five cases (Howard and Cremin, 1959; Wise, 1959; Brearley and Macdonald, 1961; Pitt *et al.*, 1961; McGill, 1961; Davis and Davis, 1966). Swelling of the tongue (Wolinetz *et al.*, 1948; Cornil *et al.*, 1949), a sensation that the tongue was too big (Meadows, 1954), and constant pain or burning of the tongue (Bowers, 1940; Post, 1949; Olivo and Spizzo, 1951) have also been noted, but local effort pain of the tongue does not appear to have been previously described.

Early recognition and treatment of giant cell arteritis is a matter of urgency. The present case has therefore been reported to show that angina of the tongue may be a presenting symptom of the disease, histological confirmation of which can be obtained from biopsy of a clinically normal temporal artery (Alestig and Barr, 1963).

My thanks are due to Dr. K. D. Lawrey for referring this patient and to Dr. G. Stewart Smith for the histological report.

A. H. HENDERSON, M.B., M.R.C.P.

Royal Devon and Exeter Hospital,
Exeter.

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Bacterial Endocarditis Presenting as Pseudobulbar Palsy

Brit. med. J., 1967, 4, 338

The changing pattern of bacterial endocarditis has been attributed to the declining incidence and severity of rheumatic fever; the increasing involvement of elderly individuals, often without cardiac murmurs; the increase of opportunistic infection; and infection with organisms formerly rarely associated (Uwaydah and Weinberg, 1965). Diagnostic delays have been prominent in the failure to reduce the mortality rate in recent years. Petechiae offer a valuable clue, being present in about half the cases, but can be readily overlooked, since few may be visible at a time. The diagnostic complexities are illustrated by the present case.

CASE REPORT

The patient, a man aged 61, had developed weakness, breathlessness, anorexia, and loss of weight in the past few months. His gait was affected and he was able to walk only progressively shorter distances, until finally he was virtually bed-ridden; simultaneously his speech became indistinct and his swallowing ability so impaired that he had attacks of choking during meals. Incontinence of urine had existed for several weeks. He had become dull and apathetic. His wife had died six months previously. Since then he had been depressed, his condition being attributed to an emotional reaction.

On examination he was extremely ill, wasted, and dehydrated, and responded very little or not at all to repeated questioning. Dysarthria was obvious when he did speak, as was dysphagia when tested with the drinking of water. A petechial haemorrhage was observed on eversion of the left lower lid but not in the optic fundi. The heart was not enlarged; an apical mid-systolic murmur was audible. The pulse was regular and rapid and the temperature was 99.2° F. (37.3° C.). No finger-clubbing, splinter haemorrhages, sternal tenderness, or splenomegaly were observed. The other abnormal physical findings were confined to the C.N.S.—exaggeration of all the deep reflexes and bilateral plantar extensor responses.

The significant results of the special investigations were: chest and skull x-ray films: no abnormalities; Hb 9.6 g./100 ml.; M.C.H.C. 28.5%; W.B.C. 12,000/cu. mm. (92% polymorphs); blood urea 38 mg./100 ml.; urine microscopy: only an occasional leucocyte; faecal occult blood examination (3) negative; total serum protein 5.5 g./100 ml. (albumin 2.8 g., globulin 2.7 g.), electrophoresis showed only moderate increase of gammaglobulin; C.S.F. examination—20 cells/cu. mm. (60% lymphocytes, 40% polymorphs), protein 70 mg./100 ml., an increase of globulin, sugar 60 mg./100 ml., and no growth on culture. Wassermann reaction of blood and of C.S.F. was negative.

A blood culture yielded a growth of *Streptococcus viridans* sensitive to penicillin and streptomycin. Treatment with both was instituted and the clinical response was soon apparent. With the improvement of his general condition a progressive reduction occurred in the neurological abnormalities, so that his gait, speech, and swallowing returned to normal and the objective neurological features and his mental apathy disappeared. A progressive rise in his haemoglobin and fall in the W.B.C. followed. The C.S.F. examined a month after the original lumbar puncture showed 5 cells/cu. mm., protein 55 mg./100 ml., and only slight increase of globulin.

DISCUSSION

Cerebral disturbances are prominent in many patients with bacterial endocarditis. Among the presentations are meningitis (sterile or purulent, especially with pneumococcal and staphylococcal infections), convulsions, subarachnoid haemorrhage, cerebral abscess, hemiplegia and other forms of paralysis of an upper motor neurone type, and rarely a flaccid palsy. Embolization, late in the course of bacterial endocarditis is not rare, even up to two years after bacteriological and clinical cure. It is now also appreciated that in the course of the infection

local inflammatory changes arise in the wall of the capillaries and arterioles, possibly as an immunological response to the infection (Friedberg, 1966). Dominating the picture may be the features of a toxic organic psychosis (Antel, Rome, Geraci, and Sayre, 1955). An analysis of 116 cases of bacterial endocarditis revealed that neurological manifestations were present in 37, and 33 of these offered an immediate diagnostic problem—15 with strokes and seven with meningitis or meningo-encephalitis (Harrison and Hampton, 1967). Thompson (1964) stressed that bacterial endocarditis may masquerade as a simple cerebrovascular lesion, particularly if no symptoms antedate the sudden onset of, for example, a hemiplegia.

Difficulties may also exist in differentiation from the cerebral effects of rheumatic heart disease complicated by embolism, and the rheumatic fever process itself can induce abnormalities of the cerebral vasculature. Both embolization and markedly diminished blood flow can lead to neurological disorders in established valvular disease (Daley, Mattingly, Holt, Bland, and White, 1951). Hutchinson and Stock (1963) observed an incidence of clear-cut recurrent neurological symptoms of short duration equal to that of cerebral embolization in patients with rheumatic heart disease, their frequency correlating with the severity of the cardiac lesion and often being precipitated by exertion. The neurological symptoms included visual features (the most frequent), vertigo, motor and sensory symptoms, and drop seizures. Cerebral emboli in patients with mitral stenosis may cause epileptic seizures; in 20 out of 22 such cases the convulsive attacks were ascribed to previous cerebral emboli (Baker and Finnegan, 1957). A useful guide is offered by Friedberg (1966): while systemic arterial embolization in mitral valve disease may occur occasionally in sinus rhythm, bacterial endocarditis should be investigated as a more probable cause.

Recognition that non-bacterial thrombotic endocarditis has clinical as well as pathological significance is relatively recent. It may simulate a bacterial infection; embolization may provide the predominant clinical manifestations, and in such circumstances, especially in a patient with cardiac decompensation, bacterial endocarditis and mural thrombi of the cardiac chambers have to be differentiated. In the third group no embolization has taken place and the valvular lesions constituted an incidental finding at necropsy. The most commonly associated diseases in the series of MacDonald and Robbins (1957) were carcinoma (36%), heart failure (30%), and vascular thrombosis (27%). Healed bacterial and healed rheumatic endocarditis require differentiation from non-bacterial thrombotic endocarditis, as does the atypical verrucous endocarditis of Libman-Sacks in patients with disseminated lupus erythematosus.

Though much less common today, a syphilitic infection must always be excluded when neurological and cardiological features coexist. Finally, the murmurs, fever, anaemia, abnormality of serum proteins, and raised blood sedimentation rate of myxoma of the auricle simulate bacterial endocarditis; petechiae and embolic phenomena add further to the possibilities of confusion (Goodwin *et al.*, 1962).

J. SHAFAR, M.D., F.R.C.P., D.P.H.,
Consultant Physician, Burnley Group of Hospitals.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Duodenal Ulcer—II

IAIN E. GILLESPIE,* M.D., F.R.C.S.

(Last week Mr. Gillespie considered the diagnosis and medical management of duodenal ulcer. This week's article deals with the indications for operation and the type of operation that can be done. It ends with a list of references to both articles.)

Indications for Elective Operation

The commonest reason for advising operation in a patient with duodenal ulcer is the failure of simple conservative medical measures to control the symptoms adequately. Few patients are considered for surgical treatment before the clinician is satisfied that the measures outlined above have been conscientiously applied, and that in spite of these measures relapses of typical ulcer dyspepsia have become more frequent, more severe, and more prolonged. It is difficult to lay down hard and fast rules such as a definite length of history beyond which operation should be advised automatically. Patients vary considerably in the periodicity of their ulcer dyspepsia, and any individual patient may himself vary in the frequency and severity of relapses from year to year. The majority of duodenal ulcer patients coming to operation have had symptoms for between 5 and 10 years,^{12 13} and an appreciable proportion have a history going back more than 20 years. Factors other than simply the length of time over which symptoms have persisted are generally taken into consideration in reaching a decision for operation in a particular patient.

When a patient complains that antacids, which formerly gave satisfactory relief, are no longer effective it seems reasonable to consider operative treatment without undue delay even if the history is relatively short. It is unreasonable to insist on waiting a fixed period of time if the patient has tried a large variety of antacid medications in adequate dosage without obtaining pain relief. On the other hand, the patient who enjoys long remissions of up to a year at a time and can fairly readily control his relapses when they occur by a simple antacid preparation may well not be advised to have surgical treatment unless some complication develops.

Loss of time from work through ulcer symptoms is another major factor, and this applies mainly to young and middle-aged men with families dependent on their continuing in regular employment. In the case of housewives symptoms interfering with their ability to perform their full household duties will also usually influence the decision towards operation. Repeated interruption of sleep by typical ulcer pain is yet another factor which might influence a decision towards surgery. When the pain begins to radiate through to the back this generally denotes a fairly severe ulcer with perhaps retroperitoneal penetration, and it is likely that surgical measures will eventually be required. Vomiting, particularly of a retention nature, suggests that pyloric stenosis is occurring, and again would usually be taken to favour operation. It is often remarkable, however, how a few days' rest in bed may allow the signs of "pyloric

stenosis" to subside, with cessation of vomiting, the disappearance of an obvious succussion splash, and shrinkage of the gastric outline on radiological examination.

Where there is a strong family history of peptic ulceration, particularly in the patient's immediate relatives, there is again a strong likelihood that operation will eventually be required, and a decision for surgical treatment may well be taken earlier than in those without such a strong family history.

It is difficult to assess the risks of complications such as perforation or haemorrhage in an individual case, but there is some evidence that patients with a previous history of haematemesis or melaena may be more prone to recurrence of this symptom. Between 30 and 50% of patients with a previous perforation of a duodenal ulcer treated by simple suture are likely to require later definitive surgery for the ulcer. There is therefore good reason to take the occurrence of either complication in the history of the patient with duodenal ulcer as being additional factors tending in favour of operation.

The question of malignant change only enters into consideration in the case of gastric ulcer, for it is virtually unknown for a chronic duodenal ulcer to become malignant.

Finally, with regard to blood groups it has been indicated that patients of blood group O, particularly those who are unable to secrete the blood group secretor substances in the gastric mucus, are slightly more likely to require surgical treatment than those belonging to other groups. However, there is recent evidence¹⁴ that group O non-secretor subjects are also more prone to develop stomal ulceration; so that if such patients are operated on they also have a slightly increased risk of further peptic ulcer trouble. In view of this confusing picture the blood group status should not influence the decision.

Risks of Operation

Every operation (like every form of effective medical therapy) is attended by some measure of risk of complication, and when advising a patient to undergo operation it is well to assess whether the severity of the disability caused by the ulcer is sufficient to justify the small but distinct risks. The mortality of an elective procedure for an essentially benign condition should nowadays generally be small, preferably less than 1%, though it is difficult to emulate the complete lack of operative deaths recorded from the admirable series of Goligher *et al.*¹⁵ In addition, a minority of patients may develop one of the variety of postoperative symptoms or symptom-complexes known to occur after all types of gastric operation. Fortunately the incidence of postoperative sequelae is quite small. Many subside with the passage of time or are controlled by simple measures, but a hard core may require repeated and complex therapeutic measures. Although some of the postoperative sequelae have a readily explained organic physiological basis, there is a distinct impression that patients with minimal history of symptoms, and those with signs of emotional instability pre-

* Senior Lecturer in Surgery, University of Glasgow.

operatively may be particularly prone to these postsurgical symptoms. For this reason surgeons generally are more confident about a trouble-free convalescence in ulcer patients having elective operation with a long severe history of dyspepsia behind them, and are perhaps a little more reluctant to accept for surgery patients showing signs of psychological abnormality. There is currently much interest in trying to assess personality and other psychometric measurements in duodenal ulcer patients in the hope that some more objective guide may be available to aid in this aspect of preoperative selection.

Type of Operation

The common aim of most elective operations for duodenal ulcer is permanently to reduce the capacity of the stomach to secrete acid and pepsin, in the belief that the hypersecretion of these substances is causally related to the ulcer. In spite of much indirect evidence this assumption remains unproved, and it may well be that the hypersecretion is simply a reflection of the underlying pathological mechanism which has caused the ulcer rather than that acid-activated pepsin has actually initiated the ulcerative process. There is no doubt, however, that in the vast majority of instances the measures taken to reduce the acid and pepsin secretion do result in healing of the ulcer and protection against further ulceration. Extending the argument that hypersecretion is an aetiological factor, there is considerable evidence that the excess secretion is vagally mediated, and for this reason vagotomy with a simple drainage procedure is currently in vogue as the elective operation of choice of many surgeons. The operative mortality seems to be acceptably low, but the incidence of recurrent ulcer is certainly higher than following gastric resection. The majority of these recurrences—if not all of them—are due to the vagotomy being incomplete, and this is perhaps the most important obstacle to the uniform acceptance of vagotomy. A drainage procedure is required to accompany vagotomy since vagal denervation alone has been found to lead to undue gastric stasis and vomiting. The two procedures most widely employed are gastrojejunostomy and pyloroplasty. Although theoretically the latter might seem a more sound physiological procedure, it is not as yet apparent whether one holds distinct advantages over the other. Perhaps the most widely discussed complication to follow vagotomy is diarrhoea. There is great variation in the reported occurrence of this symptom and its severity in different series. Most surgeons find that although there is a general tendency towards increasingly frequent bowel motions following vagotomy with drainage this amounts to disability only in a very small proportion of patients.

In an attempt to avoid vagal denervation of abdominal organs other than the stomach, various forms of "selective" vagotomy have been introduced in recent years. Claims that these procedures give adequate protection against recurrent ulceration, and diminish the incidence of other sequelae, require confirmation from further careful studies.

Adequate reduction of gastric acid and pepsin secretion can also be achieved by partial gastrectomy, and though published reports show a higher mortality rate than that of vagotomy with drainage this form of operation is less likely to be followed by a recurrent ulcer. The principal complications which may follow gastrectomy include nutritional disorders such as weight loss, steatorrhoea, protein and vitamin malabsorption, haematological defects such as iron deficiency and megaloblastic anaemia, "dumping symptoms," such as postprandial epigastric fullness, fainting, sweating, dizziness, and the desire to lie down, and bilious vomiting. The more incapacitating symptoms of the dumping syndrome and bilious vomiting fortunately occur in only a small proportion of gastrectomized patients, but the management problems they present are often extremely difficult ones. Long-term follow-ups of substantial numbers of

post-gastrectomy patients reveal a fairly high incidence of iron-deficiency anaemia and bone disorders, the signs of which often develop clinically many years after the operation.

It is still a little early to be certain about the incidence of these latter abnormalities following the simpler procedure of vagotomy with drainage, but the few preliminary reports which are available suggest that this operation may not be entirely free of such late sequelae.

The combination of vagotomy with a limited partial gastrectomy has been used in several surgical centres in the hope that removal of both the vagal and gastrin influences on gastric secretion might give greater protection against recurrent ulceration than either procedure alone. It was also hoped that with the relatively small proportion of stomach removed there be reduced chance of the troublesome postoperative sequelae met with after a more radical gastrectomy. Certainly the reported recurrent ulcer rates following this combined operation are encouragingly small. However, the mortality rate as might be expected lies intermediate between that of vagotomy with the simple drainage procedure and partial gastrectomy, and it remains to be seen whether the occurrence of postoperative sequelae will be substantially less than from either of the other two more commonly employed procedures.

One final word should be said about the management of patients once the elective operation has been performed. In spite of the rather long list of complications which may follow the various operative procedures it should be emphasized that they occur in but a small minority, and the majority of patients are able to eat normally for the remainder of their lives without fear of return of ulcer or other symptoms. They should be advised after operation that further dietary restrictions are unnecessary and that they should plan to return to a normal daily routine.

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MEDICINE TODAY

Low Back Pain

"Medicine Today" is the television series for doctors produced by the B.B.C. Advice on the preparation of the programme is given by the Association for the Study of Medical Education.

The programme on B.B.C.2 on 7 November was on the subject of low back pain. Printed below is an article prepared with the help of expert contributors to complement the television programme, which will be repeated on B.B.C.1 on 15 November at about 11 p.m.

In "Medicine Today" much of the programme was devoted to the diagnosis and management of the acute lumbar disc lesion causing pressure on the sciatic roots. Though these cases form only a small proportion of patients presenting in general practice with low back pain, the signs and symptoms of the acute disc protrusion are so clear cut that the diagnosis is rarely if ever in doubt.

The patient is usually a young or middle-aged adult male who gives a clear history of acute disabling pain following an episode of bending or lifting, usually in an "awkward" position. The pain is confined to the lumbar region initially, but within 24 to 48 hours it spreads to one or other buttock and then down the back of the thigh to the outside of the leg and as far as the outer border of the foot. There may be associated numbness or paraesthesiae and the patient often has difficulty in walking even a few steps. The pain is usually relieved by lying down flat but made worse by sitting down. Coughing and sneezing make the pain worse and it is often impossible for the patient to bend his back.

On examination the patient is found to have a flat lumbar spine with obliteration of the normal lordosis, and he usually has a so-called "sciatic scoliosis" or a list to the side opposite to the sciatica. Spinal movements other than forward flexion are often surprisingly well preserved. The hip movements are full, but when the leg is raised with the knee extended pain is produced in the back of the thigh and the leg after about 15–30° of hip flexion. If the hip is bent forward or the knee is forced into dorsiflexion an increase in pain occurs (Lasègue's sign). There is often numbness to light touch and pinprick in the L5 or S1 dermatome. The extensor hallucis longus, the tibialis anterior, or the peronei are often weak and may be wasted, and the ankle jerk is usually depressed. In addition there may be gluteal flattening on the affected side.

Treatment of the Acute Disc Lesion

The essential feature of treatment is rest in a non-weight-bearing position—in bed on a firm mattress. Some 90–95% of patients with acute disc lesions will get better on this regimen, which should be succeeded by a period of partial immobilization in a plaster jacket or a well-fitting lumbar support. Instruction should be given in spinal and abdominal exercises. It is important at this stage that the exercises should be designed and graded so as to reproduce the degree of activity to which the patient will be exposed at work or home.

Patients who do not respond to this treatment may well benefit from alternative but infrequently used conservative measures such as rest in bed on continuous pelvic or skin traction. Others may respond to extradural injections of a local anaesthetic with or without a local corticosteroid. For the remaining few laminectomy may be the treatment of choice, but discussion of the criteria on which this decision depends is outside the scope of this article.

Pain not Associated with Signs of Nerve Root Pressure

The nature of the pathological processes responsible for pain in the back not due to disc lesions is the subject of considerable debate and contention. Advice on management of patients can be based on their classification into groups with common symptomatology. The treatment that is given for these conditions is essentially empirical.

"Acute Lumbago Syndrome"

Acute lumbago is characterized by a sudden onset of severe pain in the back precipitated by minor trauma or unaccustomed exercise. There is often radiation of the pain into both legs as far as the mid-thigh. A striking feature is that with the best will in the world the patient cannot get out of bed and indeed can hardly move at all. Though spinal movements are grossly reduced there are no abnormal neurological signs. The pain is relieved if the patient lies on a hard flat surface, and analgesics such as salicylates are very effective. No treatment other than rest and analgesics is needed. It is important that the patient rests completely for ten days and then mobilizes himself for another four to seven days. Simple back exercises at home and correct instruction in lifting technique are once again important during the "healing stage," which is generally complete within a few weeks from the onset. Further attacks are not uncommon but they are usually infrequent—one or two attacks every year or so.

The aetiology of "acute lumbago" is arguable, but if the initial attack is treated inadequately, by allowing the patient up too soon, then signs of root pressure may develop. This suggests that possibly the syndrome is an acute disc lesion of some type.

Pseudo-sciatica

This term is used to describe those patients who experience a sudden attack of pain—once again after minor trauma—but in whom the pain originates in the region of one or other sacral triangle and radiates down the back of the corresponding thigh, often as far as the back of the knee. There is no limitation of movement of the lumbar spine and straight leg raising is not limited to more than 45–60°.

These patients respond very satisfactorily to a variety of treatments, including manipulation; a gentle forced rotation of the pelvis with the unaffected lower limb flexed and rotated internally often produces dramatic relief. Relief may also be given by an injection of a local corticosteroid into the tender area that can almost always be found just medial to the sacroiliac joint. This syndrome seems to have a great deal in common with the musculotendinous disorders, of which tennis elbow is perhaps the best known.

Spondylolysis

Stress fracture of the pars interarticularis of one of the lumbar vertebrae is becoming increasingly recognized as a cause of pain in the back. It is a common finding in patients who present with a history of acute pain, not disabling, associated with a definite episode of feeling "something go" in the back. The signs on examination are pain at the extremes of flexion and extension and tenderness on deep palpation at the level of the lesion. Treatment of this condition is simple. Analgesics should be given as required and the patient should wear a simple

lumbar spine support for two or three months and then discard it. The fractures usually heal within two or three months, but though a few do not unite symptoms disappear after the initial period of pain.

Lumbar Spondylarthrosis

Degenerative changes in the spine are common findings in middle-aged and elderly patients with acute or chronic pain in the back. Spondylarthrosis is essentially an "x-ray diagnosis," but the radiological changes often bear little relationship to the degree of discomfort. In general, the grosser the changes shown the less is the range of spinal movement found on examination. Treatment of patients in this group depends not on the radiological findings but on the presenting signs and symptoms. Other relevant factors are the age, sex, and occupation of the patient, the length of the history, and such variables as the treatment that has been given in the past and its effect. The patient's personality, intelligence, and pain threshold are also important.

Acute episodes of pain are best managed at first by immobilization. After bed rest for a few days the patient should be encouraged to get up and about. A simple type of lumbar spine support, such as a canvas one, may be helpful at this time. Less severe pain is often best treated with immediate mobilization—exercises, physiotherapy, hydrotherapy, or even gentle spinal mobilization by manipulation without anaesthetic through the painfree range. Many patients with chronic pain in the back benefit from simple non-addictive analgesics, and these are best given in intermittent courses. The more powerful analgesics, such as phenylbutazone and indomethacin, can also be of great benefit at times, but they too should be given for short periods only.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Habituation to Methaqualone

Q.—What can be done to cure a patient of the habit of taking methaqualone tablets 150 mg. in quantities of up to 100 tablets a week? The drug was originally given for alcoholism.

A.—Methaqualone hydrochloride, or 3,4-dihydro-2-methyl-4-oxo-3-o-tolylquinazoline hydrochloride, is a sedative-hypnotic available in Britain as Melsedin (Boots) 150 mg., and Mandrax (Roussel) 250 mg. with 25 mg. of diphenhydramine. Addiction to this drug has been reported previously,^{1,2} and the withdrawal syndrome includes delirium tremens and abnormal states of muscular tone, though this is not inevitable.³

The patient referred to provides evidence of drug dependence of the methaqualone type, and, despite our lack of experience with it, it would be wise to view the condition with the same seriousness as one would a case of severe dependence on barbiturate, alcohol, or other sedative-hypnotic. The patient should be warned that this drug is equally likely to prove destructively addictive as more familiar hypnotics, and every effort be made to have him admitted as a voluntary patient to a psychiatric unit which specializes in drug dependence. Withdrawal can be undertaken

while a careful watch is kept for the first signs of convulsions, delirium, and appropriate drug therapy may be instituted at once in order to minimize harm. A prolonged period of physical and psychological support and rehabilitation may well be needed before the patient returns to normal living.

It is to be wondered whether the alleged value of methaqualone outweighs its addictive potential.

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Rendu-Osler-Weber Syndrome

Q.—Oestrogen treatment of haemorrhagic telangiectasia has been suggested for a young woman who gets two or three nose bleeds a day from this. However, she is taking an oral contraceptive and refuses to discontinue it. Is there any way round this problem?

A.—The use of oestrogens in Rendu-Osler-Weber syndrome, as advocated by

Supportive Treatment

Many patients with lumbar spondylarthrosis are overweight. It may be difficult for the doctor to persuade the patient to slim, but this is important. Poor posture is usually attributable to environmental factors such as unsuitable seating arrangements at work, at home, or in the motor car. Considerable relief of symptoms can result from changes in the patient's environment with co-operation from the employer when this is relevant.

Understandably, some patients with backache of organic cause develop a degree of reactive depression or anxiety. This may be helped by simple psychotherapeutic measures, or treatment with tranquillizers or antidepressives may be necessary.

Non-organic Low Back Pain

When all else has been excluded there remain the patients with backache for which the most extensive investigation reveals no organic cause. Many of these patients are suffering from a depressive illness with somatic conversion symptoms, for which other evidence may be sought. They respond totally and dramatically to a therapeutic trial of anti-depressive drugs, such as amitriptyline 50 mg. t.d.s. or imipramine 25–75 mg. t.d.s. These drugs produce their effect within two to four weeks, and the response in some patients with low back pain which may have persisted for years can be astonishing.

Finally, it must not be forgotten that a number of serious life-threatening conditions may present as acute back pain. These include spinal and extraspinal tumours either primary or secondary, tuberculosis, and other infections. Occasionally intra-abdominal conditions such as peptic ulceration or even acute pancreatitis may present as an "acute back." A careful history and a full clinical examination should never be omitted.

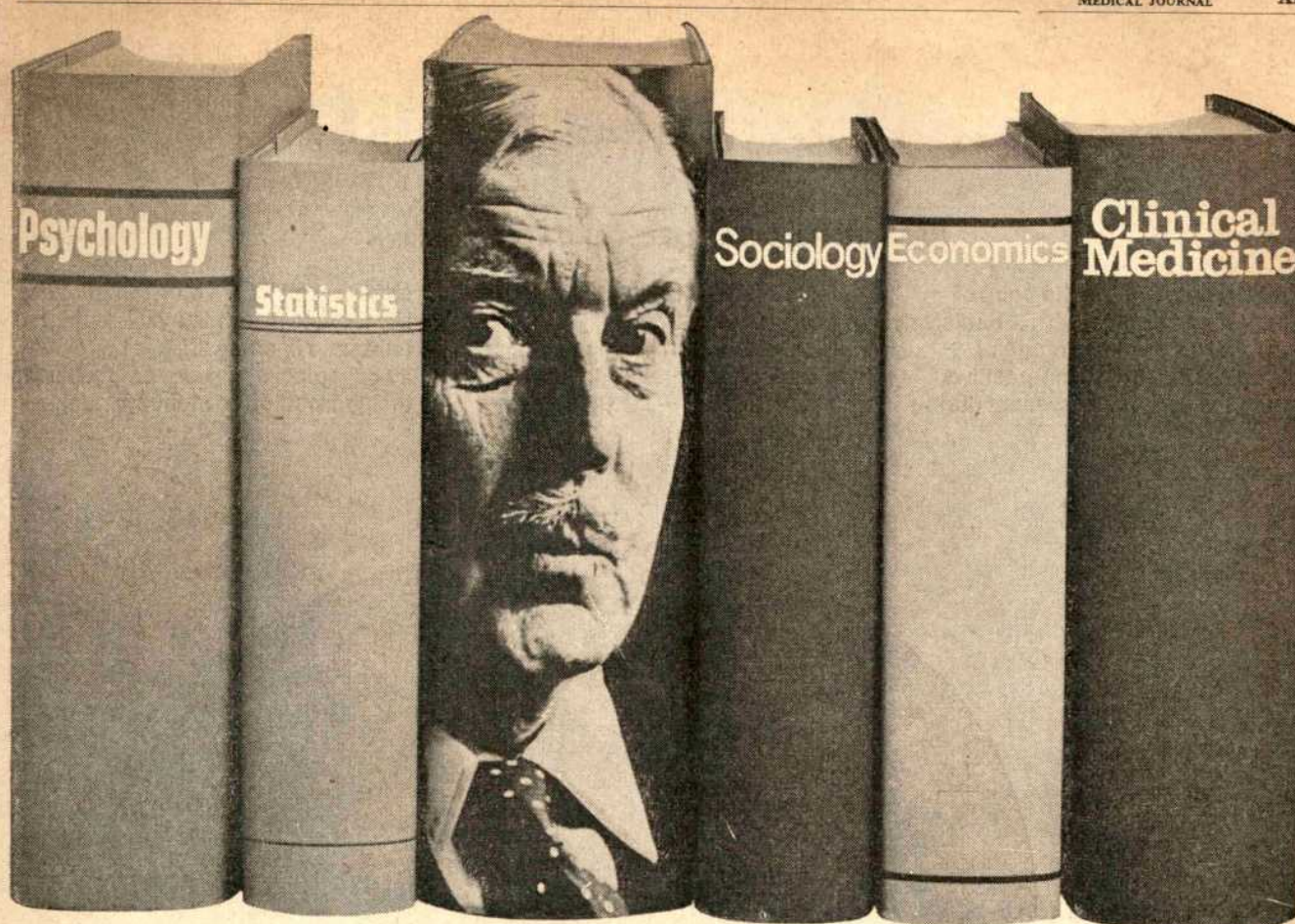
Harrison,¹ has enjoyed a modest success in this country. The elastic and muscular coats of the vascular sinuses are absent, and for that reason it is unlikely that the effect of the oestrogen is directly upon the blood vessel. Its haemostatic effect must therefore be due to the general thickening of the mucus membrane induced by the oestrogens.

All the oral contraceptives sold in this country contain either a potent oestrogen (mestranol) or else break down metabolically to yield oestrogens themselves. The dosage of oestrogen, generally about mestranol 0.1 mg. per day, is enough to exert a maximum oestrogen effect on the mucus membranes. It is unlikely, therefore, that any further benefit would be derived from additional or alternative oestrogens. The patient could perhaps be persuaded to switch to the sequential type of oral contraceptive, which would have the advantage of avoiding any progestational effect at least during the first fortnight of her cycle.

A number of alternatives to oestrogen therapy are available. Saunders² has described an ingenious form of septal dermoplasty. Stewart³ has advocated the use of deep x-ray radiation; while Golding-Wood⁴ found transantral internal maxillary ligation to be of benefit, particularly when combined with zinc ionization.

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MYCIVIN

Book Reviews

Man's Pollution of the Earth

Pesticides and Pollution. The New Naturalist Series. By Kenneth Mellanby. (Pp. 221; illustrated. 30s.) London: Collins. 1967.

Civilized man is the only unnatural animal. He manipulates his environment to reduce mortality in the youngest and to prolong life in the oldest, and even when he dies he does not surrender his carcass to the natural processes of putrefaction—it either goes up in smoke or deep down in the sterile clay. He cannot live without producing waste products from his body, but he goes to vast trouble to make sure that these are used, not to enrich the soil, but to foul the waters. He is not prepared to accept the climate as he finds it, but uses fire to adjust surrounding temperatures to his liking, and in the process forces enormous clouds of grit and gases into air that would otherwise be clean and pure. He scorns to move over the earth as fast as his own two legs will carry him, but races instead on wheeled contraptions which emit poisonous fumes as he rushes along. When he has time to stop, he is not content to eat the fruits of the natural earth, but rips and tears the land with steel, and allows only those plants to grow that measure up to his demands. And if any herb defies him, or any insect attempts to share the food in his artificial fields, he drenches them with poison. *Homo sapiens* is a highly civilized being.

Kenneth Mellanby has written a great book. It is calm, logical, and dispassionate, but deeply moving and disturbing. When facts can be given with precision, he states

them. If he can explain them, he does so; if he cannot, he says so. The book is full of facts and figures—the amount of grit deposited on one square mile, or even one square yard, per year, the amount of oxygen required to break down the daily output of faeces of one human being, the concentration of insecticide found in the fat of an Adélie penguin in the Antarctic or of a business man in America. Many of these figures are startling, but they are not given in order to startle, but because they are part of the picture. Some other parts of the picture are much more startling because they depict things that we accept almost as "natural." Draining a marsh, for example, can have a much more disastrous effect on wild life than the most poisonous chemical, and a day's ploughing of a mature pasture may exterminate a population of earthworms built up over 70 years. Traditional agriculture has, in fact, catastrophic effects on the ecology of the area in which it is practised.

Man must control his environment if he is to survive in it. Unfortunately he often cannot foresee the final result of a process which at first is obviously beneficial. Dieldrin used as a sheep dip freed the animals from the plague of fly strike; but eagles feeding on sheep carrion in the Western Highlands were poisoned, and the poison was found in their unhatched eggs. D.D.T.

(not D.D.T.) was used very successfully for midge control on Clear Lake in California; the poison was taken up and concentrated in the tissues of tiny fish, then in the tissues of larger fish that ate them, and finally, at the end of the food-chain, it killed the water birds that dived into the lake for the big fish. But death may not be the worst remote effect of chemicals used to destroy life. Genetic changes might conceivably be caused in birds or animals or in man himself. Dr. Mellanby thinks this is most unlikely, but he points out how the dangers of radiation proved far greater than the experts expected. It is difficult to find in Britain a field, an animal, or a bird without trace of pesticide, and no one can tell what the effect in 20 years may be.

This book deals with an immense problem—man's pollution of the planet he lives on. It is written with immense understanding and immense fairness. It makes fascinating, absorbing reading. The author states that an informed public opinion is essential if the problems of pollution are to be tackled intelligently. His book gives the public the necessary information and should be read by every person with enough intelligence to realize that there are such problems. The book is excellently produced, and very few errors have escaped the proof-readers, but although Dr. Mellanby writes with an easy charm, "conversationist" on page 60 is almost certainly a misprint for conservationist. The photographs vividly illustrate the text. The book will have a wide circulation and will stimulate and disturb every thoughtful reader.

A. B. CHRISTIE.

Symposium on Renal Dialysis

Replacement of Renal Function. Proceedings of the European Dialysis and Transplant Association. 1966. Vol. 3. Edited by David N. S. Kerr. (Pp. 400+xxiii; illustrated. £7 10s. 9d.) Amsterdam: Excerpta Medica. 1967.

A wide variety of papers were read at this conference ranging over the whole field of dialysis, but with a relative neglect of transplantation. The articles are published in either English or French, but unfortunately most of those in French do not have English summaries. The main section of the book consists of papers. This is followed by a report of the demonstrations shown at the conference.

Knowledge of the incidence of uraemia in the population is very important in order to assess the requirements of dialysis and transplantation. J. H. Thaysen (Denmark) estimated that there were 200 deaths per million per year in Denmark. Relating these deaths to costs at the present time S. Shaldon considers that hospital dialysis capital costs are £2,000 per annum and £2,070 a year running costs, as opposed to a capital cost of £3,500

for home dialysis and £1,210 running costs. Both N. H. Scribner and Shaldon agreed that home dialysis is preferable to hospital dialysis. It will be cheaper in the future and the patient relies on himself rather than becoming dependent on an institution. They consider that dialysis should be started early before the severe complications of uraemia such as peripheral neuritis and pericarditis become established.

W. Drukker and colleagues reviewed the European experience with recurrent dialysis. There was a mortality rate of 40% in the first six months, 33% in the second six months, 26% in the second year, and 20% in the third year. This confirmed the high rate of early complications. One of the most serious problems was the development of hepatitis occurring in dialysis units. In 19 centres there had been 40 cases of hepatitis, with four deaths occurring among patients and four deaths among staff. These rather depressing pooled results were in marked contrast to the most experienced centres, Shaldon in particular having had no deaths in the course of a year's programme of haemodialysis.

It used to be felt that with clinical recovery from acute tubular necrosis renal function

was restored to normal, but there is now an increasing amount of evidence that many patients do suffer residual renal damage. A. C. Kennedy and colleagues reported that 72% of patients recovering from acute tubular necrosis have diminished renal function, the most common abnormality being diminished glomerular filtration rate.

J. P. Merrill discussed the relation to haemodialysis of renal transplantation, and pointed out that there was no evidence from the results at the Peter Bent Brigham Hospital that prolonged haemodialysis sensitizes patients against subsequent renal transplants. This was interesting and perhaps rather unexpected. It is perhaps not impossible that some type of "desensitization" against human tissue antigens had taken place after multiple blood transfusions.

In general the discussion following the papers is interesting and constructive, and several sound points are made by "unidentified members." This volume can be recommended to all interested in haemodialysis, but those expecting to obtain up-to-date information on renal transplantation will be disappointed.

R. Y. CALNE,

Parkinsonism

Parkinson's Disease. By Leslie Oliver, M.B., B.S., F.R.C.S., F.A.C.S. (Pp. 69; illustrated. 21s.) London: William Heinemann, 1967.

With the development of new techniques, and the ability to offer hope of some new measure of relief to those who are suffering from Parkinsonism, there is a demand to know more about the present position as regards the medical and surgical treatment of the disease. This book is a communication from an expert on the subject, intended to give information to those whose work lies in other areas of medicine. It is not meant to be a textbook or work of reference for neurologists and neurosurgeons for whom the detail is inadequate, but is a small monograph in which the history and pathology of Parkinson's disease are briefly described, the medical armamentarium is summarized, and modern surgical treatment is reviewed.

The book will certainly be of interest to general practitioners and general physicians, and to nurses, physiotherapists, and social workers, who are required to collaborate in the care and management of these patients. It is therefore a pity that the social and psychological problems confronting the sufferers and their relatives are not given as much attention as they deserve. A small illustrated chapter might have been devoted to hints at the means of overcoming some of the commoner difficulties.

Those who are not surgeons are nevertheless concerned to know what aspects of this very protean condition are most likely to be helped by surgery, and to know equally precisely the contraindications to operation, the extent of benefit which may be hoped for, and the future which lies ahead. Most of this information is to be found in the book, but reference would be easier if it was brought together. Many pages are devoted to description of the operative technique favoured by the author, and other methods receive rather scant mention. As the book is likely to be referred to by nurses and radiographers, most of whom will be working with a variety of instruments, it would have been beneficial to limit the operative detail to a more concise presentation, and replace it by line drawings or photographs of one or two alternative methods and types of apparatus.

The book is to be welcomed, but it is hoped that in a future edition its usefulness will be extended.

PETER H. SCHURR.

Laparoscopy

Laparoscopy in Gynaecology. By Patrick C. Steptoe, F.R.C.S.(Edin.), F.R.C.O.G. (Pp. 92 + viii; illustrated. 40s.) Edinburgh and London: E. & S. Livingstone. 1967.

This book is a complete guide to the use of laparoscopy in gynaecological practice. The author believes that endoscopic examination of the pelvic organs by the trans-peritoneal route can give similar information to that obtained at laparotomy, and allow as detailed an examination of these organs as is now routinely applied to the vagina and cervix.

There are 16 chapters. A brief historical review is followed by more detailed chapters

on modern cold light instruments and abdominal and vaginal techniques, the author preferring the former. Indications, contraindications, and possible complications are discussed, and there are chapters on laparoscopy in the diagnosis of unruptured ectopic pregnancy, sterility and amenorrhoea, and ovarian dystrophies. The style is factual and concise and the text is so liberally illustrated by diagrams and photographs that technical points are readily understood. Of special interest to surgeons contemplating the procedure are 24 laparoscopic colour photographs of pelvic diseases.

As experience is gained in laparoscopy it is possible to perform sterilization and ventrosuspension operations in addition to biopsy, division of adhesions, and aspiration of cysts. Full details of these operations are given. The aspiration of small ovarian cysts later proved malignant may allow an early diagnosis, but seems not without risk.

There are obvious advantages for the patient in laparoscopy, if laparotomy is not subsequently required. This monograph may convince many non-believers that there is now a place for laparoscopy in gynaecology. The author is convinced of its safety and believes it an essential technique for the modern gynaecologist.

D. L. MORRISON.

Essential Information on Tropical Problems

Clinical Tropical Diseases. 4th edition. By A. R. D. Adams and B. G. Maegraith. (Pp. 582 + x; illustrated. 70s.) Oxford: Blackwell. 1966.

Since it was first published in 1953 this book has reached its fourth edition, and this in itself testifies to the need it satisfies. In this edition many useful revisions have been made, some new material has been introduced, and other parts have been brought up to date, yet it is still near its original size. The first edition contained 508 pages, and this one has increased to only 582; it remains therefore of medium size and eminently portable. The aim has continued since the book was first published to give information essential for clinical diagnosis and treatment dogmatically and concisely, avoiding speculation, and making no attempt to provide information of an encyclopaedic nature. These aims have been well maintained.

Among the new material there is an excellent section on glucose-6-phosphate dehydrogenase deficiency, and the new schistosomicide niridazole (Ambilhar) has received attention. The new developments concerning cholera and the remarkable spread of the El Tor vibrio receive prominence; there is a section on kuru, and snake-bite has been extensively revised. In the new writing the high standard set by the earlier editions has been well maintained.

The book continues to be one which the doctor in the tropics, the student of tropical medicine, and the physician in temperate climates who occasionally is confronted with tropical problems can turn to with confidence. He knows that it is authoritative, up to date, and that in it he will find essential information concisely presented.

A. W. WOODRUFF.

World Federation for Mental Health

Reflections. A Personal History and an Account of the Growth of the World Federation for Mental Health. By Dr. John R. Rees. (Pp. 178 + xxviii. \$10.00. Autographed de luxe edition \$25.00.) New York: World Federation for Mental Health. 1966.

In the subtitle of this book it is called a "Personal History"; it might therefore be expected to show the usual characteristics of autobiography, in which egotism is commonly rampant. Seldom, however, can an autobiography have shown more freedom from self-justification and display—the Little Jack Horner syndrome—than this modest record of altruistic effort. It is mainly a factual chronicle of the growth of the World Federation for Mental Health, as the second half of its subtitle indicates. Dr. Rees says in one passage that he had the privilege of visiting nearly 70 countries in the course of his work as director. Viewed from another standpoint this can be seen as evidence of the demands made upon him, which he met without regard for personal convenience.

In a tribute based upon years of close association and friendship, Dr. Brock Chisholm, former Director of the World Health Organization, says, "I have sometimes felt irritated by J.R.'s attitude, but always by what I felt was an excess of tolerance"; and he rightly adds that it is hard to distinguish between Dr. Rees's tolerance and his "pervasive love of humanity as individuals." His warm-hearted liking for all kinds of people, and his generous appreciation of what they can contribute to the common good, have obviously been powerful factors in his success in guiding three exacting organizations. He was medical director of the Tavistock Clinic, consultant psychiatrist to the Army, and director of the World Federation for Mental Health.

The book, which has forewords from intimate associates of Dr. Rees, relates the stages through which the World Federation for Mental Health has passed from its inception in 1948 to its present widespread activity. The achievements of this organization in kindling interest and stimulating organizations and governments to promote mental health have been, to a very large extent, due to the efforts of the self-effacing, resilient psychiatrist who acted for 15 years as its moving spirit.

AUBREY LEWIS.

Advice for the House-surgeon

Manual of Preoperative and Postoperative Care. By the Committee on Pre- and Post-operative Care, American College of Surgeons. Editorial Subcommittee: Henry T. Randall, M.D., James D. Hardy, M.D., and Francis D. Moore, M.D. (Pp. 506 + xiv; illustrated. £2 19s. 6d.) London: W. B. Saunders. 1967.

The newly qualified house-surgeon of today faces not only the routine note-keeping on his patients and assisting his chief in the operating theatre but also the increasingly complex problems of handling the metabolic and nutritional disturbances of major surgery.

With this in mind the present volume has been prepared by the Committee on Pre- and Postoperative Care of the American College of Surgeons. It is designed to provide a quick and concise account of recent advances in surgical metabolism and nutrition.

It therefore covers first the topics of fluid and electrolyte balance, the physiological changes of surgical stress, clotting disorders, infection, and shock. In the later chapters of the book methods of handling the pre- and post-operative care of patients undergoing surgery of the major body systems are considered, and these include the management of their common complications and of surgical emergencies. As well as general surgical considerations, cardiac, gynaecological, urological, and orthopaedic problems are considered together with a chapter on the management of burns. Useful appendices include data on laboratory tests and diets. The individual chapters have been prepared by a total of 29 surgeons, many of whom are well-known names on this side of the Atlantic. Particular mention must be made of Dr. Francis Moore, who is not only one of the editors but who also contributes an important chapter on metabolic response to injury and another on surgical nutrition.

This book will certainly prove of value to the hospital resident junior staff. The text reads easily and combines practical advice with adequate and up-to-date theoretical background. Most chapters have useful bibliographies. Here and there one detects difference in practice between the two sides of the Atlantic in, for example, the advice to discuss the cost of treatment with the patient. In most respects, however, this book covers the needs of the British house-surgeon equally as much as his American intern counterpart.

HAROLD ELLIS.

Looking after Students' Health

Student Health Services in Great Britain and Northern Ireland. By Professor Alex Mair. (Pp. 236+xii. 42s.) Oxford: Pergamon, 1967.

This is a disappointing book. Despite the fact that student health services have existed for several decades in the U.K. and overseas, there is considerable confusion and lack of knowledge about them. The administrative, medical, and psychiatric problems and the complexities of this kind of work are ill-understood among both university personnel and doctors generally. There is thus a real need for comprehensive, accurate, up-to-date, and detailed information, and for discussion of some of the critical issues.

Professor Mair has attempted to tackle the problem on the basis of replies to questionnaires circulated in 1960. The result cannot fairly be described as "a comprehensive account of what the student health service is in Britain today." It is a piecemeal assortment of data, much of which is manifestly obsolescent, and in respect of services introduced since that time non-existent. The services of, for example, London (City University), London (Central Institution), Sussex University, and Birmingham (Aston) are not mentioned.

The contents of the book naturally reflect the kind of questions asked in the questionnaire. Readers expecting to find discussion of topical issues of major importance in student health work, such as late adolescent development, learning problems, unwanted pregnancy and contraception, and drug-taking, will search in vain.

Professor Mair is an advocate of a preventive approach on the lines of school or industrial services, rather than the compre-

hensive service which attempts to accept full treatment responsibility for individual students. In this he differs from the 1966 report of the Royal College of Physicians (the earlier reports only are referred to in the book) and with the consensus view in the British Student Health Association. The particular difficulties of adopting a preventive approach in relation to mental health—in which prevention in this setting mainly means early identification followed by skilled management—are not fully discussed. Indeed, little impression of this type of activity can be gathered from the book; counselling is equated with guidance and reassurance, though we are told that it is "time-consuming if done thoroughly."

Other aspects of preventive work receive more thorough consideration, although there is little about environmental safety, accident prevention, and laboratory safety, and the possible role of a safety officer in the university.

Some points, well and strongly made, certainly deserve the emphasis the author gives them. For example, his point that no student should leave for reasons of academic failure without the fullest investigation of his mental and social well-being is extremely important. How often is this attempted in British universities today? He also argues that services should be university services covering all members of the community, rather than student health services—a view which most of those working in the services would endorse, given that sufficient support could be obtained.

In conclusion, this is a book with many shortcomings, but nevertheless it does contain a great deal of information and raises many points. It will certainly prove a controversial work which will be widely read and discussed.

CHRISTOPHER J. LUCAS.

Books Received

Review is not precluded by notice here of books recently received.

In Vivo. The Case for Supramolecular Biology. By Hans Selye, M.D., Ph.D., D.Sc., F.R.S.(C.), F.I.C.S.(Hon.). (Pp. 168. \$5.95.) New York: Liveright. 1967.

Cortical Evoked Potentials in Man. By Ludovico Bergamini, M.D., and Bruno Bergamasco, M.D. (Pp. 116+xi; illustrated. \$11.50.) Springfield, Illinois: Charles C. Thomas. 1967.

Claude Bernard and Experimental Medicine. Collected Papers from a Symposium commemorating the centenary of the Publication of *An Introduction to the Study of Experimental Medicine* and the first English translation of Claude Bernard's *Cahier Rouge*. Edited by Francisco Grande and Maurice B. Visscher. (Pp. 210+120; illustrated. \$8.95. Paper \$4.95.) Cambridge, Mass.: Schenkman. 1967.

The Venereal Diseases. A Book about Sexually Transmitted Infections. By R. D. Catterall, M.R.C.P.Ed. (Pp. 160; illustrated. 15s. Paper 7s. 6d.) London: Evans Brothers. 1967.

Arthritis and Rheumatism. By W. S. C. Copeman, C.B.E., F.R.C.P. (Pp. 128; illustrated. 12s. 6d. Paper 6s.) London: Evans Brothers. 1967.

The Effects of Abnormal Physical Conditions at Work. Edited by C. N. Davies, D.Sc., F.Inst.P., P. R. Davis, Ph.D., M.B., B.S., L.R.C.P., M.R.C.S., F.Inst.Biol., and F. H. Tyrer, M.A., M.R.C.S., L.R.C.P., D.I.H. (Pp. 185+viil. 21s.) Edinburgh and London: E. & S. Livingstone. 1967.

Accidents to Children. What to do in an Emergency. By Maurice Ellis, F.R.C.S. (Pp. 96; illustrated. 12s. 6d. Paper 5s.) London: Evans Brothers. 1967.

The Cell Periphery, Metastasis and other Contact Phenomena. By Leonard Weiss. (Pp. 388; illustrated. £5 8s.) Amsterdam: North-Holland. 1967.

Alcoholism Explained. By Dr. Lincoln Williams. (Pp. 127. Paper 6s.) London: Evans Brothers. 1967.

Communication in Science. Documentation and Automation. Ciba Foundation Volume. Edited by Anthony de Reuck and Julie Knight. (Pp. 274+xi; illustrated. 60s.) London: J. & A. Churchill. 1967.

Statistics for Biologists. By R. C. Campbell. (Pp. 242+xi. 40s.) London: Cambridge University Press. 1967.

Review of Physiological Chemistry. 11th edition. By Harold A. Harper, Ph.D. (Pp. 522; illustrated. 50s.) Oxford: Blackwell. 1967.

Dynamic Aspects of Biochemistry. 5th edition. By Ernest Baldwin, Sc.D., F.I.Biol. (Pp. 465+xiv. 55s.) London: Cambridge University Press. 1967.

Introduction to the Anatomy and Physiology of the Nervous System. By David Bowsher, M.A., M.D., Ph.D. (Pp. 180+viil; illustrated. 15s.) Oxford: Blackwell. 1967.

Fundamentals of Acid-Base Regulation. 3rd edition. By James R. Robinson, M.D., Ph.D., Sc.D.(Cantab.), F.R.S.N.Z., F.R.A.C.P. (Pp. 109+xiv. 12s. 6d.) Oxford: Blackwell. 1967.

Chemotherapy of Psychiatric Disorders. By Peter Dally, M.B., F.R.C.P., D.P.M. Introduction by William Sargent, M.B., F.R.C.P., D.P.M. (Pp. 156+viil. 42s.) London: Elek. 1967.

Anaesthesia for Neurosurgery. By R. G. B. Gilbert, M.B., G. Fred Brindle, M.D., and Anibal Galindo, M.D. (Pp. 213+xv; illustrated. 85s.) London: J. & A. Churchill. 1967.

Marital Tensions. Clinical Studies towards a Psychological Theory of Interaction. By Henry V. Dicks, M.A., M.D., F.R.C.P., F.B.Ps.S. (Pp. 354+xiv. 42s.) London: Routledge & Kegan Paul. 1967.

Preventive Medicine. Edited by Duncan W. Clark, M.D., and Brian MacMahon, M.D. (Pp. 897+xix; illustrated. 70s.) London: J. & A. Churchill. 1967.

Middle Articles

CONTEMPORARY THEMES

Clients of Alcoholism Information Centres

GRIFFITH EDWARDS,* M.A., D.M., D.P.M.; MARION KELLOG FISHER,* B.A.
ANN HAWKER*; CELIA HENSMAN,* M.A.

IN CO-OPERATION WITH THE NATIONAL COUNCIL ON ALCOHOLISM AND THE GLASGOW, GLOUCESTER, AND LIVERPOOL
ALCOHOLISM INFORMATION CENTRES

Brit. med. J., 1967, 4, 346-349

In Britain alcoholism is a condition which causes embarrassment and perplexity. The alcoholic is often ashamed to seek help, and if he does want help he may be uncertain where to find it. The National Council on Alcoholism, a voluntary organization inaugurated in 1963, has sought to meet this problem by fostering the setting up of alcoholism information centres and has encouraged and assisted local community councils on alcoholism, in various parts of Britain, to open centres which break away from the rescue mission and "Skid Row" aura which so often clings to alcoholism. The centres have been set up in better and central areas of towns; furnishing and décor are of good quality and tend to suggest a modern office suite rather than a clinic. The policy has been to employ staff with wide practical experience of helping the alcoholic rather than to look for counsellors with professional training.

An important part of the job of a centre is that of making contact with the local community and by means of visits, talks, pamphlets, articles in local newspapers, etc., ensuring that the existence of the centres' services is widely known. The hours of opening vary from centre to centre. The aim is to provide help which is friendly, confidential, and immediate, and the door is open to the alcoholic, his spouse, the employer, or any other concerned person or agency. The work of the centres is seen as that of sorting out immediate problems, and directing toward help, rather than providing treatment or long-term counselling.

In 1966 the staff of the Alcohol Impact Project were approached by Colonel Peter Perfect, the executive officer of the National Council on Alcoholism, with the suggestion that the research team should carry out a survey of the work of the three longest-established centres.

Method.—A precoded structured questionnaire was evolved which could be used at an initial interview without interfering with the helping relationship. Staff of the Glasgow, Gloucester, and Liverpool centres then administered this questionnaire each to a consecutive series of 100 clients. The collection period differed slightly between the three centres, but averaged about four months. Data from the 300 completed schedules were analysed on the University of London's I.B.M. 7090 computer.

Of the 300 clients 264 were men and 36 were women. Data on the men are presented in detail, and results on the women are given more briefly.

* From the Alcohol Impact Project Addiction Research Unit, Institute of Psychiatry, Maudsley Hospital, London S.E.5.

Male Clients

Twenty-three per cent. of the male clients had been referred to the centre by a doctor, 20% were self-referred, 14% had been brought or sent along by the spouse or other member of the family, 9% had been referred by a probation officer, 5% had been brought along by a friend other than family member, and the remaining 29% had been referred from a wide variety of agencies, which include Alcoholics Anonymous, Family Welfare and Marriage Guidance, personnel officers, clergymen, etc.

The mean age was 43.1 years (S.D. 9.4). Forty-nine per cent. had been born in England, 39% in Scotland, 9% in Northern or Southern Ireland, and 2% in Wales; 1% gave other places of birth. Forty-eight per cent. of clients were married, 16% single, 24% separated, 9% divorced, and 3% widowed. Social class determined according to the Registrar-General's Classification (General Register Office, 1966) (Table I), shows that there has been a slight tendency toward downward drift.

TABLE I.—Male Clients: Socio-economic Class by Occupation

Class	"Best"	"Now"
I (professional)	6	6
II	22	18
III	48	41
IV	18	23
V (unskilled)	6	12

Eighty-six per cent. described a pattern of continuous drinking and 14% a pattern of bout drinking. Ninety per cent. of male clients had experienced "morning shakes," and 76% of these had been in the habit of taking a morning drink to relieve shakes. All but 5% had experienced amnesias for the previous evenings, and 37% had at some time attempted suicide.

Thirty-two per cent. had not been on a drunkenness charge, 51% had been convicted and fined only, 17% had been convicted and gaoled. Twenty-eight per cent. had been convicted of driving when drunk. Twenty-five per cent. had been in prison for offences which were not technically "drunkenness" offences but which the clients believed to be a direct consequence of their drinking.

Only 22% of clients believed their general practitioner to be unaware of the drinking problem. One per cent. had not seen a general practitioner during the previous year—56% had seen their doctor during the preceding month, 10% during the preceding one to two months, and 14% in the preceding two to

three months. Forty-four per cent. had personally sought help from their doctor, while 30% believed that the wife had consulted the doctor for assistance. However, 74% said that during the previous year they had attempted to "fool" a doctor, and had given false reasons for requiring a medical certificate.

Employment

At the time of interview only 50% were in full-time employment; 4% were in part-time employment, 13% off sick with a job to which to return, 32% unemployed, and 1% retired. That the working population under study consisted of others besides transients and casuals is suggested by the finding that 23% of clients had been with their present employer for less than six months, 15% for 6 to 12 months, 13% for one to two years, and 49% for more than two years. Further evidence on this point is the finding that only 5% of men gave less than one year as their longest period with one employer ever, while 65% gave more than five years as the longest period spent in one job.

The mean time off work for those sick or not employed at the time of interview was 6.5 months: the distribution was in fact skewed, with 75% of the non-working having been out of work for six months or less, and 25% having been out of work for periods ranging from six months to five years. When replies from the total sample of 264 men to a question on days lost from work due to drinking during the previous year were analysed it was found that only 2% stated that they had lost no time from work, and the average number of days lost during the year was 86 (S.D. 82). Only 10% thought that they had received any promotion at work during the previous five years, only 24% believed that drinking had not interfered with promotion, and 47% were in a lower-paid job than their immediately previous employment. Eleven per cent. were certain that during the previous year their drinking had contributed causally to an accident at work, while 32% thought that their drinking might in some way have been implicated in such an event. Seventy-five per cent. had at some time lost a job because of drinking and 12% had been sacked more than five times because of drinking. Thirty-eight per cent. had been dismissed because of the drinking during the immediately preceding year.

Many also gave a history of frequent lateness at work and Monday morning absenteeism due to drinking (Table II).

TABLE II.—*Male Clients: Frequency of Unpunctuality and Monday Morning Absenteeism During Previous Year*

Frequency	Late at Work %	Absent on Monday morning %
Never	9	7
Rarely—once or twice per year	20	27
Quite often—once or twice per month	44	40
Frequently—more than twice per month	22	21
Not applicable—unemployed, retired, etc. . .	5	5

Sixty-two per cent. stated that they had on occasion brought a bottle into work with them, and 12% were doing this every working day. Eighty-eight per cent. were at times having a drink before coming into work, and all but 9% said they could occasionally contrive to keep drinking throughout the working day.

Sixty-nine per cent. of male clients had during the previous year received some warning from their employers, and 59% had indeed been warned about their drinking more than once during that year. Fifty-two per cent. of men said they believed that the company had no consistent policy as regards drunkenness, a further 22% were unsure on this point, and only 26% felt they really knew where they stood. Fourteen per cent. said that the company simply ignored drinking. Fifty-eight per cent. of the clients stated that other employees in the firm had definitely lost a job because of drinking, while 53% had heard of fellow employees being warned. Where there was a com-

pany doctor—in 31% of instances there was no one holding this position—49% of clients said it would be impossible to consult him because of the drinking problem, 36% were unsure whether it would be wise, 11% felt it possible but had not done so, while 13% had indeed sought advice and help from this source.

During the preceding year 74% of clients had sought help from a general practitioner, 55% from a hospital, 44% from Alcoholics Anonymous, 26% from a probation officer, 25% from a minister of religion, and 21% from a marriage guidance counsellor.

Women Clients

The mean age of the women was 44.9 (S.D. 10.5)—not significantly older than for men. The distribution for place of birth and marital status closely resembled male distributions. The general impression is of less severe involvement in pathological drinking: 41% reported continuous drinking, 76% had experienced morning shakes (45% of these had been in the habit of taking a morning drink), and 12% had not experienced amnesias. The incidence of attempted suicide was similar—33%. Only 18% had been charged with a drunkenness offence, and half of these had been to gaol. None had been charged with drunken driving. Six per cent. had been in gaol for some other offence connected with drinking. Rather closer contact was being maintained with the general practitioner—76% had seen their doctor during the previous month. The number in employment was too small to allow any meaningful analysis of the impact of drinking on work. Women seem to seek help from much the same agencies as men.

Discussion

Did this study get at the truth? Proper caution is necessary before accepting any information given by alcoholics that has not been validated, but, if anything, the results probably err toward underestimating rather than overestimating the damage which drinking has done to these people's lives—a man is more likely to conceal the fact that he has been in prison than to invent a story that he has served a gaol sentence. With questions such as whether the general practitioner or employer knows of the client's drinking, or whether the firm has a consistent policy, what is being reported is simply what the client believes to be the case. Moreover, the interviewers were not trained research workers, though they had very considerable experience in talking to alcoholics and forming good and easy relationships, and the structured design of the questionnaire obviated many difficulties.

Who Comes to the Information Centres?

If the information centres are attracting anything like the "average" alcoholic, then our findings are a powerful corrective to the view that the ordinary alcoholic is a drifting down-and-out. The centre clients are quite different from those of London's Skid Row (Edwards *et al.*, 1966) (Table III). The social background of the person who comes to the alcoholism information centre closely approximates to that of the ordinary socially integrated citizen.

The demographic characteristics of men in this study may be compared with those of Alcoholics Anonymous members

TABLE III

	Information Centre	Skid Row
Semi-skilled or unskilled males	35%	88%
In one job for more than 5 years	65%	6%
Married or had been married at some time	84%	36%
Still married	48%	0%

(Edwards *et al.*, 1967) and patients attending a National Health Service hospital (Edwards and Guthrie, 1967).

This study also answers the question whether people who come to information centres are suffering from alcoholism of the same type and degree as those who go to doctors. By any definition the majority of clients of information centres are indeed "real" alcoholics. Ninety per cent. of the men studied here had suffered from morning shakes—a symptom which may be regarded as pathognomonic of severe alcohol dependence. The figure for Alcoholics Anonymous was 84%, for hospital patients 100%, and for Skid Row 92%.

Why do people go to an information centre? Why are they asking for help at all? The answer to this part of the question seems to be simple—these are people who are undergoing a great deal of suffering. We did not attempt to analyse the impact of their drinking on their physical or mental health, but that 37% of men and 33% of women have attempted suicide is some indication of the degree of social damage which is being undergone. Breakdown of marriage, entanglement with the law, and failure at work are some of the elements of chaos—the personal suffering of the alcoholic is not something to be forgotten in the statistics (Lowry, 1967). It would be too optimistic to suppose that the relative under-representation of subjects in the older age groups among clients of information centres is just explained by older people having generally got the treatment they required or having reverted to normal drinking (Davies, 1962; Kendell, 1965); it seems likely that this finding is in part a hint of the diminished life expectancy of the alcoholic.

The question why it is to the information centre that these alcoholics turned perhaps has its answer in the fact that the alcoholic who in this country today wants help can have a very frustrating time finding it. His confusion often seems equalled by the bafflement of those to whom he turns.

The frequency with which the alcoholic seeks to mislead his doctor when asking for a certificate illustrates another aspect of the confusion. Perhaps one reason why the information centres are attracting business is that this reflects the consequences of a system of medical training and qualifying examinations which put little stress on the understanding of personal problems and social distress.

Impact on Industry

The statement has recently been made that alcoholism is costing the country's industry millions of pounds a year (National Council on Alcoholism, 1965). Only very rough estimates of the number of alcoholics in Britain are available, but in 1948 the World Health Organization (1951) made a guess that there were about 350,000 alcoholics, 75,000 of them being "chronic alcoholics," in England and Wales. If the W.H.O. figure is even anywhere near correct, multiplying up the losses to industry caused by the 264 men attending the three information centres studied by a factor to give the total national impact of alcoholism on industry would suggest a quite astonishing figure. The cost to various welfare services would also be enormous. The findings that 50% of male clients were out of work at the time of interview, that 38% had been sacked because of their drinking in the previous year, that the average days missed from work during the preceding year was 86 days, that only 1.5% had not lost time from work during that year, the data on lateness and Monday morning absenteeism set out in Table II, all this suggests an industrial disease deserving the most urgent attention. Quite apart from actual time lost from work, there is the question of inefficiency while still at work: some measure of this aspect of the problem is suggested by the 76% who believed that their promotion has been blocked and by the 11% who say that they have caused accidents by their drinking, and inefficiency is hardly to be wondered at when 88% of clients were occasionally drinking

before work, 62% sometimes bringing in a bottle, and 90% sometimes drinking throughout the day. Quite terrifying risks are being taken.

As for sacking as a solution, the alcoholic will usually simply go and find another job, and take his unsolved problem with him. The State will for a period pay out some more sickness or unemployment money, and then another firm takes on the problem where it was left off. The 12% who have been sacked more than five times present extreme examples of this process of circulation.

Future of Information Centres

Besides their specific value in giving help to alcoholics, these information centres probably have a wider importance. They provide an interesting example of what must surely be the new trend in mental health, of the effort to reach out into the community rather than to sit back in the hospitals. In America the approach to drug addiction seems to be taking very much this direction.

There can be no doubt that information centres are reaching the alcoholic, but whether, having reached him, they are able to take appropriate action is another question. It would seem likely that workers in these centres, widely knowledgeable as they are about the networks of local referral systems and local availability of treatment resources, are providing an extremely useful service; but, in the end, the limit to what they can achieve is set by limits of availability of treatment and rehabilitation. Recently, after the most useful stimulus provided by a Ministry of Health (1962) memorandum, regional hospital boards have set up a number of special units for the treatment of the alcoholic: it is to be hoped that energetic community-orientated treatment services, coping with the needs of every type of alcoholic rather than with the few who can benefit from intensive inpatient psychotherapy, will now be developed on the basis of existing units, and on the basis too of the very considerable skill and experience gained by the staff who have been running these regional units.

When such community treatment services are developed, alcoholism information centres would clearly continue to play a very important part within them. Surely sooner or later the information centres must be given official and permanent financial backing rather than that their survival should depend largely on their ability to raise money from charity. The staff of these centres will also of course go on playing a valuable part as educators. Rational planning, education of the public, and better education of many specialist groups are all urgently needed if chaos is not to be perpetuated.

Summary

By the use of a structured questionnaire information was obtained on 100 clients attending each of three alcoholism information centres—Glasgow, Gloucester, and Liverpool.

People making use of these information centres are very largely citizens with a normal background of social integration—the lack of similarity with the Skid Row stereotype is stressed. Clients come to these centres because they are confused regarding where else to turn.

Besides their importance because of the service they are giving to alcoholics, these information centres are of wider significance in the example they provide of a "reaching-out" type of community approach to mental health.

Appendix: Location of Information Centres

Cardiff and District Council on Alcoholism and Drug Dependency, Dyfrig House, Fitzhamon Embankment, Cardiff (Tel.

32127). East Midlands Council on Alcoholism, The Dan'l Lambert, Albion Hill, Leicester. Glasgow Council on Alcoholism, 141 Bath Street, Glasgow C.2 (Tel. City 3111). Gloucester Council on Alcoholism, 11 Barton Street, Gloucester (Tel. 22682). London Alcoholism Information Centre, 25a Wincott Street, London S.E.11 (Tel. Rel 0456). Merseyside Council on Alcoholism, 14 "B" The Temple, Dale Street, Liverpool 2 (Tel. Central 0300 and 1372). Staffordshire Council on Alcoholism, 48 Greengate Street, Stafford. Centres are also currently being established in Edinburgh and Herefordshire.

We wish to thank Dr. D. L. Davies, Senior Director of the Alcohol Impact Project, for his continued encouragement. Our thanks are specially due to Colonel Peter Perfect and Miss E. M. Keys, of the National Council on Alcoholism, to the members of the Medical Committee of the N.C.A. (chairman at that time Dr. H. D. Chalke), who gave much help at the planning stage, and to the staff and directors of the three co-operating information centres—Mr. John

Gray (Glasgow), Mr. Michael Taylor (Gloucester), and Mrs. W. H. Kenyon (Liverpool). Mrs. Barbara Kinsley, Mr. Michael Clark, and Mrs. Hedi Firth kindly helped with statistical analysis. We thank Mrs. Julia Polglaze and Miss Ethane Cross for all their secretarial work. The study was supported by a grant from the Bethlem Maudsley Research Fund.

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CONFERENCES AND MEETINGS

Uses of Niridazole

[FROM A SPECIAL CORRESPONDENT]

A conference on the pharmacological and chemotherapeutic properties of niridazole and other antischistosomal compounds was held by the New York Academy of Sciences from 10 to 13 October.

Professor BRIAN MAEGRAITH (Liverpool) opened the meeting by outlining the magnitude of the world problem of schistosomiasis, which is estimated to afflict 200 million people or roughly 1 in 10 of the world's population. Repeated courses of different schistosomicides are at present advocated for the cure of individuals in highly endemic zones, but Dr. A. H. MOUSA (Cairo) described trials aimed at mass chemoprophylaxis. In view of the possible theoretical development of resistance to any single drug and of toxicity due to them, he had employed combinations of subtherapeutic doses of antimonial and non-antimonial drugs in different schedules in infected mice. Despite variable results the combination was encouraging, particularly since there were different biochemical effects between antimonial and non-antimonial schistosomicides. Mice that had been infected with *Schistosoma mansoni* continued to excrete non-viable eggs for up to one year after treatment with niridazole (Ambilhar) even although there were no longer signs of active parasitism. Dr. C. R. LAMBERT (Basle) referred to them as black eggs or empty shells.

Niridazole is rapidly absorbed and accumulated in the vitellogenic gland of the female worm, and decrease in worm length and in the size of the worm ovary shows a clearcut dose-effect relationship. Dr. H. P. STRIEBEL (Basle) emphasized this sensitivity of the female and the relative refractoriness of male-worm testes to such treatment.

Orally administered radioactive niridazole is slowly absorbed from the gastrointestinal tract over several hours, and then rapidly broken down by a nitroreductase enzyme system in the liver. Dr. J. W. FAIGLE and Dr. H. KEBERLE (Basle) pointed out that this combination of slow absorption and rapid metabolism ensured a uniform concentration

of niridazole in the blood throughout the period of its absorption.

Professor A. W. WOODRUFF and his co-workers at the Hospital for Tropical Diseases (London) had compared the value of toxicity of sodium antimony tartrate, antimony dimercapto-succinate, sodium antimony gluconate, Anthiomaline (anthiolimine), lucanthone, and niridazole, bearing in mind the useful practical definition that a schistosomicide must be capable of eradicating heavy and light infections of all strains from persons of different racial, residential, and other characteristics when given in a regimen easy to apply under varying conditions. The main disadvantage of niridazole was the neuropsychiatric disturbance which particularly complicated its use in hepatosplenic bilharziasis.

Hepatosplenic Disease

Professor A. M. COUTINHO and Dr. A. M. DOMINGUES had carefully studied 52 patients in Brazil receiving niridazole for the hepatosplenic form of the disease. In 20 treatment had had to be stopped because of side-effects, which included psychoses, often with suicidal tendencies, in 19 and convulsions in four patients. Serial electroencephalograms had shown changes in 15 of 18 patients studied. In the intestinal form of the disease only two of 30 patients had developed any of these complications. To some extent these side-effects could be minimized by the administration of barbiturates and tranquillizing agents. Dr. A. ABDALLAH (Cairo) described episodic excitement, euphoria, and hallucinations from the fourth day of treatment onwards; and also mental disorientation, generalized convulsions, and localized muscle tremors and spasms. Though the overall incidence of toxicity was less than 1%, it had been found to rise to about 28% in adults with *S. mansoni* infection and the hepatosplenic form of the disease. This was unlikely to be due to hepatocellular poisoning, for

serum-transaminase levels and bromsulphalein excretion were essentially unimpaired during treatment. Dr. A. RUAS, studying similar patients in Mozambique, had noted that liver biopsies showed no histological change after niridazole therapy compared with pretreatment sections.

The cerebral sequelae may be related to portal-systemic venous shunting, which is a feature of hepatosplenic schistosomiasis. This would allow niridazole to reach the brain without being metabolized by the liver. Dr. J. W. FAIGLE and Dr. H. KEBERLE (Basle) demonstrated high peripheral blood levels of the drug in patients with hepatosplenic schistosomiasis. Professor SHEILA SHERLOCK (London) believed that the mechanism was analogous to portal-systemic encephalopathy, in which products of bacterial action on protein bypassed the liver and induced hepatic coma. Impairment of liver function would facilitate the effect; hence the increased frequency in the malnourished and in older patients rather than children.

Despite its toxicity in hepatosplenic disease, it was agreed that niridazole was the drug of choice in *S. haematobium* infections. Dr. V. CLARKE (Rhodesia) had found that such infections were easily cured by niridazole in a dosage of 25 mg./kg. body weight for five to ten days—an experience which proved universal. Dr. G. RAFFIER (Ivory Coast) felt that the excellent therapeutic and prophylactic results obtained in vesical bilharziasis allowed her to predict its eradication by a mass campaign comprising niridazole for the bilharzial patients, together with a molluscicide for destruction of the intermediate host, the snail.

Dr. F. FONTANILLES (Basle) summed up the situation succinctly by balancing the risks of treatment (including the effect on the myocardium of some schistosomicides) with the tolerability and efficacy of niridazole in mass campaigns—particularly of children suffering from *S. haematobium* infections, in which it was of unequalled efficacy and suitable for outpatient therapy.

Extracorporeal Filtration

Dr. B. H. KEAN and Dr. E. I. GOLDSMITH (New York City) described an ingenious method of recovering adult schistosomes, based on their peculiar localization in the portal circulation. The portal blood was diverted through a catheter inserted in the splenic vein and was returned to the circulation through a saphenous vein after being filtered extracorporeally. The worms were mobilized from the intestinal venules by the intravenous injection of antimony and were trapped in the filter as they passed towards the liver. Up to 2,000 worms might be recovered in a single procedure. So far, however, haemofiltration of the perivesical plexus for *S. haematobium* infection had been unsuccessful.

Dr. C. H. TAMBURRO and Dr. C. M. LEEVY (New Jersey) had extended the observations by assessing the immunological response of patients with active infestation who were being dewormed by means of extracorporeal filtration of their portal vascular beds following antischistosomal treatment. A serological schistosomiasis plasma card

test using a cercarial antigen emulsion had been found easy, highly specific, and effective in screening an endemic population in a non-endemic area for schistosome infestation. This semiquantitative method of measuring antibody titre was related to the degree and severity of infection. Antibodies, produced against cercarial antigen, were found to be 7S globulins of the IgG fraction; they were predominantly responsible for the hypergammaglobulinaemia seen in active infestation. A direct correlation was apparent between severity of infestation, height of cercarial antibody titre, and level of IgG in all 17 patients with tissue evidence of schistosome eggs.

Other Infections

Dr. S. J. POWELL (Durban) demonstrated that niridazole was highly effective in both bowel and liver infections. A trial of niridazole with dehydroemetine revealed that it was just as effective as chloroquine in liver abscess. Nevertheless, the efficacy of combi-

nations of well-established amoebicides and the advent of metronidazole was thought to leave little place for niridazole in the treatment of amoebiasis.

Dr. G. RAFFIER (Ivory Coast) and Professor O. LUCAS (Ibadan) emphasized the broad-spectrum, antihelminthic value of niridazole, which was highly effective in the treatment of strongyloidiasis and dracontiasis. The recommended dose was 25 mg./kg./day for one week, administered in divided doses twice daily. Absence of parasites in the stools and an improvement in health were rapidly achieved in most patients with strongyloidiasis, and likewise there was an elimination of the guinea-worm in almost all subjects infested with *Dracuncula medinensis*, with a corresponding rapid relief of pain, tenderness, and swelling. It was also noted that the worms were extracted more easily and there was less tendency for fresh worms to emerge. Niridazole was well tolerated, and minor side-effects were controlled by antihistamine drugs.

The transactions of the Congress will be published by the New York Academy of Sciences.

HOSPITAL TOPICS**Organization of Hospital Work in Scotland**

[FROM A SPECIAL CORRESPONDENT]

Clinical Organization

Under the auspices of the Scottish Home and Health Department a conference was held in B.M.A. Scottish House in Edinburgh on 2 November to consider the first report of a Joint Working Party on the "Organization of Medical Work in the Hospital Service in Scotland" (see *B.M.J.*, 4 November, p. 291). Among those attending the conference were representatives of the Central Department, regional boards, boards of management, and hospital medical staff.

The Working Party, which consisted of members nominated by the Department and the Joint Consultants Committee (Scotland), was appointed in December 1965 by the Secretary of State for Scotland with the following terms of reference: "To consider what developments in the hospital service are desirable in order to promote efficiency in the organization of medical work." The Chairman of the Working Party was Dr. J. H. F. BROTHERSTON (Chief Medical Officer of the Scottish Home and Health Department), and Dr. J. G. M. HAMILTON (Chairman of the Scottish Joint Consultants Committee) presided over the conference.

In his opening remarks Dr. HAMILTON pointed out that the detailed study of the remit had been undertaken by subgroups of the Working Party, but the report now presented represented the joint and agreed view of the Working Party as a whole. He emphasized that the conclusions were in no sense to be regarded as instructions to anyone; they were recommendations for discussion and consideration by all concerned—at national, regional, and hospital levels.

Introducing the chapter of the report dealing with clinical organization, Dr. BROTHERSTON said it seemed to be inevitable that medical development tended to outstrip organization. The present pattern of grouping in individual firms or units, each operating more or less independently, dated from older and simpler times, and was well suited to preserve continuous consultant responsibility in patient care. With the increasing complexity of specialist service, however, it was becoming evident that this system might not give the best results either for patients or for teaching. The problem was to organize without adversely affecting independent consultant responsibility. The Working Party believed that this could be achieved by the larger-scale organization in "divisions" which it recommends. The corresponding working party for England and Wales had independently reached the same conclusion.

Touching on the advantages of the proposed divisional system, Dr. Brotherston spoke of its greater flexibility in deployment of beds to meet the needs of developing specialties with much less disturbance than was now the case. Other variable needs—such as those arising from epidemics, seasonal changes in morbidity, intensity, and type of patient care needed—would all be more readily met. The system could provide an effective means of forming and transmitting collective opinion and advice on hospital policy and development. This would supplement, not replace, the role of medical staff

committees. So far as training was concerned, while the present organization provided the obvious advantages of apprenticeship, it was difficult under it to provide the variety needed for a complete training in the modern situation. This would be more easily achieved under the proposed plan. It would also be easier to develop methods of evaluating work done in hospitals.

The Working Party had adopted the term "patient-care evaluation" as more nearly expressing what was in mind than the American "medical audit." Speaking of the possibility of improved co-ordination with other specialties and services, Dr. Brotherston drew attention to the similarity of their own recommendations to many of those in the Salmon Report on nursing organization. In conclusion, he said the Working Party believed that clinicians would have to interest themselves actively in organization and administration if they were to play their full and necessary part in the "tactics and strategy" of the Health Service.

Consultant Responsibility

Sir JOHN BRUCE (S.E. Region and Joint Working Party) thought that some among the senior clinicians might regret the passing of the old order under which they had long worked happily, and suspect the change to be a sort of committee system. The proposals were, however, designed to preserve the principle of consultant responsibility and, he believed, would be welcomed by the younger

group. The "divisional" type of organization was not in fact new and had been in operation in some specialties in several areas for some time. This was also true of so-called medical auditing.

Dr. P. MACARTHUR (N.E. Region) doubted whether the divisional organization could be introduced voluntarily, and argued in favour of divisional chairmen being appointed by regional boards from among the senior clinicians, as proposed by the English working party. The appointment should be for five years. Mr. W. M. FARQUHARSON-LANG (N.E. Regional Board and chairman of the Departmental Committee on Hospital Administration) thought the proposed organization could lead to improvement in the medical advisory arrangements for hospital boards. It would be necessary to provide effective administrative support for the chairmen of divisions and for the committee of chairmen. In reply to Dr. W. P. U. KENNEDY (S.E. Regional Hospital Junior Staff Group) Dr. BROTHERSTON said the place of junior staff within the organization had not been forgotten in the deliberations, but would need more discussion "on the ground." Other matters raised by speakers included the financing of effective medical auditing and the role of medical superintendents under the scheme.

Dr. C. W. CLAYSON (Western Region and Joint Working Party), introducing Chapter II on medical staffing, said the Working Party had recognized at an early stage that the basis of any discussion on staffing problems must be the existence of a chronic shortage of doctors. In spite of an increase over the past dozen years of 30% in senior and nearly 60% in junior staff, there was still a serious shortage. The numbers in general practice meanwhile were actually falling. The factors creating this situation would continue to operate, and hence there was a need to relieve medical staff as much as possible of non-medical duties by providing them with technical and secretarial assistance, and for delegation by consultants of duties which could be undertaken by appropriate intermediate staff. The Working Party had concluded that one paramount need was to foster reintegration of hospital and general practice, which would be to the benefit of both.

Other sources of staff were part-time employment in hospital of local authority doctors engaged in specialist preventive work in the paediatric, geriatric, and mental health fields; married women doctors; and retired doctors. This would mean a substantial expansion of the medical assistant grade, with a compensatory reduction in the registrar establishment—which would be desirable in the interests of a better balance between staffing and training needs.

Dr. JOHN SMITH (Scottish Home and Health Department) felt that the association of general practitioners with the hospital was most important. A recent survey had shown that there were twice as many aspirants to a hospital career as there were likely vacancies, whereas only half the number needed for general practice wished to enter it. He felt sure that many in both groups would be well content with a career that combined the two. The combined local authority and hospital appointment would also be attractive to many.

Dr. A. ALLISON (Western Region) and two other speakers expressed concern about the proposed expansion of the medical assistant grade. This might lead to a recurrence of the old senior hospital medical officer problem. Dr. CLAYSON did not think this likely under the new organization, though there might be problems in connexion with delegated responsibility.

Use of Beds

Mr. A. H. JACOBS (Western Region and Joint Working Party), introducing Chapter III—Alternatives to Traditional Systems of Hospital Care—said the Working Party were concerned to know whether the present system of admission to and treatment in hospital provided both the best and most economic use of hospital beds. They had reached the conclusion that several changes could usefully be made—including planned admission to hospital (with separation of the emergency and waiting-list cases); development of selective patient grouping according to clinical need; and the allocation of beds to provide this flexibility. Several categories could be distinguished, such as routine acute care beds (including intensive nursing care beds); intensive therapy beds; and short-stay beds, perhaps divided into overnight and observation beds, and five-day beds.

Dr. MACKAY HART (Western Region and Joint Working Party) said building changes would be needed to put many of these ideas into effect, but quite a lot of them could be realized without this. Dr. ERIC SAMUEL (S.E. Region) thought there was room for better planning of radiological, laboratory, and other investigations of inpatients. Several speakers suggested, and Mr. JACOBS agreed, that a great deal more information would be needed before many of these changes could be approved and adopted.

Mr. N. G. C. HENDRY (N.E. Region and Joint Working Party), in introducing Chapter IV on Operational Research, discussed the techniques involved and their application to medical work generally and hospital work in particular. These covered such things as routine statistics, assessment of standards of care, and work study. The cynic, he said, might argue that people could spend so much time investigating the work they were doing that they ended up doing no work at all. The Working Party were convinced that great benefit could come from intelligent use of these methods, and they recommended further strengthening of the Health Department's Research and Intelligence Unit.

"Communications"

Mr. E. U. E. ELLIOTT-BINNS (Scottish Home and Health Department) spoke briefly to Chapter V on Communications, pointing out that the term "communications" was not altogether satisfactory, but it was difficult to find a more suitable one. It was concerned essentially with ways and means of getting information to those for whom it was necessary or useful. He drew the attention of the conference to two of the Working Party's proposals—namely, the establishment of some kind of "staff college," which would be concerned with the study of and training in

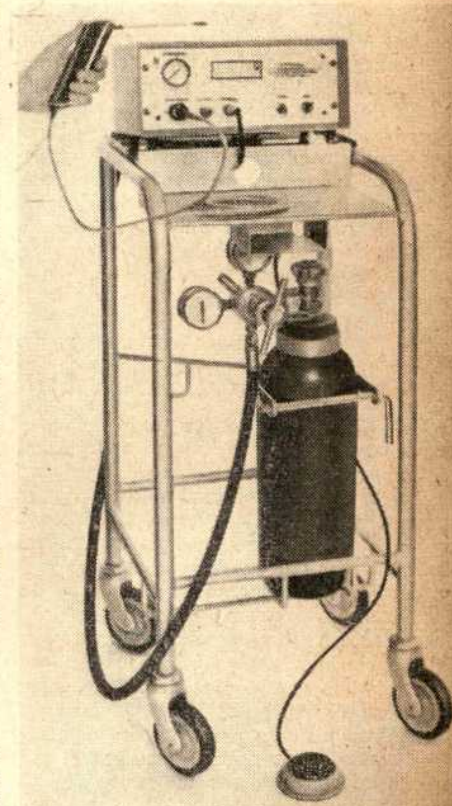
management, and the appointment of a small standing committee representative of the various interests to devise and keep under review the channels of communication within the service.

In closing the meeting Dr. HAMILTON said that the Department hoped very much that the report and its recommendations and proposals would be thoroughly and critically discussed by doctors and others all over the country.

NEW APPLIANCES

Prototype Cryosurgical Probe

Mr. P. MCKELVIE, Institute of Laryngology and Otology, London, and Mr. O. H. SHABEEN, Guy's Hospital, London, write: This prototype cryosurgical probe is 15 cm. long, the low temperature tip being 1.5 by 0.5 cm. Operating from a cylinder of carbon dioxide, it reaches minus 40° C. in one second and defrosts electrically in eight



seconds. It is autoclavable, light, and portable, and is particularly suitable for the destruction, with haemostasis, of small lesions accessible in the upper air and food passages, though its general applicability is widespread.

It is manufactured by Spembley Products Ltd. and distributed through Keeler Ltd., London.

Correspondence

Letters to the Editor should not exceed 500 words.

Postoperative Gas Gangrene

SIR,—Your leading article "Postoperative Gas Gangrene" (14 October, p. 68) is a timely reminder of the unexpected and, fortunately, unusual risk run by the patient after surgery. This risk exists despite exhaustive efforts to control the environmental and personal sources of *Clostridium welchii*. I believe clostridial cellulitis and myositis occur more commonly than is realized.

Since the opening of a small hyperbaric oxygen unit three years ago 16 cases of post-operative and post-traumatic gas gangrene have been admitted from a relatively small population. Answers from a group of orthopaedic surgeons indicated that more than 50 cases had occurred in a population of three million in five years. You state that gas gangrene is a rare and terrifying disease, as indeed many diseases have been prior to methods of control.

Gas gangrene, however, has yielded over the last 10 years to a most effective form of treatment, hyperbaric oxygen, first reported by Boerema.¹ Van Zyl,² reporting on 200 cases treated all over the world, revealed a mortality rate of 2.9% when excluding those moribund on admission and dying within 24 hours. At our unit³ we have had patients in extremis with toxicity and confusion recover within hours, and had only one death in 16 patients with established gas gangrene. The cause of death was liver and renal failure.

The improvement is caused by transporting oxygen in plasma to the ischaemic tissues and preventing the elaboration of toxins by *Cl. welchii*. It is the ischaemia and anoxia which prevent penicillin destroying the organisms in the wound, and these proceed to produce toxins which cause tissue necrosis and even death.

Hyperbaric oxygen treatment renders the patient fitter for surgery and limits the procedure to excision of sloughs, with avoidance of dramatic amputations. There are facilities for hyperbaric oxygen treatment in many centres in the United Kingdom, and it is surprising that you did not refer to this therapy in your welcome article. Indeed, it is in the United Kingdom that so much of the impetus and development of the hyperbaric oxygen facilities has occurred. It is to be hoped that, while the evaluation of this therapy in other fields proceeds, the opportunity is not lost for rendering this life-saving method to the victims of surgery and trauma.—I am, etc.,

ROY H. MAUDSLEY.

Heatherwood Orthopaedic
Hospital,
Ascot, Berkshire.

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- 2 Van Zyl, J. J. W., *Proc. Third Internat. Conference on Hyperbaric Medicine*, ed. I. W. Brown and B. G. Cox, 1966, p. 515. Washington.
- 3 Maudsley, R. H., and Colwill, M. R., *J. Bone Jt Surg.*, 1966, 48B, 584.

Abortion Act

SIR,—While most doctors are in favour of greater latitude under the law, many may now be wondering whether the latest legislation on abortion, like that on road traffic, has taken sufficient account of the increased burden it places upon the overworked general practitioner. It was fairly obvious that there were not enough gynaecologists for the law to demand their involvement; but is there really any good reason to suppose that general practitioners are in a better position to take over even the whole consultative element from the present criminal practitioners?

The introduction of social grounds is going to call for a great deal of fact-finding and assessment which, to say the least, will require an enormous amount of liaison with the social and welfare services. For instance, the emotionally disturbed expectant mother who already has an overcrowded home will not only present a need for general-practitioner psychotherapy and a certificate to the housing authority but the possibility of abortion will have to be considered. Ethically, this might be regarded as the last resort, but patients and housing committees may well tend to favour it for its relative simplicity. Once precedents are established in any one family or district it will become increasingly

difficult for any doctor to stand out against abortion becoming accepted as the remedy for many of the social evils that have long been crying out for fundamental solution.

The present law, for all its harshness and injustice, has enabled the doctors to take up a position with regard to abortion that is sufficiently simple and well-defined to render administration by them relatively easy. The new law will inevitably far more often depend on the interpretation and judgement of general practitioners, with a much greater need for thorough investigation of the grounds. These, as we have seen, will range over a very wide field. Thus as time goes on there will develop another considerable factor to be taken into account by members of the public in making their choice of doctor from a competitive profession. This would become increasingly significant if Governments ever decided to reverse the policy of giving more and more work to fewer and fewer medical practitioners. In this context one may wonder what remuneration there will be for the abortion service and how it will compare with that relating to the Mental Health Act.

Although one would not wish to quarrel with the House of Commons' decision that two medical practitioners should be responsible for

administering the new law to patients, it may be felt that in practice considerations such as those to which I have alluded make a wider and more impersonal system desirable. In relation to the Mental Health Act the nomination of local standing referees has worked very well, and possibly something like this idea could grow up as an unofficial institution suited to the Abortion Act and the needs of some areas. Incidentally it is possible that we may even evolve the surgeon-abortionist to replace his criminal counterpart and take the load off the shoulders of gynaecologists whose operation and waiting lists will probably remain full enough without any additional work.

Undoubtedly there is a lot to be said for leaving room for natural evolution of the detailed administrative machinery for coping with all the problems that can be foreseen. However, there can be no objection to the consideration of possible ways of dealing with the whole situation during the six months before we are actually called upon to cope with it. I would like to propose for consideration the appointment of "local abortion committees." There would be permanent membership recruited from obstetric committees and public health authorities or other sources of medical, legal, and social expertise. Whether cases for abortion should be submitted compulsorily or voluntarily, or whether the patient, her doctor, or local health visitor or any other witnesses of fact or opinion should attend meetings, are matters to be decided in general or in any particular case. Obvious advantages of such a system are the relatively consistent and impersonal decisions and precedents that would arise out of it. It would also tend to be more efficient and less onerous than the separate and varying personal efforts of different pairs of general practitioners. This especially because judicial and sociological ability will be comparatively more important than medical science.—I am, etc.,

Eye,
Suffolk.

J. SHACKLETON BAILEY.

Hiatus Hernia and Coronary Disease

SIR,—Dr. M. Atkinson's masterly account of hiatus hernia (28 October, p. 218) requires some comment. As he states in his final paragraph, hiatus hernia is extremely common in elderly patients with coronary disease, so that we often encounter chest pain from the combined lesions. Anginal pain may be conditioned by a number of coincident extra-cardiac diseases—for example, gall-bladder disease, cervical spondylosis, and notably by hiatus hernia, especially the para-oesophageal type, in which cardiac pain may occur mainly or even exclusively at night or after meals.

I have now seen so many patients with serious coronary insufficiency dragged from their beds to be radiographed in an inverted posture and at much peril that some warning is needed. Patients with this combined lesion may die in their anginal attacks. One of my patients reached the stage when he refused to eat and passed the night on a chair. When he died suddenly his wife was so sure that

the trouble arose from the stomach that she demanded a postmortem, which showed advanced coronary disease with old occlusion and a hiatus hernia, the size of a tangerine.

Dr. Atkinson states that hiatus hernia may cause pain down both arms, though he qualifies this by remarking that such pain is usually cardiac. In my experience it is always cardiac. Certainly before such symptoms are attributed to hiatus hernia careful electrocardiographic investigation is required, and, whenever possible, a record during the pain should be obtained. This can sometimes be accomplished by laying the patient flat or by a mild exercise test immediately after a good lunch.

Dr. Atkinson mentions the diagnostic difficulty in such cases and warns us that the consequences of error may be serious. I am sure that he will forgive me for emphasizing this particular point.—I am, etc.,

London W.1,

D. EVAN BEDFORD.

Surgery in Pulmonary Tuberculosis

SIR,—I am concerned that your leading article on surgery in pulmonary tuberculosis (21 October, p. 127) might be misunderstood. I imagine that some of the implications which might be drawn from it were not in fact intended by the writer, but I feel I should draw attention to them in case other people also misconstrued his intentions. The first indication for surgery mentioned is the most surprising: "those patients with cavitated disease who after six months of adequate chemotherapy are still producing positive bacillary tests, particularly where the original organism showed an appreciable degree of resistance to the standard antituberculous drugs." Many physicians would now agree that if proper treatment is given to a newly diagnosed case (streptomycin, P.A.S., and isoniazid, in appropriate rhythm and dosage) the sputum of all patients who do not die within the first week or two should convert to negative. Cultures were negative in about 98% of my own series at six months, but the remaining 2% converted by 10 months. Genuine failure will occur only if the patient has initial drug resistance to more than one of the three drugs used or he has not taken his treatment. In the former case this should be known by three months after starting treatment, and appropriate alteration of chemotherapy should ensure later sputum conversion. Cavitated tuberculosis should be treated under sufficient supervision to ensure that the patient takes his drugs. Surgery may perhaps be justified in some patients with localized disease known to have organisms resistant to all the standard and some of the reserve drugs, and perhaps this is what the author really had in mind.

In suggesting some of the other indications for surgery the writer does not make clear the necessity for ensuring that active tuberculosis has been eliminated. Such patients will require at least 18 months of effective chemotherapy to ensure them against relapse, no matter when operation has been carried out or what its nature.

We have done so little surgery for tuberculosis over the last 10 years that it is difficult to comment on the suggestions regarding thoracoplasty, which have the nostalgic flavour of past controversy. Nor is it easy

to comment on the suggestions regarding the resection of intrathoracic lymph-glands in primary tuberculosis, which I have, perhaps incorrectly, never regretted not having done. On the other hand, I am happy to be able to agree that there is a definite place for surgery in infection with atypical mycobacteria, which are at present so much less controllable with chemotherapy.

I feel that this article, I am sure unintentionally, has been slightly haunted by ghosts out of the past. I hope I will be forgiven for a little gentle exorcism.—I am, etc.,

JOHN CROFTON.

Department of Respiratory
Diseases,
University of Edinburgh.

SIR,—In your leading article "Surgery in Pulmonary Tuberculosis" (21 October, p. 127) you mention the treatment of enlarged tuberculous mediastinal glands in children by repeated bronchoscopic aspiration or alternatively by thoracotomy and excision or evacuation of these glands. Lest medical staff working in areas where primary tuberculous infection with enlarged mediastinal glands is still seen should conclude that surgical treatment is the best method, I should like to draw your attention to a study conducted at this hospital on 383 child patients. The results of this study were presented at the annual conference of the British Tuberculosis Association at Oxford in 1965.¹

All children admitted to the hospital suffering from primary pulmonary tuberculosis with consolidation-collapse from 1952 to 1959 were carefully followed up for periods ranging from 6 to 13 years. Bronchoscopy was done in only 12 patients, and in these two showed normal appearances, five oedema of the mucous membrane, one a block by granulation tissue, one a block by external gland pressure, two showed strictures, and one a stricture with sinus formation. Thoracotomy was not resorted to early in treatment but only if after a period of expectant treatment the consolidation-collapse failed to clear. In fact only 21 children (5.2%) required thoracotomy—ten had a lobectomy, seven a segment resection, one a lobectomy with removal of glands, two a segmental resection with removal of glands, and one removal of glands only. The end results of treatment were satisfactory in 338 patients who were traced; 41 were lost sight of. Two children who had recovered well died after discharge—one from appendicitis and one from a road accident, and two died early in the course of treatment from tuberculous meningitis.

This study has not yet been reported in full, as a further follow-up is being carried out in a group of children who showed marked clearing of calcium deposition from the affected segments of lung and/or from calcified mediastinal glands. Quite large masses of calcification have been found to disappear gradually from the lungs over periods of three to ten years, a phenomenon not thought to be so common previously. Sweany² has described peculiar phagocytic cells in the lung which arise from basic reticulum cells in the lung or from monocytic cells which come in from the blood stream. He showed that they have the capacity to reabsorb calcium deposits from the lung tissue. I mention this because, although one is aware of the severe lesions which occur in primary tuberculosis with consolidation-collapse, and of the excellent work done in this connexion by Seal *et al.*,³ nevertheless our

long-term results of conservative treatment lead to the conclusion that surgery should not be undertaken under one year from diagnosis; in fact, Harley Stevens⁴ suggested 18 months. A graph of the time at which x-ray clearing of the consolidation-collapse appeared in our series showed peaks at two to three months and seven to nine months. Treatment by bronchoscopic aspiration is of limited value, a finding also borne out by Bentley and Grzybowski.⁵

The human body appears to have remarkable powers of healing if given time, and in young children the experience of repeated bronchoscopy, which can be hazardous, or of major chest surgery are probably best avoided.—I am, etc.,

JOHN B. MORRISON.

Abergele Chest Hospital,
Abergele, North Wales.

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Body Building on Drugs

SIR,—I have recently been approached by a person who is interested in body building and weight lifting and who has asked me if I would consider giving him anabolic steroids. He alleges that a very large percentage indeed of the top flight of both body-builders and weight-lifters take these drugs, and he feels that he would have gone further if he had taken them. He also says that there is a ready availability of these drugs on the "black market." I feel under some moral pressure in this case, as he will abide by my decision whether I give them or not, but not winning competitions will entail undoubted financial loss in his line of business.

My object in writing to you, Sir, is four-fold. (1) To bring more into the open a newer aspect of drug-taking. (2) To inquire whether your readers feel it is justified to prescribe this class of drug for body building, bearing in mind the side-effects—quite apart from the ethical aspect. (3) To ask whether the governing bodies of these sports feel a stand should be taken against such artificial methods of "training." (4) To inquire whether the easy detection of persons being given steroids is feasible at competitions and games.—I am, etc.,

Westcliff-on-Sea,
Essex.

D. E. PEARSONS.

Epidemic Keratoconjunctivitis

SIR,—After an interval of eleven years epidemic keratoconjunctivitis has returned to the Clyde Valley conurbation (for report see page 366). The causal agent, adenovirus type 8, is very hardy. Though poorly infectious by casual personal contact in European or North American conditions, this virus is highly contagious and transmitted easily by the fingers, instruments, and medicaments of the ophthalmologist or in the industrial ambulance room. Infections of medical,

paramedical, and nursing staff have been observed in the present outbreak, as in the past. Scrupulous attention to hygiene and sterile techniques is necessary to stop the spread of this infection, which can cause painful disability for many weeks with residual corneal opacities. Since fingers seem particularly likely to transfer infection, it would be advisable to use disposable gloves for manipulating eyelids when rushed conditions prevent thorough cleansing of hands between patients.—I am, etc.,

Department of Infectious
Diseases,
Glasgow University.

N. R. GRIST.

Obstetric Forceps or Vacuum Extractor

SIR,—Your leading article (23 September, p. 753), inspired by the excellent paper of Schenken and Serr,¹ makes certain dogmatic pronouncements over and above their findings. Such is the influence of the *B.M.J.* that these should be questioned forthwith before they become accepted as orthodox doctrine on this topic.

You state that forceps are to be preferred for the management of delay or foetal distress in the second stage because "delivery will be quicker." Certainly it will, but application of forceps requires either a formal pudendal nerve block or a general anaesthetic, both of which take some minutes to organize. The hazards of the latter you ignore. It is debatable whether the combination of minimal anaesthesia and vacuum extraction is in fact much slower than a properly anaesthetized forceps delivery.

"Delivery is safer because a doctor cannot hope to apply the forceps correctly and effectively until he has checked the position of the occiput." To be certain of the position of the occiput a general anaesthetic may be required, and this carries its own risks. Manual rotation and forceps extraction are definitely easier to perform under general anaesthesia. This is in marked contrast with deliberate application of the cup to the occiput when the latter is posterior, using local infiltration anaesthesia, or at most a pudendal block. In the majority of cases the unique ability of the vacuum extractor to promote flexion of the foetal head is then followed by autorotation and a comparatively rapid occipito-anterior delivery. The minute force often necessary to produce this manoeuvre makes it one of the most aesthetically satisfactory obstetric procedures.

"Damage to the scalp by necrosis at the site of the application of the vacuum cup is not uncommon." Nearly all writers in fact agree that it is extremely rare unless traction is continued for longer than 40 minutes.

You conclude, "The vacuum extractor has no place on the district or in a general-practitioner maternity unit." This appears to be in direct opposition to Schenker and Serr's conclusions: "its principal advantages . . . are the lack of necessity for general anaesthesia . . ." (surely of great value in such units) and "the correction of pathological vertex positions such as persistent occipitoposterior and deep transverse arrest" (most general-practitioner obstetricians would agree that these cause them more anxiety than the rest of operative obstetrics put together). They further conclude that,

"with respect to the mother, the vacuum extractor is a relatively safe instrument as compared to the forceps." "The danger of ascending infection appears to be minimal (5 to 6%) as compared to 15.3% in forceps deliveries. . . ."

The enormous value of the vacuum extractor in one general-practitioner unit has been previously described.² Subsequent experience of a further 40 cases has confirmed this view. Naturally the instrument has its limitations, but the fact that it has largely replaced the forceps in several countries on the Continent, whose results compare favourably with our own, must speak for itself.—I am, etc.,

A. J. M. CAVENAGH.

Brecon, South Wales.

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- ² Cavenagh, A. J. M., *Practitioner*, 1965, 194, 396.

Prevention of Rh-haemolytic Disease

SIR,—We read with interest Professor C. A. Clarke's article (7 October, p. 7) and the leading article (same issue, p. 3) on prevention of Rh-haemolytic disease. In this hospital we have been using 1-ml. doses of Rh human immunoglobulin ("RhoGam," Ortho, U.S.A.) for the past 18 months in a trial to prevent Rhesus sensitization in women at risk.¹ To date we have injected 45 patients. The following case is of interest, particularly in the light of Professor Clarke's article.

The patient's first pregnancy ended in an abortion at 12 weeks in February 1965. Evacuation of the uterus was required, but no transfusion. Her blood group is A Rh-negative, genotype cde/cde (rr) and no antibodies were present; and that of her husband A Rh-positive, CDe/CDe (R₁ R₂).

In her second pregnancy (expected date of delivery 22 April 1966) she received an intramuscular injection of antirubella gammaglobulin at the 11th week. The pregnancy proceeded normally, no versions were performed, and no antibodies were present at the 32nd week. She had an easy forceps delivery at 41 weeks' maturity, there being no difficulty in the third stage. Cord blood showed direct Coombs test negative, and the baby's group was A Rh-positive (D); maternal blood sample two hours post delivery showed a foetal cell count per 50 low-power fields of 15, and no antibodies were detected. In view of the leak of foetal cells she therefore received an intramuscular injection of 1 ml. RhoGam 32 hours after delivery; there was no reaction, local or general. Foetal cell counts after injection showed that the cells had been completely cleared within 24 hours, and remained clear; antibody test at six weeks showed a titre of two; and four-months and six-months post-injection tests showed no antibodies.

Between her second and third pregnancies she had six normal periods until the last one on 21 December 1966. She received no injections of any description, and there was no question of a miscarriage.

In her third pregnancy (expected date of delivery 28 September 1967) no antibodies were detected at the 22nd or 32nd weeks of pregnancy; external cephalic version was performed on three occasions, at the 37th, 39th, and 40th weeks. She had a normal delivery at term of a living child after a labour lasting five and a half hours. The direct Coombs test on the cord blood was strongly positive; the baby's group A Rh-positive (D); the serum bilirubin 1.75 mg./100 ml., and the haemoglobin 14.89 g./100 ml. The maternal blood taken two hours after delivery showed no foetal cells; anti-C + D

antibodies were present—complete antibodies to a titre of 16, incomplete to a titre of 256.

It may be of significance that the immunized case in the Liverpool trial, and in ours, both had antirubella globulin during the previous pregnancy. We feel confident that the immunoglobulin we use, which has an anti-D titre of 20,000 to 80,000 by Coombs technique, cleared the foetal erythrocytes from the maternal blood, as four counts subsequent to its injection failed to reveal any circulating cells. Whether the globulin prevented sensitization at that time is open to question, though no evidence of antibody formation appeared in the interval between the second and third pregnancy.

Another point of interest is whether the rapid rise of antibodies after the 32nd week was related to the three external versions performed, which could have caused significant transplacental foetal bleeds.

The success figures Professor Clarke quotes from the various centres are so impressive that it seems important to investigate every failed case in detail in order to discover the cause.—We are, etc.,

N. P. WALSH.

S. R. HEWITT.

Portiuncula Hospital,
Ballinasloe, Ireland.

REFERENCE

- ¹ Walsh, N. P., Sr. Simon Peter, and Hewitt, S. R., *J. Irish med. Ass.*, 1966, 554, 190.

Acute Industrial Poisoning

SIR,—The use of poisonous gases in warfare has been rightly condemned, but it seems that we may not be so fortunate to avoid being gassed in peacetime. Recently property not far from a hop-processing plant in Kent was inundated by clouds of sulphur dioxide gas emanating from the plant. The immediate result was the defoliation of apple-trees, burning of grass, and withering of rose and fruit bushes. Those people who were in the way of the gas experienced distress in breathing. After-effects are difficult to assess.

In my own case a minor viral infection a week or so later turned into an acute bronchitis requiring several weeks' sick leave and treatment with antibiotics. It appears the growers are well aware of the destructive nature of this gas, as they make sure their own crop is fully gathered before liberating the sulphur dioxide. It would be interesting to know if any of your correspondents have experienced this form of acute industrial poisoning. Clear Air Acts aim to protect city populations from chronic poisoning due in some measure to sulphur dioxide. It would seem that some legislation is needed to protect the public against an acute hazard of this sort.—I am, etc.,

East Farleigh,
Nr. Maidstone, Kent.

DENIS APIVOR.

Vasectomy for Contraception

SIR,—In view of the increasing public interest in vasectomy more surgeons are being approached to perform this operation. As a surgeon who has been working in a male infertility clinic for 20 years I would like to point out some of the pitfalls.

Counsel's opinion for the Medical Defence Union states that the operation is illegal if done only for the purpose of birth control.¹ To cover the surgeon legally it is essential to have a second opinion from a general practitioner, a psychiatrist, or a gynaecologist to the effect that further pregnancies are likely to endanger the mental or physical health of a man's wife.

The surgeon should discuss the operation of bilateral vasectomy, and its implications, with both partners, and obtain the written consent of both husband and wife to the operation.

At operation it is wise to excise 1 cm. from each vas deferens, and both open ends should be ligated with linen thread or silk, rather than catgut. If the excised portions are sent for microscopic examination there can be no doubt that the vas deferens has been tied. Congenital abnormalities of the vas deferens are more common than one thinks.² One per cent. of all men attending an infertility clinic have bilateral absence of the vas deferens; a smaller number have absence of one vas. I have found one case of duplication of the vasa, and probably more will be found as vasectomy becomes more common.

After bilateral ligation of the vas deferens semen analysis must be carried out at monthly intervals for some months to make sure that the seminal reservoir is completely empty of spermatozoa. The patient must be told that contraceptive measures are required until he has had at least one azoospermic ejaculate. If spermatozoa in fair numbers persist for more than three months the possibility of faulty technique, or duplication of the vasa, must be considered and an exploratory operation performed.—I am, etc.,

DONALD YOUNG,

Warrington Infirmary and
Dispensary,
Warrington.

REFERENCES

- ¹ *Medical Defence Union Annual Report*, 1949.
- ² Wells, C., and Kyle, J., *Scientific Foundations of Surgery*, 1967, p. 358. London.

Institutional Care of the Mentally Subnormal

SIR,—Professor T. McKeown and Dr. Ian Leck have recently reminded us (2 September, p. 573) that numbers of patients in hospitals for the mentally subnormal are not in need of hospital care. Attempts are being made in many areas to transfer such patients to the care of local authorities, and local authorities are increasingly providing hostels to meet this need. Transfers from hospital to local authority hostels are typically arranged by having local authority representatives interview selected patients, both to assess their suitability as hostel residents and to enable an estimate to be made of the number of hostel places that the local authority need provide.

At the present moment, for a variety of reasons (delays in building programmes, etc.), a considerable proportion of patients accepted for local authority hostels tend still to be on waiting-lists three or more years after their initial interview. Delays such as this are not something with which the mentally subnormal can happily cope, and from interviews I have conducted with 34 such patients on a waiting-list for one local

authority hostel it is clear that they are on the whole very disappointed people indeed. Instead of interviewing patients and accepting them for "hostel X to open in four years' time," can we not postpone the interviews until hostel places are actually available? It may be argued by local authorities that patients must be interviewed in advance in order to plan the number of hostel places needed, but statistics for planning purposes can in fact be obtained by other means (vide McKeown and Leck). It is hoped that the present situation, whereby numbers of patients are suffering disappointments through transfers to local authority hostels not being speedily effected, will not be allowed to persist.—I am, etc.,

ALISON C. CAMPBELL.

Department of Social and
Preventive Medicine,
University of Manchester.

SIR,—I would like to comment on your leading article "Place of the Mentally Retarded" (2 September, p. 567) and the article by Professor T. McKeown and Dr. I. Leck (same issue, p. 573), but lack of space restricts me to a few remarks only.

Ever since the inception of mental health departments of local authorities increasing numbers of mentally handicapped children have been brought to the authorities' attention with subsequent requests for their disposal. From the practical aspect, therefore, more placements will have to be found for them in the near future, both in the community and in hospitals. You quote that large numbers of institutionalized mental defectives could be placed in open employment. The implication that any chronic institutionalized patient could be easily integrated into community life is somewhat contrary to past experiences. It applies even more so to the severely mentally subnormal patient who constitutes a large proportion of chronic institutionalized patients of most hospitals for mental subnormality. As a considerable number of them suffer from an additional physical disability, an even greater obstacle to open employment is thereby created. This was discussed elsewhere.¹

If we consider the high-grade subnormal patients, especially those without physical handicaps, then their place should certainly be in the community. But let it be stated here there is an understandable reluctance on the part of hospitals to discharge their brighter patients, the ones for whom community facilities were essentially designed, because these patients fulfil a most useful function in the daily running of the hospitals with their present-day acute staff shortages. Professor McKeown and Dr. Leck suggest that responsibility for training should be transferred from the local health authority to the education authority and a group of resident patients transferred to the local health authority. As for educationally subnormal (E.S.N.) pupils these are already under the care of the education department, although some children needing psychiatric advice are sometimes reluctantly and belatedly sent to child guidance clinics.

When, however, we consider the "ineducable" pupil (an objectionable term) we are confronted with quite a different problem. He represents the lower grades of mental subnormality, and the present system of junior training schools and attached special care units under the

aegis of the mental health departments provides the most suitable environment for such a handicapped child. I would therefore make a plea for the retention of mentally subnormal in junior training schools under medical direction, but suggest closer collaboration with the education department for readier consultation and referral from one professional discipline to the other. What about those children who reach the arbitrary school-leaving age for handicapped pupils at 16 years? If junior training centres were administered by education departments do Professor McKeown and Dr. Leck suggest that the same departments should continue to care for those post-school adolescents when they enter adult training centres—quite a novel function for an education authority—or should mental health departments then take over with the introduction of yet another new set of welfare officers?

One other point requires mentioning. The staff of child guidance centres should be brought together under one department, not Education, as at present, where all services for the adolescent cease when he reaches the age of 16, but Health, which could thus form a more closely knit unit in conjunction with the local mental health department. This team then would continue to counsel and guide the teenage patient during those formative and impressionable years until he qualifies for treatment and supervision by an adult department. It should be noted that facilities for the older teenager are almost non-existent at present and by the time he has reached the age of 16 he is "either too old for the child guidance clinics or too young for adult departments of hospitals," and thus receives little or no counselling or guidance.

The suggestion made in your leading article which may cause difficulties in practice refers to the mixing of patients with various types of mental disabilities in one centre. The behaviour and temperament of subnormal people is often totally different from that of trainees suffering from other mental afflictions. Further, one trusts that the remark about the transfer of resident patients to local authority establishments will not be construed to mean the wholesale transplantation of inmates of chronic hospital wards into the community. It should be reiterated that the mentally subnormal, with or without physical defects, who require nursing attention or medical care cannot be contained in any community hostel, and owing to the chronicity of their mental state require hospitalization for the remainder of their lives.—I am, etc.,

London N.3.

U. P. SEIDEL.

REFERENCE

- ¹ Seidel, U. P., *Int. J. soc. Psychiat.*, 1966-7, 13, 42.

Hypercalcaemia and Malignant Tumours

SIR,—Although he found it "longish," Mr. W. M. Keynes (23 September, p. 799) might not have found the discussion on the mechanism of the hypercalcaemia in malignant tumours "less interesting" than the rest of our paper (2 September, p. 590) if he had read it with attention. His statement that "hyperplastic parathyroid glands have not been found in such patients" is contradicted by our quotation of the work of Massaro and Owen,¹ and of Krane and Roth,² who found chief-cell hyperplasia. We quoted an additional point in favour of a mechanism mediated via the parathyroids³ in that removal of these glands has caused lowering of the serum calcium.

Mr. Keynes is right that some tumours produce a parathyroid hormone-like substance,

as shown by direct evidence quoted by him and by ourselves, but this does not remove the possibility that in the other cases the effect is produced via the parathyroids. His parade of facts such as the prompt fall in the serum calcium after surgery, the absence of skeletal metastases, and the hypophosphataemia, all of which could equally well occur with either mechanism, and his reference to Albright's suggestion in 1941⁴ that tumours of non-parathyroid origin might produce a substance with the activity of this hormone avail nothing. The latter prognostication merely indicates how far advanced in his thought this individual was, and in fact no such hormone was found in that case by the methods then used. Furthermore, in so far as it is not totally irrelevant owing to the different hormone system involved, Mr. Keynes's reference to the work of Liddle *et al.*,⁵ who found corticotrophin, or a closely related polypeptide, in tumour tissue, supports the possibility of an indirect hormonal effect.

As we stated, direct evidence alone in each case will be the final answer. We would be genuinely grateful if Mr. Keynes, if he forgives us our sharpish reply, or anyone else, could assay the tumour in our case for hormonal activity, as we still have half of it in the deep-freeze. The patient remains entirely well three years after operation.—We are, etc.,

W. E. MEDD.

Kingston Hospital,
Kingston-upon-Thames,
Surrey.

N. J. STRICKLAND.

Guy's Hospital,
London S.E.1.

A. M. BOLD.

St. Thomas's Hospital,
London S.E.1.

REFERENCES

- Massaro, D. J., and Owen, J. A., *Amer. Rev. resp. Dis.*, 1962, 85, 727.
- Krane, S. M., and Roth, S. I., *New Engl. J. Med.*, 1964, 270, 898.
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- Case Records of the Massachusetts General Hospital, 27461, *New Engl. J. Med.*, 1941, 225, 789.
- Liddle, G. W., Island, D. P., Ney, R. L., Nicholson, W. E., and Shimizu, N., *Arch. intern. Med.*, 1963, 111, 471.

Swallowed Dental Reamer

SIR,—It is common practice to adopt a conservative regimen in the management of swallowed sharp foreign bodies, surgical removal being indicated if the object does not pass or if signs of penetration occur. This report of an unusual dental accident illustrates the value of early accurate radiological diagnosis as an indication for emergency surgery.

A 28-year-old ex-dental nurse was having a root filling performed when the dentist dropped the reamer into her mouth (Fig. 1). She realized the dangers of swallowing and attempted not to do so. However, the reamer could not be found and the patient was therefore sent to the local hospital, where x-rays of the chest and abdomen were interpreted as showing no foreign body. Two hours after



FIG. 1.—Magnified view of dental reamer. Actual length 3.1 cm. Diameter of haft 0.5 cm. Though superficially resembling a Malay Kris, it is a fine spiral drill.

returning home the patient began to experience ill-defined colicky epigastric pain and sought a second opinion. Physical examination indicated no abnormality apart from minimal epigastric tenderness. A plain abdominal x-ray film showed the shadow of the reamer in the right abdomen (Fig. 2). There was no free intraperitoneal gas. Although the reamer lay in a position corresponding to the vertical part of the duodenal loop, the lateral projection showed it too far anteriorly to be in the duodenum. Therefore the patient was given a mouthful of barium. Further films showed the reamer fixed in the pyloric antrum, the wall of which it had penetrated (Fig. 3). Emergency laparotomy revealed it firmly embedded in the wall of the antrum, which was impregnated with

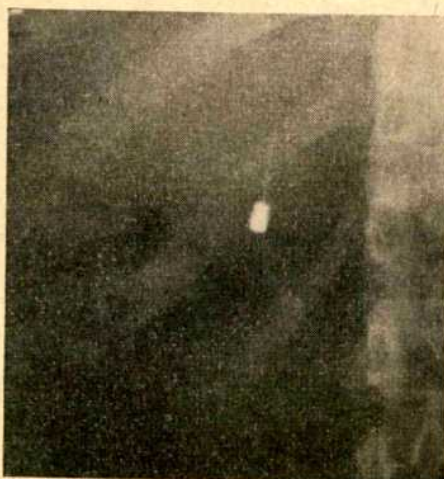


FIG. 2.—Supine abdominal film showing reamer lying vertically to the right of the spine. Is it in the duodenum?

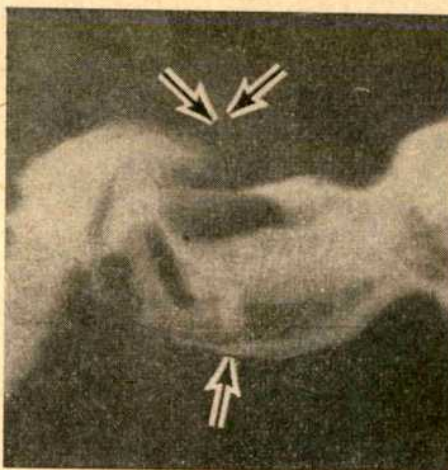


FIG. 3.—Barium meal film (rotated view) showing reamer having penetrated wall of antrum. Indication for immediate operation.

dental amalgam. The reamer and adjacent wall were removed, and the patient made an uninterrupted recovery, leaving hospital on the fifth postoperative day.

This experience demonstrates that barium contrast examination is a safe, speedy, and accurate method not only in assessing location but also penetration of the bowel wall by a sharp pointed object.—We are, etc.,

R. A. D. BOOTH.

D. K. M. TOYE.

J. ALEXANDER WILLIAMS.

General Hospital,
Birmingham 4.

Dyspepsia

SIR,—Dr. N. F. Coghill's paper on dyspepsia (14 October, p. 97) condenses a great deal of clinical wisdom into a small space. The presence of one or more of the following symptoms or signs could also be helpful in pointing to a demonstrable organic cause in the differential diagnosis between "organic dyspepsia" and that which remains of uncertain cause after investigation:

- (1) Abdominal pain sufficiently severe to wake the patient up.
- (2) Localized abdominal pigmentation from frequent use of a hot-water bottle.
- (3) Waterbrash (defined as a sudden outpouring of saliva).—I am, etc.,

H. J. GOLDSMITH.

Liverpool Regional Urological
Centre,
Sefton General Hospital,
Liverpool 15.

Paraproteins and Bence Jones Protein

SIR,—Dr. E. N. Wardle (7 October, p. 56) is quite right in that the Bence Jones protein excreted in the urine does not absolutely represent its total daily production, but to what extent in man is unknown. In the very recent paper he quoted¹ it was clearly shown that only some 20% of a 1–2 μ C intravenous dose of ¹³¹I-labelled Bence Jones protein appeared in the urine of mice. Much of the remaining 80% appeared to have been catabolized by the kidneys of the mice. However, the amount of protein involved is not stated; it may have been only a milligram or so, and no effect of dose-load was investigated.

In the other paper he quoted² it is also clear that, with apparently normal renal function, two patients excreted only 10% of their slight Bence Jones production, up to 3 g./day being catabolized. With the enforced retention and high blood levels following on renal failure three other patients catabolized up to 50 g./day, presumably throughout the body tissues. However, with Bence Jones proteinuria of 1–20 g./day in the absence of renal failure (as in most of our patients) I can find no data to show how much Bence Jones protein is catabolized, or how important is the role of the human kidney. Certainly among very many patients with renal diseases due to causes other than myelomatosis I have detected no gross excess of light chain excretion (above 10 mg./day). Therapy with γ G-globulin did not result in any significant increase in light chain excretion,³ and Putnam's⁴ original work showed that Bence Jones proteinuria reflected largely the *de novo* synthesis of Bence Jones protein, not a catabolic breakdown product of whole myeloma immunoglobulin.

Thus Bence Jones proteinuria does indicate abnormal synthesis. In the M.R.C. Myeloma Trial survival of patients producing only Bence Jones protein is already significantly worse than in those with comparable Bence Jones proteinuria but also with a parent myeloma protein. Thus the latter patients produce more paraprotein daily, run the same risk of renal failure, but, presumably because their myeloma cells can still make some whole immunoglobulin, they do not appear to be as malignant as the former. This is the as yet unpublished evidence for the statement that the shift to only "the production of

Bence Jones protein indicates further differentiation" (misprinted as "differentiation" under Fig. 2).¹ Irrespective of the proportion catabolized, Bence Jones proteinuria seems to carry a worse prognosis. I hope this has clarified the issue.—I am, etc.,

JOHN R. HOBBS.

Royal Postgraduate
Medical School,
London W.12.

REFERENCES

- 1 Wochner, R. D., Strober, W., and Waldmann, T. A., *J. exp. Med.*, 1967, 128, 207.
- 2 Solomon, A., Waldmann, T. A., Fahey, J. L., and McFarlane, A. S., *J. clin. Invest.*, 1964, 43, 103.
- 3 Vaughan, J. H., Jacob, R. F., and Gray, B. A., *J. clin. Invest.*, 1967, 46, 266.
- 4 Putnam, F. W. and Miyake, A., *J. biol. Chem.*, 1958, 231, 671.
- 5 Hobbs, J. R., *Brit. med. J.*, 1967, 3, 699.

* We regret this error.—Ed., *B.M.J.*

Glucagon and Intravenous Glucose Tolerance

SIR,—Mr. D. A. Turner and his colleagues (21 October, p. 145) claim that "it is unlikely that glucagon-induced elevation of plasma insulin levels is responsible for the superiority of oral over intravenous glucose tolerance." They may be right, but their own data are inconclusive. Thus the two individuals in their series who received the low-dose glucagon infusions (0.6 µg./min.) showed only small increases in blood sugar levels compared with the control infusion, yet showed definite differences in plasma insulin levels. Had the authors tried an even lower rate of glucagon infusion, it is at least conceivable that the insulinotropic effect might have remained, while the glycogenolytic effect was lost. It is conceivable because that is the trend suggested by the authors' own figures.—I am, etc.,

R. J. JARRETT.

Department of Medicine,
Guy's Hospital Medical School,
London S.E.1.

Intestinal Spirochaetosis

SIR,—In reference to the letter by Dr. S. C. Dyke (21 October, p. 176) we wish to point out that Dr. A. G. Shera described a form of granular proctitis, which he termed "the strawberry lesion" and which he claimed was due to Vincent's organisms originating in an oral or pharyngeal infection. He also found that many of the patients had vitamin-C deficiency. A fully illustrated account is found in the *British Journal of Surgery*.¹

The connexion between this condition and the one we recently described (16 September, p. 718) remains to be established. The organism we described averages only 3 µ in length and appears as a pure growth on the epithelial surface, while the spirochaete Dr. Shera found in swabs of the rectal lesions averaged 11 µ in length and was invariably associated with fusiform bacilli. This perhaps indicates that these conditions are not identical.—We are, etc.,

W. A. HARLAND.

F. D. LEE.

Pathology Department,
Western Infirmary,
Glasgow W.1.

REFERENCE

- 1 Shera, A. G., *Brit. J. Surg.*, 1962, 50, 68

SIR,—Drs. W. A. Harland and F. D. Lee have misinterpreted normal intestinal microvilli cut tangentially as spirochaetes ("Intestinal Spirochaetosis," 16 September, p. 718). Their original interpretation "staining of the brush border" is correct.—I am, etc.,

CLAUDE O. BURDICK,

Chief, Anatomic Pathology,
Department of the Army,
Pathology Service,
William Beaumont General Hospital,
El Paso, Texas, U.S.A.

Dysmenorrhoea

SIR,—Your leading article (21 October, p. 125) repeats several fallacies which I had hoped were long interred. The "psychogenic" theory of dysmenorrhoea may be convenient for the doctor, but it is hardly comforting to the unfortunate victim of crippling uterine colic to be told that "it's all up here" when she knows "it's all down there." And therapeutically the theory is of little or no value. I had also thought that the "hypoplasia of the uterus" and "stenosis of the cervix" theories were nowadays totally abandoned. Neither has any anatomical or pathological basis. It is similarly disappointing to see aspirin and a "healthy psychological outlook" (whatever that may mean) and "attention to exercise" still prescribed. Nothing depresses a patient more than such predictably ineffective treatment.

The basis of the pain, as you somewhat reluctantly agree, is hypercontraction of the uterus, postulated by Muir 30 years ago, and the coincident ischaemia still remains the most satisfactory explanation. The cause of the myometrial hypersensitivity is less precise, but it is almost certainly connected with inflammatory and degenerative changes found in the tracts and ganglia of presacral nerves removed from these patients.¹ This is supported by the beneficial effects of sympathectomy, which acts not only by severing the sensory pathways but also by cutting off contractile efferents. Dydrogesterone acts similarly by partially paralysing the myometrium. A great many patients are relieved by the contraceptive pill, and this must remain the initial treatment of choice. For those unable to tolerate hormone therapy dilatation of the cervix is generally advocated. But this procedure is effective only when the endocervical sympathetic plexus is ruptured, and this is attained only by using the higher grades of bougies—a process which you rightly associate with possible future incompetence. In any case, it helps only a quarter of the patients. Much superior is alcohol-injection of the pelvic plexus.² This is simple and safe with proper technique, and gives a cure rate of 70%.—I am, etc.,

London W 1.

A. DAVIS.

REFERENCES

- 1 Davis, A. A., *J. Obstet. Gynaec. Brit. Emp.*, 1933, 40, 481.
- 2 — *Clin. Obstet. and Gynaec.*, 1963, 8, 754.

Railroading in Retinal Vessels

SIR,—Dr. P. J. Tomlin's interesting comments on this phenomenon (16 September, p. 722) deal with cases of restored circulation after cardiac arrest.

It may be worth pointing out that it is incorrect to assume, as is commonly done, that "railroading" necessarily signifies a

state of cardiac arrest. I recall, when a houseman in neurosurgery, being informed during the night that an adolescent girl had died. She had been in deep coma with an incurable intracranial lesion, and was on continuous positive pressure respiration. On examining her, heart sounds were inaudible. The fundi showed the characteristic fragmentation of blood in the vessels, which is often said to be a sign of death and *ipso facto* of cardiac arrest. However, the fragments were moving along in one direction in a faintly pulsatile fashion, and cardiac arrest was clearly not present. Later, during the same night, I was again notified of the patient's apparent death, but it was eerie to find as before that the movement of the blood fragments showed persistence of a sluggish circulation with a regular though faint pulsation. It was only during the following morning that death was deemed to have finally occurred.—I am, etc.,

Halliwick Hospital,
London N.11.

P. D. L. JOHN.

M.A.O. Inhibitor Headache

SIR,—Dr. C. A. H. Watts has reported (28 October, p. 238) two cases where blood-pressure readings were found to be near-normal soon after onset of severe headache associated with monoamine oxidase inhibiting drugs. His observations provide interesting confirmation of an earlier report¹ suggesting that the blood pressure is not always raised in patients taking monoamine oxidase inhibiting drugs who develop such headaches.

It may not be generally known that the majority of these headaches, which can be not only devastatingly severe but also protracted over some days, can be swiftly relieved by the slow intravenous injection of 5 mg. phenolamine (Rogitine). Furthermore, it is interesting that this measure appears to be as effective in the normotensive¹ as in the hypertensive setting.²—I am, etc.,

R. K. RONDEL,

Medical Adviser,
Ciba Laboratories Ltd.
Horsham, Sussex.

REFERENCES

- 1 Bethune, H. C., Burrell, R. H., and Culpin, R. H., *Lancet*, 1963, 2, 1233.
- 2 — and Ogg, G. J., *Amer. J. Psychiat.*, 1964, 121, 245.

Early Discharge of Maternity Patients

SIR,—Early discharge of maternity cases is now an established procedure in many areas (26 August, pp. 517 and 520); the advantages and disadvantages are well known, and there is no need to recount these. Above all, in areas where there is a shortage of beds it is a means of offering the safety of confinement in hospital to a large number of women. Mothers at high risk are more willing to enter hospital knowing they can return home early, and the problem of the home which is inadequate for confinement but adequate for nursing is solved. What was an emergency arrangement has proved so popular with patients that there is no doubt it has come to stay. However, for the smooth running of such a scheme good planning is necessary, and these plans will depend on the structure of the community to be served.

Thorpe Coombe Maternity Hospital is in Walthamstow in the outer London area. It has a total of 70 beds for antenatal care, first stage of labour, and the lying-in period. Since planned early discharge was introduced four years ago confinements have increased to over 2,000 annually. The hospital serves three local authorities, and for the success of the scheme close co-operation is essential. Patients for early discharge are selected during the antenatal period by a consultant. The request may come from the mother herself or her family doctor, or the hospital may ask if she is able to be nursed at home after 48 hours. Selected mothers sign an agreement and provide the hospital with the name and telephone number of their doctor and district midwife. In all cases the home is visited and assessed by a district midwife, thus ensuring her co-operation, and the general practitioner and local authority are notified. These plans having been made well in advance, discharge from hospital can proceed as a smooth routine. The antenatal care of the patient is shared by the hospital, general practitioner, and district midwife, so that she is known to all concerned.

Before discharge all mothers and infants are seen by the obstetric registrar, and in case of doubt are referred to a consultant obstetrician or paediatrician. If necessary they are detained in hospital for longer than 48 hours. Each morning the ward sister notifies a clerk of the patients for early discharge and she then informs the family doctor and midwife. The patient, who has been up and about, leaves by private transport accompanied by a relative. This has proved a satisfactory arrangement and an ambulance is seldom required. Very few patients have needed readmission to hospital. In one of the areas concerned these mothers are cared for by a retired midwife working part-time, in the other two areas by the full-time midwives. In addition to mothers booked for early discharge those booked for home confinement who are admitted in late pregnancy or labour are allowed home early provided they are fit.

The arrangements described were arrived at by trial and error accompanied by good will. They are simple and require no elaborate administrative machinery. They provide additional safety for many mothers and infants, and this makes the additional work worth while.—I am, etc.,

D. JOAN BRYSON.

Thorpe Coombe Maternity Hospital,
Walthamstow, London E.17.

Fallacies in Four Fevers

SIR,—I support the suggestions for shortening the official period of infectivity of childish fevers (7 October, p. 41). But might it not be better to go even further?

School epidemics are poorly controlled by exclusion of children with infectious fevers. It is much less inconvenient, and often less unpleasant as well, to suffer these illnesses when young. Therefore I believe it would be better to abandon ineffective attempts at control, and instead try to infect as many children as possible. In order to do this I propose that *general policy* be one of inclusion, rather than of exclusion, of well but infectious children with rubella, mumps, and chicken-pox. Infectious measles children are not in any case well enough for school.

This policy would only be general, and schools could at any time declare a season of exclusion during important exam terms and the like. Families with special reasons for not wanting an infectious member would keep their children from school, but should in logic exclude also all uninfected members from public places during the epidemic.—I am, etc.,

Bury St. Edmunds,
Suffolk.

JOHN E. HODGKIN.

SIR,—Professor R. S. Illingworth's short article (7 October, p. 41) was as usual full of common sense, and I am in complete agreement with his conclusions. With regard to school exclusion of cases and contacts of the common infectious diseases, the following recommendations were adopted in Oxford in February 1963:

Disease	Minimum Period of Exclusion from School provided child appears well	
	Patients	Family Contacts
Chicken-pox	Seven days from appearance of rash; all the scabs need not have separated.	There is no routine exclusion of contacts of any of these infectious diseases but individual children may be excluded on the advice of a general medical practitioner or a school medical officer.
Dysentery (Sonae)	Until complete cessation of diarrhoea.	
Measles	Seven days from appearance of rash.	
Mumps	Until disappearance of all swelling.	
Rubella	Five days from appearance of rash.	
Scarlet Fever	Until clinical recovery.	
Whooping-cough	Until clinical recovery.	

There has been no subsequent occasion on which there has been cause to regret departing from the more rigid criteria laid down in the Ministry of Education Memorandum 1956, which is of course advisory rather than mandatory.—I am, etc.,

Oxford.

JOHN F. WARIN,
Medical Officer of Health,
City of Oxford.

Treatment of Poisoning by Anti-depressant Drugs

SIR,—Dr. A. B. Masters (30 September, p. 866) and Dr. C. A. Fuge (14 October, p. 108) both draw attention to sudden relapse and death after seeming recovery from the effects of an overdose of a tricyclic drug. In their original paper (9 September, p. 663) Dr. C. M. Steel and his colleagues also noted this unusual outcome.

It is of great practical and theoretical interest to know the cause of these sudden relapses. They may perhaps be directly caused by persistence of the drug or one of its metabolites, but it is also possible that they result rather from some special feature of the drug-induced illness, and only indirectly from the drug itself. Thus Dr. Steel and his colleagues warn against the risk of precipitating circulatory collapse by allowing patients to be physically active as soon as they seem to have recovered from the overdose. The drug leaves a cardiovascular sensitivity behind it, and physical strain might cause relapse.

I wish to draw attention to the possibility of permanent brain damage which may arise

where there is a long delay in instituting treatment. Status epilepticus, hypotension, and hyperpyrexia damaged the brain in the following case:

A normal boy weighing 12.7 kg. and aged 14 months was able to crawl and use five distinct words. He opened a screw-cap bottle and took four to eight tablets of desipramine hydrochloride (Pertofran, Geigy, 100-200 mg.). His parents put him to bed, where next morning he was found to be unrousable. When he reached hospital, 15 hours after his overdose, he was in status epilepticus, with clonic convulsions every five minutes, a weak irregular pulse (40/min. at apex), blood pressure unrecordable, and a rectal temperature of 41° C. Electrocardiogram showed a chaotic mixture of ventricular and supraventricular tachycardia with wide QRS complexes.

Intravenous thiopentone and 100 mg. hydrocortisone were given. Fourteen hours after admission fits had ceased, the blood pressure was 80/50 mm. Hg, pulse was 190 at the apex, and the E.C.G. showed regular ventricular tachycardia. Procaine amide, 50 mg. intravenously over five minutes, produced a slower but irregular ventricular rhythm. Next morning, however, systolic blood pressure was 100 mm., pulse 120 regular, and E.C.G. showed sinus rhythm, but the patient remained unrousable. Two days later convulsions returned, and 15 were noted in the next 13 hours in spite of renewed thiopentone. They ceased when 14 g. urea was given intravenously over half an hour (as 30% "Urevert") to reduce cerebral oedema.

Thereafter the child made only a partial recovery. After 19 days an E.E.G., kindly performed by Mr. D. Lee (Warneford Hospital), showed a medium voltage arrhythmic slow wave pattern in all leads without evidence of any cortical activity. When seen five months later he lay sucking his thumb, rhythmically emitting a constant feeble whine if it was pulled out of his mouth. He could take his weight on his legs, but could not maintain his balance for standing or sitting. His pupils reacted to light, but there was no comprehension of visual stimuli. He opened his mouth to receive food when a spoon touched his lips. Hunger and discomfort caused wailing. Pain made him turn from supine to prone in evasion.

The special feature of this case was the long delay in instituting treatment, as in Dr. Masters's case.

I am grateful to Dr. Desmond MacCarthy for permission to publish this case.

—I am, etc.,

Woodstock,
Oxford.

W. R. EDWARDS.

Acute Necrotizing Encephalitis

SIR,—In your leading article (30 September, p. 812) referring to a recent report by two of us¹ on eight cases of acute necrotizing encephalitis you state that, "If an exploratory biopsy is carried out, however, necrotic brain only will be found. . . ." This might seem to imply that cerebral biopsy is of no value in establishing the diagnosis of acute necrotizing encephalitis, when in fact the reverse is the case. In four of the five original cases, and in two more recently encountered, examination of a cerebral biopsy disclosed the characteristic histological features of acute necrotizing encephalitis.

You also observe that it is still uncertain if acute necrotizing encephalitis is due to direct virus invasion or represents yet another antigen-antibody reaction, and whether herpes virus is the only cause or the only one so far demonstrated. We have now encountered 10

cases in which the clinical and pathological features were typical of acute necrotizing encephalitis. From five of these brain biopsy material was examined by virus isolation studies and four yielded herpes simplex virus; three of these have been previously reported.² In all seven cases from which suitable tissue was available for electronmicroscopic study virus particles belonging to the herpes group have been identified.³ This seems convincing evidence that most cases of acute necrotizing encephalitis are due to direct invasion of the brain by herpes simplex virus.

The possibility of the successful treatment of acute necrotizing encephalitis with idoxuridine⁴ makes it vital to establish the diagnosis of herpes simplex encephalitis as early as possible in the disease before neuronal necrosis is advanced. As the results of virus isolation, the testing of paired sera for complement-fixing antibodies, and electronmicroscopic examination are unlikely to be available for several days, histological examination of brain biopsy material is likely to remain the most important means of making an early diagnosis. Fluorescent antibody studies for herpes simplex virus may also be of considerable value in making a rapid preliminary diagnosis, but their reliability in herpes encephalitis has not yet been adequately assessed.—We are, etc.,

J. HUME ADAMS.

W. BRYAN JENNETT.

Institute of Neurological
Sciences,
Glasgow.

CONSTANCE A. C. ROSS.

Regional Virus Laboratory,
Ruchill Hospital,
Glasgow.

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Diet and Diverticulitis

SIR.—One is well aware of the important contribution to the understanding of diverticulosis coli by Mr. N. S. Painter (12 August, p. 434), and his studies on the pressures generated by segmentation.¹ However, the constant fact remains that both sigmoid volvulus and diverticulosis occur in Ethiopians on the same diet and under the same conditions, although admittedly the former is much more commonly recognized. It is incorrect to state that these "African natives living on a tribal diet do not develop diverticulosis."²

Dr. B. Yovanovich in a busy hospital practice reports an unchanged radiological incidence of approximately 30 cases annually of diverticular disease in Ethiopians.³ These barium enema studies show great variation in the length and diameter of the colon, and there must be many other factors than the simple theory advanced by Drs. Cleave and Campbell of the effects of refined and unrefined carbohydrate eating habits.—I am, etc.,

ERIC GOULSTON.

Faculty of Medicine,
Haile Selassie I University,
Addis Ababa, Ethiopia.

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Courtesy between Colleagues

SIR.—A few years ago¹ I wrote to you complaining about the Institute of Directors' Medical Centre examining patients of mine without my reference. This produced some interest from *The Times*,² and also from other doctors who were kind enough to write to me supporting my complaint.

Soon afterwards I met the director of the institute, and he promised to do his best to get in touch with the general practitioner before examining his patients. I regret that this has not yet happened with my patients, and I have been concerned to find that they

still receive a carbon copy of the verbose report sent to me. Recently I spent a rather difficult time going through such a report, paragraph by paragraph, with the patient concerned, and doing my best to explain it and reassure him.

Is the long-established tradition of courtesy and contact between medical men passing?—I am, etc.,

P. B. SCHOFIELD.

Walton-on-Thames,
Surrey.

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Prospects for Hospital Doctors

SIR.—While the Health Departments are to be congratulated for attempting to give some guidance on prospects by publishing the official figures for 1965 and 1966 (*Supplement*, 24 December 1966, p. 240, and 7 October 1967, p. 3), the profession should not be blinded by their star-studded appearance or fail to compare these sets of figures with those found in HM.64(94) [a Ministry of Health circular in 1964 on hospital medical staffing structure]. Such an exercise is thoroughly depressing.

In terms of whole-time equivalents (W.T.E.) boards in England and Wales considered an additional 1,806 consultant posts ought to be created by September 1968. This figure of 1,806 was scaled down to the so-called median figure of 1,095, which incidentally had the effect of reducing the target for additional posts in general medicine from 194 to 113, in general surgery from 150 to 64, in pathology from 201 to 109, in psychiatry from 281 to 205, and in obstetrics and gynaecology from 109 to 48—to mention a few of the larger specialties. From the time the boards made their returns in 1964 to September 1966 406 W.T.E. new consultant posts had been created and for the three-year period September 1963 to September 1966 this gave a figure of 603.9 W.T.E. new posts. This left the need to create a further 689 new posts by September 1968 if even the scaled-down figure of 1,095 (406+689) was to be reached.

It is to be noted that in the Ministry's recent tables the column showing expected consultant vacancies is based on the sum of the average annual expansion rate over the last three years plus the expected existing posts which might fall vacant (if it is a good year for the actuary). The average consultant expansion over the three-year period 1963–6 was 202. Projected to September 1968 this should add 404 posts (if the present rate is maintained)—285 short of the already scaled-down target and 996 short of the target the boards themselves thought should be aimed at in the original reviews.

Recently I investigated what plans hospital boards had made for expansion in psychiatry over the next three years. Senior administrative medical officers were extremely helpful, but the results of this survey painted a very different picture from that suggested by the Ministry's charts and in no way reached the expansion figures these anticipate. In summary, if boards were to have reached the original review target by September 1968 they would have needed to have plans for an additional 201 posts (100 per annum for each

of the two years 1966–7, 1967–8); to reach the scaled-down median target plans for 140 (70 per annum); and for the Ministry's latest target plans for 33 per annum. In fact they had plans, albeit tentative in many cases, for an average of 13 new posts per annum over the next three years. And this despite the fact that there are some 200 senior registrars in training. Appalling though this is in a specialty where consultants are trying to practise modern psychiatry with ridiculously heavy case loads—the number of inpatients alone can be as many as 200–400 (600 is not unknown)—an equally important point is what would be revealed if similar investigations were made at board level of the expansion they have in mind for other specialties?

Meanwhile the service suffers and the work load on existing consultants increases, encroaching more and more on time that could be devoted to postgraduate teaching and research. Senior registrars—nearly 700 of whom are over 35 years and 161 over 40 years—to say nothing of the many excellent registrars with appropriate qualifications and training, become more disenchanted and emigrate.

In such a situation to increase further the number of junior staff of either registrar or medical-assistant type is no answer. The former merely intensifies the bottleneck problem. The latter grade, while it may prove to be the answer for getting general practitioners and others back into the hospital, is unsuitable for highly trained specialists waiting in the queue for consultancy. Indeed, the very creation of assistant posts could have the much more sinister effect of suppressing the proper expansion of the consultant grade, with the inevitable result of consultant work being performed by junior grades and all the understandable resentment that produces.

Since I am assured that the Central Advisory Committee on Consultant Establishments never turns down a needed consultant post, the conclusion must be that either hospitals are not asking for them or boards are failing to forward requests that are made.

The machinery is obviously going wrong somewhere. The time must have come for each specialty to lay down objective criteria on which hospitals could base their need for consultants. If this is not done and implemented soon an increasing number of potential consultants will continue to emigrate.—I am, etc.,

EDMUND A. HARVEY-SMITH,
Chairman,
Hospital Junior Staffs Group,
British Medical Association.

Kingston,
Surrey.

Casualty Staffing

SIR,—On examining the recently published figures (*Supplement*, 7 October, p. 3) for medical staffing in the National Health Service at registrar and S.H.O. levels one should under "traumatic and orthopaedic surgery" really read "casualty." If the departments which are major employers of these grades are compared the following figures are obtained. The total numbers are given in brackets, followed by the percentage of graduates born in the British Isles (as estimated from the Tables).

Specialty	Registrars	S.H.O.'s
Pathology	(231) 62%	(143) 56%
Anaesthetics	(506) 60%	(343) 53%
Psychiatry	(433) 59%	(153) 47%
General medicine	(615) 63%	(456) 46%
Paediatrics	(158) 47%	(205) 45%
General surgery	(676) 48%	(657) 37%
Obstetrics and gynaecology	(369) 42%	(449) 37%
Ophthalmology	(126) 49%	(92) 24%
Traumatic and orthopaedic	(314) 34%	(377) 19%
Otolaryngology	(131) 33%	(101) 19%

In the specialties of anaesthetics, pathology, and psychiatry it is probable that most, especially of the home-produced graduates, will eventually stay in these specialties, and the numbers in general medicine, general surgery, and obstetrics and gynaecology are helped by preregistration regulations. In casualty only a small proportion can hope to be recruited to consultant rank and the only inducement to take a casualty post at present is the requirement for F.R.C.S.

The casualty departments are mainly staffed by overseas graduates, and as the medically underdeveloped countries expand their postgraduate training this supply will diminish. While being grateful for their services, there are too many casualty departments being staffed by those without previous hospital experience in this country or sufficient training for such responsibility. The present system is also unfair on the overseas graduates. More than six months in a casualty department as S.H.O. grade is a waste of time, but it is my impression that too many are drifting rather aimlessly from casualty post to casualty post simply because they are relatively easy to obtain.

In some quarters it has been suggested that casualty departments should be staffed by consultants or medical assistants. To cover 24-hour duties and holidays this would mean a minimum of four for every casualty department. Even if the medical manpower situation were less critical I am certain that candidates in sufficient numbers would not be forthcoming. It would also be very expensive. The separation of accidents from other casualties would not solve the problem. It would mean two sets of 24-hour services in place of one. Someone must do the triage.

While agreeing there is a need for more consultant supervision in many casualty departments, I am sure that the solution lies with those who are in or destined for general practice. To be an effective casualty officer the general practitioner must be free of his practice commitments when in casualty. This would mean an average of one to two weeks whole-time casualty duty or its equivalent for all general practitioners every year. Because

of the differences in distribution between general practitioners and casualty departments this might mean working several miles from home. I believe that six months in a casualty department does allow younger doctors to see many of the types of emergencies that he is going to meet in general practice and at the same time have more experienced advice at hand. If such appointments were to be a prerequisite for entry into general practice it would help general practitioners' training and solve the staffing problem of casualty departments.

It would be interesting to hear the views of general practitioners, since I am very sure that before long the Ministry will be forced, out of sheer necessity, to place this bone of contention on their plates.—I am, etc.,

London W.1.

GUY RIGBY-JONES.

Approval of Emergency Treatment Service

SIR,—I cannot let Dr. M. Mundy's letter (4 November, p. 299) pass without commenting on some of his assertions concerning the B.M.A. Emergency Treatment Service.

It was decided to make use of the Telephone Answering Service a condition of joining the deputizing part of the service, because experience has shown that receipt of messages from patients by the control centre second-hand, or even third-hand, frequently through the doctor's receptionist or caretaker, can lead to misunderstanding and delay in visiting the patient. Direct telephone contact between the person requesting medical attention and the nurse at the control centre leads in our view to a quicker service for the patient. In those provincial centres where the service is operating subscribers are quite satisfied with this arrangement, and the chances of confusion over the relay of messages are minimized.

Our experience is also that doctors welcome the opportunity of the combined facilities, as it enables them to enjoy their time off without the need to provide cover for the telephone. While undoubtedly problems over the mechanical transfer of calls do occur, these are not common enough to be a serious danger to the efficiency of the service. The suggestion that the Telephone Answering Service provides an economic cushion against losses incurred in running the deputizing service is totally false. In fact the Answering Service is provided at less than an economic cost.

It was considered to be inappropriate for the Association to sponsor a service which would enable doctors to contract out of all their evening and week-end responsibilities, and with this in mind the Central Advisory Committee originally recommended a maximum of 25 calls per month—a level which it was considered would have made it impracticable for doctors to transfer to the service all their out-of-hours work. For those doctors who wish to contract out of evening and week-end duties the new general-practitioner contract provides the necessary mechanism.

In the event, experience in the centres already operating shows that 12 calls per month is the average demand by doctors. Furthermore, it has been drawn to the attention of the Central Advisory Committee that

there are a number of doctors, particularly in London, who wish to transfer only a limited number of calls, or alternatively whose level of evening or night calls is rather lower than average and for whom the 25-call contract would be unnecessarily expensive. A revised contract which should be acceptable to these doctors has been drawn up.

As to the recommendation by Dr. Mundy that "The organizers must adopt a much more realistic attitude towards a viable Emergency Treatment Service" I can only answer that we have a large number of satisfied subscribers in the seven centres where the service is operating. Surely I need comment no further.—I am, etc.,

London W.C.1.

IVOR M. JONES.

Consultants' Views of General Practitioners

SIR,—I have been in general practice in the East End of London since 1921. Prior to 1948 I had eminent specialists out for consultation. To mention a few: Dawson of Penn, Horace Evans, Tommy Horder, Victor Bonney, Louis Carnac Rivett, and Russell Brain. These men always observed strict protocol and always paid complimentary remarks re my treatment both to patients and relatives.

In my experience the consultants I have met since 1948 are men of the same calibre, in dealing with the general practitioner, as the illustrious names I have mentioned. It would be a very sad day for the profession should any acrimony develop between consultants and general practitioners (16 September, p. 735).—I am, etc.,

WILLIAM BELTON.

London E.17.

Menace of Smoking

SIR,—There is not much reason behind the intemperate attacks in the *B.M.J.* (23 September, p. 753, and 14 October, p. 113) and in the press on the smoking of tobacco generally.

I raise a voice on behalf of the many millions of men who have enjoyed smoking moderately (as I have done for the last 50 years) and who have met death, or must encounter death, from causes other than can be placed squarely against smoking.

What appears to have been lost sight of are these points. Quick-dried cigarette tobacco is probably the killer and this possibly has been marketed only in the last two decades. There has been a clear distinction between pipe tobacco and cigarette tobacco, but this is now overlooked. Cigarette-smoking was a very, very common indulgence at the time of the 1914–18 war, and one might still name the type of cigarette rubbish that was the troops' ration. The utmost anxiety, the poorest food, the cheapest cigarettes, and a shilling a day was their lot. If ever there should have been a spate of lung cancer it should have been in the third decade of the twentieth century.—I am, etc.,

Hexham.

RICHARD BELL.

Vocational Training for General Practice

SIR,—Dr. Frank Gray chides me gently (21 October, p. 177) for my comment in the G.M.S. Committee debate on 7 September (*Supplement*, 23 September, p. 135) that conditions should be created in general practice in which young graduates could continue to practise medicine in the way they have been trained. The debate was about vocational training for general practice and the subject was the report produced by a subcommittee of which I was the chairman. My observations were made in my reply to points raised during the debate.

The situation must be viewed with the 1967 recommendations of the General Medical Council as to basic medical education in mind.¹ These say that basic medical education should give "the student knowledge of the sciences upon which medicine depends and an understanding of the scientific method." They also set a single objective for all doctors up to the time of full registration and define the object of basic medical education as being "to provide doctors with all that is appropriate to the understanding of medicine as an evolving science and art." . . .

In the pre- and post-registration hospital appointments graduates have at their disposal all the resources needed to investigate and treat patients and they are unlikely to seek careers in a branch of medicine where similar resources are not available. There is thus an immediate danger to recruitment to general practice unless it is clearly seen to offer the conditions that graduates want. Of course changes in the administration and organizational aspects of general practice are just as essential as simple access to departments of medical science in order to allow full expression of the art of medicine by doctors.

Dr. Gray speaks from a lifetime of experience in practice, but I believe there is no great separation between his viewpoint and my own, both of which are concerned to advance general practice as a branch of medicine well able to offer a challenge to a due proportion of able graduates now and in the future.—I am, etc.,

London W.8.

DONALD C. BOWIE.

REFERENCE

¹ *Recommendations as to Basic Medical Education*, 1967. General Medical Council.

Mileage Allowances

SIR,—The letters from Drs. D. L. Bennett and R. J. Purnell (21 October, p. 177) are an oversimplification of a very complex situation, and the interim mileage allowance which has been negotiated by the B.M.A., although far from acceptable to the members of the Committee concerned, should not lead to the suggestion made by Dr. Bennett that, "the junior medical staff have no faith in the B.M.A., and . . . large numbers of senior medical staff see no reason for returning to the fold."

Horsepower, in relation to the internal combustion engine, was originally computed upon a basis related to the bore of the engine cylinder, but variations in the stroke of the piston, leading to considerable differences in the volume, necessitated a reappraisal of the formula. At one time it was considered that 100 c.c. was equivalent to one horsepower, but in recent years the tendency has developed

for engines to be "over-square"—that is, with a bore exceeding the stroke. The efficiency of the engine is of course dependent upon many factors, but a modern engine of 1159 c.c. at 5,200 r.p.m. can develop, for example, 47 brake horsepower, but owing to the relatively large bore the rating on the old basis would be as high as 15 horsepower. I stress this point because it must be appreciated that any attempt to devise a mileage allowance based upon horsepower, an outmoded term, rather than cubic capacity measured in c.c., is quite impracticable as a basis for future negotiations.

The difficulty of adhering to the horsepower formula was recognized by local authorities employing doctors in the public health service at least as long ago as 13 July 1956 in Medical and Dental Council circular No. 29, when it was decreed that in the case of cars registered on or after 1 January 1947 10 h.p. would henceforth be equated with 1199 c.c. for the purpose of calculating mileage allowances. The General Whitley Council, which considers mileage allowances for all hospital employees, adopted the 10 h.p./1199 c.c. equivalent basis system in General Whitley Council circular No. 70 dated 3 January 1966 (applicable from 1 November 1965), but at that time the Staff Side of Medical and (Hospital) Dental Committee B refused to accept the increase of only ½d. a mile which was offered, since this was considered to be totally inadequate. This figure of ½d. a mile has now been replaced, on an interim basis only and without prejudice to continuing negotiation, by a figure of ¾d. a mile. It should be appreciated that, since negotiations must be carried out through the General Whitley Council, which has already accepted the figure of 1199 c.c. as equivalent to the outdated concept of 10 h.p., all future computations must be assessed upon a cubic capacity rather than a horsepower basis.

Although some hospital medical and dental staff may have been fortunate enough to have had their mileage allowances calculated upon the old concept that 10 h.p. is equivalent to 1000 c.c. instead of the 1199 c.c. defined by the General Whitley Council, it is surely unreasonable to indict the B.M.A. on this account. Realizing that in some instances an apparently unfair situation might arise, care was taken to write in a "no detriment" clause in the official circular N/C154/17B, which was issued by the Ministry in July 1967 to the secretaries of all regional hospital boards; boards of governors; hospital management committees; clerks of executive councils; joint pricing committees, and the dental estimates boards to the effect that: "where an officer . . . whose car in use at 30 June 1967 was over 10 h.p. but not over 1199 c.c., continues to use that car, he may retain the old rates until he changes his car. . . ."

The new rates of mileage allowances, which are effective from 1 July 1967 and will be published in G.C. circular No. 76, compare with the old rates as follows:

Old Rates		New Rates	
Cars up to 10 h.p.		Cars up to 1199 c.c.	
First 2,000 miles	7½d. per mile	8½d. per mile	
2,001–7,000 miles	6d. " "	6½d. " "	
Over 7,000 miles	4½d. " "	5d. " "	
Cars over 10 h.p.		Cars over 1199 c.c.	
First 2,000 miles	9½d. per mile	10d. per mile	
2,001–7,000 miles	7½d. " "	8½d. " "	
Over 7,000 miles	6½d. " "	6½d. " "	

While it is appreciated that the owner of, for example, a Morris 1100 will not for the present time be any better off, he will certainly not, owing to the "no detriment" clause, suffer

any reduction as Dr. Bennett suggests. The recently introduced 1250 c.c. engine for this model will of course place such a new vehicle in the higher mileage rate group.

The B.M.A. went to great lengths and considerable expense to prepare, through the Economist Intelligence Unit, assisted by representatives of the Automobile Association and Royal Automobile Club, a very comprehensive memorandum dealing with current motoring costs, which was not, however, acceptable to the Management Side of Committee B, and it is not always fully appreciated that it is extremely difficult to persuade the General Whitley Council that hospital medical and dental staff should receive preferential rates and conditions as compared with other hospital staff. Despite this, an interim increase of ¾d. a mile instead of ½d. a mile has been achieved; there is a "no detriment" clause to protect staff with cars previously rated on the 10 h.p./1000 c.c. basis; and further negotiations are being pursued to the maximum extent possible.—I am, etc.,

N. L. ROWE,

Member, Negotiating Subcommittee of Central Committee for Hospital Medical Services.
Woking, Berks.

Points from Letters

Lithotomy Position for Forceps

Dr. R. M. PEBERDY (Droitwich Spa, Worcs) writes: In the two years that I spent as senior house officer anaesthetist I and my colleagues in our anaesthetic team dealt with rather more than the average number of these cases, as one consultant obstetrician preferred general anaesthesia for his forceps deliveries. . . . It was always the rule that the patient should be anaesthetized with the legs down, and that intubation with a cuffed tube should always be performed. Only when the anaesthetist was satisfied that the trachea was protected by the cuffed tube and pack were the legs raised to the lithotomy position, which undoubtedly seemed the most convenient position for forceps delivery and other obstetrical manoeuvres. Also an efficient, working, frequently tested sucker was always provided wherever an anaesthetic was given (a portable sucker formed an essential part of the flying squad anaesthetic equipment). By means of these precautions, which took very little extra time or effort, the incidence of regurgitation was, I believe, reduced and if it did occur was comparatively easily dealt with.

Drugs and Schizophrenia

Dr. J. A. McCLUSKIE (Sydney, Australia) writes: I wonder if it was a coincidence that your leading article "Antibodies in Schizophrenics" (2 September, p. 569) was followed on the next page (p. 570) by your article on "S.T.P." It would be a peculiar turn of coincidence if underworld research into new hallucinogenic drugs did produce one which could be identified in the tissues of schizophrenics.

"Mediflash"

Dr. R. W. COCKSHUT (London N.W.4) writes: The famous flashing green-light application form states: "(2) only to be used in emergencies; . . . (6) if improperly used light will be withdrawn." What interesting implications there are here. It appears that the B.M.A. approves of a doctor being followed and questioned, and of the patient being questioned, so that someone (it could only be the police) could be satisfied that the call was a true emergency. A report then made to the B.M.A. would result in the green light being confiscated, never to be used again.

Obituary Notices

L. E. C. NORBURY, O.B.E., M.B., B.S., F.R.C.S.

Mr. L. E. C. Norbury, consulting surgeon to the Royal Free Hospital, to St. Mark's Hospital, West Middlesex Hospital, and Belgrave Hospital for Children, died on 31 October at his home after a short illness. He was 85.

Lionel Edward Close Norbury was born at the Cape of Good Hope on 9 January 1882. His father was a Barts man, Sir Henry



Norbury, K.C.B., Director General of Naval Medical Services. Lionel was educated at Merchant Taylors' School, and St. Thomas's Hospital Medical School, where he had a distinguished career as a student, taking the Cheselden medal, the Beane scholarship, and other prizes. He

qualified with the Conjoint diploma in 1904 at the age of 22, and graduated M.B., B.S. the following year. He passed the F.R.C.S. examination in 1906 at the age of 24 in the distinguished company of Lord Webb-Johnson and Sir Gordon Gordon-Taylor, but he had to wait until the following year, when he was 25, to receive the Diploma of Fellowship. He held resident surgical appointments at St. Thomas's Hospital, and in 1911 was appointed assistant surgeon to the Mildmay Mission Hospital, London. He served as captain in the R.A.M.C. throughout the first world war, and was appointed O.B.E. After demobilization he rapidly established himself as a sound general surgeon, and was elected surgeon to the Royal Free, St. Mark's, and West Middlesex Hospitals, and to the Belgrave Hospital for Children.

His merits were appreciated by the Royal College of Surgeons, where he became an examiner in surgery, a member of Council, and vice-president. He was Bradshaw lecturer in 1948, and Hunterian orator at the Royal College of Surgeons in 1953. He took an active part in medical societies, and was president of the Medical Society of London, and also orator to the Hunterian Society in 1955.

His general training gave Lionel Norbury an all-round interest in surgery, and although he had a special interest in proctology his surgical field was very broad. He had no special interest in research, but applied himself completely to the relief of individual patients. He took a personal responsibility for every case, public or private, and devoted himself wholeheartedly to the patient from the beginning to the end of treatment. He was scrupulous in all that he did, and no detail was too much trouble. He would carry out the first dressings of his major operations himself on all cases in hospital. He was always available, and on his duty

week in hospital he would always come and operate himself on emergencies, right up to the time of his retirement from hospital practice. Norbury was popular with his students, and his teaching was always clear, simple, and practical. He took a keen interest in examinations, and when he was on the Court of Examiners he never missed a single examination in his twelve-year period of office. He was a kindly examiner, and, although he demanded a high standard, his friendly disposition always helped to get the best out of his candidates.

Lionel Norbury was an outstanding example of the cultured professional gentleman. He had a splendid, impressive figure, tall and handsome, and he was always of a cheerful, friendly disposition. He was very happy in his private life. At the height of his career,

before the second world war, his home in Harley Street was a centre of social as well as professional activity, where his devoted wife, Grace, and their four charming daughters were the focus for many happy gatherings of youth and culture. At week-ends Norbury kept open house at Cowden, entertaining many of their friends with swimming and tennis parties, while he himself always took an active part and was never too tired for another set of tennis.

Lionel Norbury will be remembered by many doctors and patients with gratitude for his kindness and humanity. He had about him the rich glow of Christianity. His death will be mourned by many friends, but while they will be saddened by the loss of a great and good man they will be grateful to have had the privilege of having had his friendship. We extend our deep sympathy to his wife and to his daughters.—G. Q.

R. HALE-WHITE, M.C., M.A., M.D., M.R.C.P.

Dr. R. Hale-White, president of the Fellowship for Freedom in Medicine, a prominent figure in the profession and a practitioner of uncommon kindness and understanding, died on 31 October at the age of 72.

Reginald Hale-White, son of the late Sir William Hale-White, was born on 12 June 1895, and received his early education at Uppingham. During the first world war he



(Lawson)

joined the King's Own Yorkshire Light Infantry. He was severely wounded in the Battle of the Somme, and was invalided out of the Army. For his distinguished services he was awarded the Military Cross. Entering King's College, Cambridge, he graduated B.A., and took the M.A. in 1920. His father having been physician to

Guy's Hospital, and his uncle, Sir Alfred Fripp, having been surgeon, it was only natural that he should undertake his clinical studies at Guy's. Here, after qualifying with the Conjoint diploma in 1922, and graduating B.Chir. the following year, he held appointments as house-surgeon, house-physician, and resident obstetric officer. In 1924 he took the M.R.C.P., and proceeded M.D. a year later. He became principal medical officer to the Alliance Assurance Company and to the Imperial Life Assurance Company of Canada. He was also a senior medical examiner for the Scottish Widows' Fund and Life Assurance Society. He always loved people, and

quickly became established as a much esteemed general practitioner in London. The scrupulous and unhurried care of his patients over a period of nearly 40 years gave him an unrivalled experience of human nature and of the practice of medicine—for 20 years before the National Health Service, and as a stern critic of the N.H.S. after its inception.

It surprised no one that Lord Horder invited Hale-White to join him in founding the Fellowship for Freedom in Medicine in 1948, and to become its vice-chairman shortly afterwards. On the death of Lord Horder in 1955 he became chairman of the F.F.M., until he decided a year ago to give up the chair; he was then immediately elected its first president. From its beginning he threw himself heart and soul into the work of the Fellowship, not because he did not believe in the principle of a national health service (for he stated again and again that the Fellowship and he were in favour of making the resources and advances of medicine available to every man, woman, and child), but because he thought that since the start of the N.H.S. what used to be about the most dignified human contact, the doctor-patient relationship, had practically disappeared. He deplored that more and more the Ministry of Health seemed to think that the Service was run for the benefit of the "Elephant and Castle." His forceful way of speaking, his carefully chosen words, the transparent honesty of his views, and his great capacity for making friends made him one of the natural leaders in the medical profession—and one who was never afraid to criticize or to make constructive suggestions at meetings, in the lay press, or in the medical journals.

His record of service to the British Medical Association was substantial. From 1944 onwards he was elected year after year as a

member of the Representative Body. From 1946 to 1949 he was chairman of the St. Marylebone Division, he served on the Council of the Association from 1948 to 1957, and he was secretary of the Metropolitan Counties Branch from 1950 to 1952 and its chairman in 1955-6. He was a valued member of the Journal Committee between 1956 and 1965, and of the Private Practice Committee from 1959 to 1966. In recognition of his many services Hale-White was elected in 1964 a Fellow of the Association.

Apart from his medical activities, his great interests were painting, sculpture, and music, which gave him many hours of pleasure each week. The sympathy of all of us will go out to his widow, and to his only son.—E. C. W.

G. R. writes: Bobbie will be sadly missed and mourned by many. His patients will remember a tireless doctor who contrived to be friend and counsellor to each of them. His practice came from all walks of life, and Bobbie was somehow able to see into the hearts as well as the strictly physical problems of all his patients. Without exception they adored him. His colleagues at the B.M.A. and the F.F.M. will remember him as an ardent champion of the rights of the individual doctor. He was unsparing in his vigilance on our behalf, and yet throughout retained a real sense of humour and a great facility for words. He never overestimated his own importance, though he was always ready to help and advise and to give freely of his time. He could, and did, delegate responsibility, and if he asked you to do a job he trusted you to put into it the same enthusiasm as he would have done himself—and left you to get on with it. His many friends will miss a warm-hearted family man who never allowed his professional responsibilities to erode his private life. He loved the countryside, especially the Sussex Downs, where he made his home. He was a keen gardener and a domesticated husband. Amid his family, which included his beloved Labrador Alex, he was a relaxed and simple man. His retirement never presented him with any problems, for with his love of opera, which took him regularly to Glyndebourne and Covent Garden, and of pictures, which took him travelling, there was always more than enough to do. He was a connoisseur of good food and civilized comfort. He clearly enjoyed life to the full—a quality that was infectious—and time spent with Bobbie was always satisfying, and all too quickly passed.

W. HOFFER, PH.D., M.D., L.R.C.P.&S.ED.
L.R.F.P.S.GLASG.

Dr. W. Hoffer, a leading psychoanalyst, and consultant in psychotherapy at the Maudsley Hospital, died very suddenly in London on 25 October. He was 70.

Willi Hoffer was born in the Austrian village of Luditz on 12 September 1897, and had his schooling in Pilsen. After serving in the Austrian Army from 1915 to 1918 he entered the faculty of philosophy at Vienna University, where he read biology and psychology, the latter interest being due to the influence of August Aichhorn. He entered into personal analysis with Herman

Nunberg, and was soon launched on a psychoanalytic career. In 1922 he received his Ph.D. for a thesis entitled "The Scientific Basis of the Use of Play in Education," and in 1923 he was elected a member of the Vienna Psychoanalytical Society. He then entered the medical faculty and obtained his M.D. in 1929, after which he proceeded to spend three years in part-time work at psychiatry in Professor Otto Pötzl's department. Meantime his gifts had been recognized by his analytic colleagues, and he was given much responsible work in training and in editing. He wrote a number of psychoanalytic papers, nearly all concerned with play, childhood, and adolescence. The Nazi annexation of Austria in 1938 led Dr. and Mrs. Hoffer (herself a psychoanalyst) to migrate to England. Once again Hoffer had to undertake medical studies, as well as perfect his English, and in 1943 he obtained the triple qualification of the Scottish Colleges.

Since the second world war Hoffer came to occupy an increasingly prominent place not only in London but also in international psychoanalysis. Apart from publishing various valuable papers himself, he did much editing work. From 1945 he was co-editor of *The Psychoanalytic Study of the Child*, and from 1947 to 1959 he was editor of the *International Journal of Psycho-Analysis*. He was also a leading training analyst and teacher at the Institute of Psycho-Analysis. The very high esteem he enjoyed led to his election as president of the British Psycho-Analytical Society in 1959, a position he held until 1962. Hoffer was equally recognized in the international field, becoming a vice-president of the International Psycho-Analytical Association in 1957, and honorary vice-president in 1963. American honours included the Abraham Flexner lectureship in 1954 and his appointment as Sigmund Freud Anniversary Lecturer in New York last year.

He was appointed in 1954 consultant in psychotherapy at the Maudsley Hospital, and until his retirement from the National Health Service five years ago he contributed a great deal to broaden the postgraduate education of large numbers of registrars, with whom he was very popular. Indeed, his capacity for inspiring affection and friendship was one of his leading characteristics. What will be remembered most vividly by all who knew him is the warmth and simplicity of his personality. His many friends will miss him sorely. His wife died in 1961; there were no children.—W. H. G.

F. A. PICKWORTH, B.SC., M.B., B.S.

Dr. F. A. Pickworth, a former consultant pathologist to Birmingham hospitals, died at his home in Bournemouth on 22 October after a long and distressing illness. He was 78.



[Lotte Meitner-Grat

Frederick Alfred Pickworth, son of Dr. A. J. Pickworth, was born at Lakenheath, Suffolk, on 31 August 1889, and was educated at East Anglia School, Bury St. Edmunds. He began work as a pharmacist in Lincoln, and after serving an apprenticeship he qualified M.P.S. and finally obtained the Ph.C. in 1910. In 1913 he obtained the B.Sc. with honours in chemistry, and the following year qualified as a public analyst, after which he worked for a time as an analytical chemist. Deciding to take up medicine as a career, he entered Charing Cross Hospital Medical School and qualified with the Conjoint diploma in 1921, graduating M.B., B.S. a year later. At Charing Cross Hospital he became house-physician to Sir James Galloway and to Dr. Gordon Holmes. In 1923 he was appointed pathologist to the Birmingham Mental Hospital, and as research officer to the Joint Board of Research for Mental Diseases, working under Sir Frederick Mott. In 1926 he succeeded Sir Frederick as director of the Board of Research.

In 1935 Pickworth published his first book, *Chronic Nasal Sinusitis and its Relation to Mental Disorder*. He always gave special attention to the capillary blood supply to the brain, and developed special staining techniques which are still widely used. His major work *New Outlook on Mental Disease* was published in 1952, and he retired three years later.

In his later life Dr. Pickworth spent his time studying natural history, and was a great pond-hunter and botanist. Living as he did near the New Forest, he spent much of his time there.

In 1930 he married Jane Wylie Stocks, a medical officer at Hollymoor Mental Hospital. He is survived by his widow and three children, one of whom is a general practitioner. He will be missed by his many friends and relatives. The greatest sympathy is extended to his widow and children.—R. C. B.

W. C. FOTHERGILL, M.D., D.M.R.E.

Dr. W. C. Fothergill, a former consultant radiologist at Darlington Memorial Hospital, died suddenly on 28 September after a heart attack in the hospital with which he had been associated for 35 years. He was 67.

William Crichton Fothergill, an only child, was born in 1900 into a family with strong connexions with the Society of Friends, the medical profession, and the North Yorkshire dales. A delicate child, he was never physically robust, and took no part in sport, although he was a keen motorist in his early years and enjoyed canoeing, making trips down the Thames and Moselle in 1935. He received his medical education at Edinburgh University, graduating M.B., Ch.B. in 1923, took the D.M.R.E. in 1925, and proceeded M.D. in 1930. He held a post in Portsmouth for a time, and was senior assistant radiologist under the redoubtable Rutherford Morison in Edinburgh. In 1931 he set up practice in Darlington. He was appointed honorary radiologist to the Darlington Memorial Hospital, becoming consultant at the inception of the National Health Service. He retired from this post on reaching the age limit in 1965.

Fothergill was an amateur engineer and craftsman of considerable ability, and was an early and outstanding exponent of colour photography. Some of his early Autochrome and Dufaycolor transparencies can stand comparison with anything produced in this day of the colour slide. For many years he was a member of the Royal Photographical Society, of which he gained the associateship. He was a founder member and first president of the local camera club. A man of wide culture, he held strong views, often forcibly expressed, on a number of subjects, but basically he was shy, and one of the gentlest, most generous, thoughtful, and courteous of men.

His retiring nature prevented him from making many intimate friends, but he had a very wide circle of acquaintances who held him in high regard. They will miss his tall courtly figure and his pertinent comments on the matters of the day.—O. H. W.

J. KRUSZYNSKI, M.D.

Dr. J. Kruszyński, senior lecturer in histology in the University of Liverpool, died on 14 October, aged 64.

Jan Kruszyński was born in Poland on 12 August 1903, and studied medicine at the Stefan Batory University of Wilno. In his second year his beautiful histological drawings came to the attention of Professor J. S. Alexandrowicz, and soon led to a junior appointment to the teaching staff of the department of histology. He graduated M.D. in 1930, and attained the degree of Docent in 1936. He remained at the histology department at Wilno until he was captured by the Russians in 1939. He was a prisoner of war until 1941 and never cared to discuss his terrible experiences during that period. He joined the Polish Army in Russia in 1941, being appointed pathologist to a military hospital, with which he served as it travelled across the Caspian Sea to Italy, via Egypt, Palestine, Iraq, and Persia. He reached Britain in 1947, and was appointed assistant lecturer in histology at Liverpool in 1948, lecturer in 1950, and senior lecturer in 1963.

Jan Kruszyński was a gentle, self-effacing scholar who gave service of inestimable value to the department, and to the Medical School as a whole. He had a profound knowledge of classical histology, its literature, its methods, and results. His artistic gifts made him a superb illustrator of histological appearances; he went to untold trouble on the students' behalf in preparing demonstrations and lectures illustrated by the clearest of diagrams and drawings. He was always ready to share his wide experience of histological appearances, and was consulted by colleagues from many different departments about their problems. His own special research interest was in inorganic histochemistry; from an early stage of his career he was interested in microincineration and became recognized internationally, through lectures and published papers, as the chief authority in that field.

His hobbies reflected his artistic interests; art galleries, photography, engraving, and country walking. He will be sorely missed, not only for his professional accomplishments, but for his cheerful, modest personality and

the complete integrity of his character. Our sympathy goes to his widow.—N. M. H.

Rev. M. HATFIELD WRIGHT

M.B., CH.B., D.O.M.S.

The Reverend Hatfield Wright, formerly ophthalmic surgeon to the Swindon group of hospitals, died at his home in Liddington on 29 September. He was 69.

Morden Hatfield Wright was born on 28 December 1897. During the first world war he was a lieutenant in the Shropshire Light Infantry, and was wounded and taken prisoner in Europe in March 1918. After demobilization he entered the University of Edinburgh, where he graduated M.B., Ch.B. in 1924 and very soon afterwards married a fellow student. Both joined the Church Missionary Society and went to Gairo Hospital, combining medicine with missionary work. His 16 years in Africa were spent mostly at Omdurman Hospital in the Sudan. Much of his work was concerned with diseases of the eye, and his skill in this branch was self-taught during this period. During the second world war he joined the Army as an eye specialist, and became Southern Command senior ophthalmologist based on Wheatley Hospital, Oxford. After demobilization he took the D.O.M.S. in 1947. In 1949 he was appointed ophthalmic surgeon to the Swindon group of hospitals. He was chairman of the Swindon Division of the British Medical Association in 1960–1. He retired from his hospital appointment at the age of 65, and was ordained into the Church of England, continuing some private ophthalmic work while a curate at Liddington.

His friends and patients will remember him as a quiet, unassuming, conscientious man. Scrupulous and neat in his surgical work, he would always visit his patients afterwards, and his colleagues on the hospital staff thought highly of his work.

He leaves a widow, Dr. Mary Wright, and two daughters.—J. K. M.

N. J. L. ROLLASON, M.D.

Dr. N. J. L. Rollason, a general practitioner in Coventry for more than 40 years, died at his home in Coventry on 30 September. He was 84.

Norman John Lancelot Rollason was born in Smethwick on 6 May 1883, and was educated at Five Ways Grammar School and Birmingham University, graduating M.B., Ch.B. in 1905, and proceeding M.D. in 1908. After house appointments at the Queen's Hospital, Birmingham, he joined the late Dr. John Orton in general practice in Coventry, where he rapidly became a well-loved family doctor. During the first world war he served as a surgeon lieutenant-commander in the R.N.V.R., and from 1914 to 1964 he served continuously on committees concerned with medical administration. When he retired from active work an illuminated scroll recording his 50 years' service was presented to the executive council in the presence of the Lord Mayor of Coventry by the Coventry Local Medical Committee. During the second

world war he rendered valiant service at the time of the air raids on Coventry.

He had a distinguished record in the St. John Ambulance Association, and in 1957 was created a commander of the Venerable Order of St. John of Jerusalem. For many years he was the vicar's warden at St. Laurence's Church, Foleshill, Coventry, and secretary and treasurer of the Parochial Church Council. He loved Freemasonry, for there he felt he could relax away from his busy practice, and was a past Master of the St. John's Lodge of Freemasons and an officer of the Provincial Grand Lodge of Warwickshire. A member of the British Medical Association, he was a representative at the Annual Meeting in 1921 and 1922 and again in 1931. He was an enthusiastic angler and every holiday would be spent fishing in Scotland and later Leintwardine.

In 1908 he married Elizabeth Mary Oakden. After a wonderfully happy life together he looked after her devotedly during her last illness until she died in 1957. They had no children.—R. S. R.

H. C. MILLER, B.A., M.D.

Dr. H. C. Miller, a general practitioner at Cressage, Shropshire, died suddenly at his home in Shrewsbury on 27 October. He was 63.

Herbert Crossley Miller was born on 31 October 1903. After some years in holy orders he decided to enter the medical profession, and graduated M.B., Ch.B. from Edinburgh University in 1940. He held house appointments at Brighton, Stourbridge, and Hove. During the second world war he served for a time as surgeon-lieutenant in the Royal Naval Volunteer Reserve, but was invalided out. He then set up with his wife in general practice at Cressage, Shropshire. In addition he held an appointment at Cross Houses Hospital, near Shrewsbury, and was a justice of the peace. In 1962 he proceeded M.D., and was awarded a gold medal for his thesis entitled "The Social Medicine of an Ageing Rural Community."

J. H. F. B. writes: Dr. H. C. Miller, "Dusty" Miller to his many friends, came comparatively late to medicine; when he took up medicine in Edinburgh in 1935 he was curate at St. John's Episcopal Church, Edinburgh; aged 32 at the time, he seemed to the rest of us in the year a very senior person, indeed. He never regretted abandoning for medicine what was a career of great promise in the Church. He had tremendous gifts of warmth and personality, and inevitably became a leader among the students of his time. Like the rest of them, he was engulfed by the war and served for a time in the Navy; but was invalided out with an arthritis of the spine, which finished his aspirations to a career in surgery. He and his wife, also a doctor, set up in practice in Cressage, Shropshire, where he became the complete country practitioner, held in respect and affection by everyone, and actively involved in the life of his community. He served on the bench as a justice of the peace for many years. It was his intimate knowledge and understanding of the life of his patients which gave his book *The Ageing Countryman* the qualities of a

classic. It was based on a survey—supported by the National Corporation for the Care of Old People—of geriatric problems in rural Shropshire. Recently ill-health forced him to retire from practice; but he continued to hold a part-time appointment in geriatrics. His wife and five children survive him.

**J. A. ADAMS, B.A., M.B., B.CH.
B.A.O., L.M.**

Dr. J. A. Adams, formerly in general practice at Sowerby Bridge, Yorkshire, died in a nursing-home at Camberley on 23 October. He was 100.

John Andrew Adams was born in Ulster on 19 January 1867, and was educated at Queen's College, Galway, graduating B.A. with honours in 1888, and M.B., B.Ch., B.A.O. in 1890, obtaining the L.M. at Coombe Hospital, Dublin, in the same year. After a short period as assistant lecturer in anatomy at Queen's College, he held house appointments at the Halifax Infirmary, Yorkshire, before settling in general practice at Sowerby Bridge in the West Riding of Yorkshire, where he continued in a large practice until his retirement before the second world war. He also held the appointment of medical officer of health to Sowerby Urban District Council. A member of the British Medical Association, he was chairman of the Halifax Division from 1922 to 1924.

A.R.D.A. writes: An able and vigorous man of fine physique, Dr. Adams was held in very high regard for his professional skill and integrity and for the kindly way in which he worked. A much-respected figure, he took an active interest in local affairs, both medical and administrative. He was an active member of the B.M.A. for many years. Dr. Adams leaves behind him his devoted wife, Beatrice, and a son and two daughters.

A. W. RATTRIE, M.C., M.B., CH.B.

Dr. A. W. Rattrie, one of Cumberland's longest practising general practitioners, died in hospital at Scorton, Yorkshire, on 8 September, at the age of 82.

Alexander William Rattrie was born in 1884, and received his medical education at Edinburgh University, graduating M.B., Ch.B. in 1910. As an undergraduate he had a distinguished career, and was awarded medals in histology, pharmacology, medicine, and forensic medicine, and in addition received a major award in clinical surgery. He held house appointments at Hull, Dudley, and Wolverhampton before returning to Edinburgh to study his special interest, tuberculosis, under Professor (later Sir Robert) Philip. At the outbreak of the first world war he volunteered for service with the R.A.M.C. and was awarded the Military Cross at Cambrai in 1918 for gallantry in evacuating the wounded from an advanced dressing station while under intense shell-fire from the enemy. During this operation he himself was gassed. After demobilization with the rank of major he went into general practice, joining the late Dr. Sanderson in

Maryport in 1920. In due course Dr. Rattrie's two eldest sons joined the practice. He was a referee to the Ministry of Pensions, and examined Service recruits during the second world war. He was a life member of the B.M.A. and a founder member of the Royal College of General Practitioners and of the West Cumberland Medical Society.

On his retirement in 1965, after over 45 years of unbroken service as their general practitioner, his many grateful patients presented him with an illuminated address and cheque. Doubtless many of them recalled the years of depression in West Cumberland when, despite trying times, Dr. Rattrie still rendered them his usual dutiful attention and treatment, often without any financial reward. Those of us who were privileged to know him more personally will always remember him as a genial and generous host, a keen conversationalist, and never happier than when enjoying his occasional game of chess or bridge, both of which he played with more than average ability.

To his wife, two sons, and daughter we offer our sympathy.—J.F.

**Sir ARCHIBALD GRAY, K.C.V.O.
C.B.E., T.D., LL.D., F.R.C.P., F.R.C.S.**

Sir ARTHUR MACNALT writes: It is with sorrow that I hear of the death of Archibald Gray (obituary, 21 October, p. 178), for we had been close friends for over 60 years. When I came down from Oxford to University College Hospital to complete my medical education I was appointed clinical clerk to Sir John Rose Bradford in 1905. Gray was then his house-physician, and he taught the clerks well, not only in the wards in taking histories and examining patients but also tutorially. At noon each day he would take us into his room and interrogate us on the ward work of the morning, explaining signs and symptoms and giving valuable instruction in medicine. When in 1908 I was Bradford's house-physician Gray was resident medical officer, and was equally kind and helpful. He came of a medical family. His father was a surgeon, and he told me that one of his forebears was a naval surgeon who was present at the Battle of Navarino. Gray had a brilliant and comprehensive medical education. In addition to his knowledge of medicine he had taken the F.R.C.S., and had been a valued house-surgeon to Sir Victor Horsley. We all considered—and rightly too, I think—that he could have specialized successfully in any branch of medicine or surgery. His original intention was to be an obstetrician, and he was the first obstetric registrar to be appointed at University College Hospital. Unexpectedly, he was asked by the hospital authorities to embrace another medical career, a most unusual experience. The eminent dermatologist, Henry Radcliffe Crocker, was retiring, and there was no one to succeed him. Gray was sent to the University of Berne to study skin diseases, and on his return was appointed dermatologist to his hospital. It says much for Gray's rapid acquisition of dermatological knowledge, and for the flexibility which a sound medical education gives, that he speedily attained distinction in his new field of work.

Gray's talents and advice as a medical administrator at the War Office were most valuable to me when I was seconded from the Local Government Board to that department for inspection of camps and infectious disease hospitals and epidemiological work in the first world war. We often met both officially and socially during those anxious years. He will be sorely missed as physician, medical administrator, and loyal friend.

S.C.S. writes: In none of the several obituary notices and appreciations that have appeared about the late Sir Archibald Gray (obituary, 21 October, p. 178) is there any mention of an activity that was in his later years very dear to his heart. I refer to his connexion with St. John's Hospital for Diseases of the Skin, and to the associated Institute of Dermatology. Both of these institutions owe much to him. He was an original member of the first Board of Governors of the hospital from 1947 until 1959, and it was largely due to him that the Institute was founded in 1947. He was its chairman from its inception until 1960. During these years under his wise guidance the Institute, at first merely affiliated to the British Postgraduate Medical Federation, increased in influence and importance in dermatology until in 1957 it achieved full federation. In the years that followed, the Institute had the benefit of his unrivalled knowledge of university and medical administration. Today, two years after he finally retired from the Committee of Management, the Institute may fairly claim to have become the academic seed-bed of dermatology. Indeed, the Institute is a permanent memorial to his energy and devotion.

J.D.F. writes: It does not seem to be generally known that Sir Archibald Gray (obituary, 21 October, p. 178) had every intention of becoming a gynaecologist. In about 1908 two young gynaecologists were on the staff of University College Hospital, and there did not seem to be any likelihood of a vacancy in that specialty for many years to come. He was then gynaecological registrar at University College Hospital, and during this time he performed what I think was the first caesarean Wertheim operation ever to be carried out in England. He always had a great sympathy and understanding for the work of gynaecologists, and personally he helped me in more ways than one.

E.C. writes: When the University of London Officer Training Corps was formed in 1909 Sir Archibald (obituary, 21 October, p. 178) was one of the first to join. He recruited "C" Company, which then included men of both University College and Middlesex Hospitals. Gray told me there was soon to be a war, and I joined up as a cadet, although at the time I was doing a house appointment at U.C.H. At the very beginning, men from all faculties drilled together. The four years I served with the O.T.C., from private to sergeant, were of the greatest value to me in my subsequent 35 years of service in the R.A.M.C. and A.M.S. Gray was a keen, able, and efficient officer; many of his cadets did splendid service in the 1914 war, and subsequent years. In 1908 he was made a Fellow of University College, London, and at the time of his death was the second senior Fellow.

News and Notes

EPIDEMIOLOGY

Epidemic Keratoconjunctivitis

We are indebted to Dr. J. C. TAYLOR, of Glasgow University Department of Infectious Diseases, for the following report:

In shipyards and engineering works on the Clyde and in steelworks in Lanarkshire an epidemic of keratoconjunctivitis is in progress. A few cases occurred in July, but the epidemic situation developed in September. The peak appears to have been reached in the last week of September, and there is evidence of reduced momentum. The disease has affected metal workers mainly, but also several office workers in the industries concerned. In addition, several industrial ambulance-room attendants have been involved.

To date 27 viruses have been isolated at the Regional Virus Laboratory, Ruchill Hospital, Glasgow. These consisted of 21 strains of adenovirus type 8, 2 of adenovirus type 3, and 4 of herpes simplex virus. By serological methods evidence of recent infection with a member of the adenovirus group has been found in 36 patients. Herpes simplex virus has been found only in patients who are

not metal workers, while both strains of adenovirus type 3 were from shipyard workers. By contrast adenovirus type 8 has been isolated from 5 patients not employed in the shipbuilding or steel industries, and further epidemiological investigations are in progress. With these exceptions all strains of adenovirus type 8 and all significant titres of antibodies to adenovirus have been from employees in the shipbuilding, engineering, and steel industries.

The last epidemic of keratoconjunctivitis on Clydeside was in 1956 and was also caused by adenovirus type 8.

Narcotic Drugs

From 1965 to 1966 the number of addicts in the United Kingdom known to the Home Office increased by 422 (45.5%). The total in the latter year was 1,349. The drugs concerned were morphine and its derivatives and analogues and cocaine. Of the

1,349 addicts 886 were males and 463 were females. Of the same total 329 were aged under 20.

Between 1965 and 1966 93% of the increase in the number of known addicts was of people below the age of 35, and 90% of the increase was of addicts using heroin. The numbers of known addicts using heroin increased by 73%.

Illicit trafficking in the United Kingdom was mainly in cannabis, which was smuggled by a variety of routes. There was also smuggling of opium on a small scale. Illicit trafficking in manufactured narcotics was largely confined to small-scale peddling of heroin overprescribed by a few medical practitioners.

Approximate total quantities of narcotic drugs seized were: raw and prepared opium 17 kg., cannabis 193 kg., cannabis resin 65 kg. Convictions relating to illegal possession or use of opium numbered 36, manufactured narcotic drugs 242, and cannabis 1,102. (Report to the United Nations by Her Majesty's Government in the United Kingdom of Great Britain and Northern Ireland

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 21 October (No. 42) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included) Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	3	0	2
Dysentery ..	229	38	102	1	2	362	36	109	19	8
Encephalitis, acute..	1	0		0		1			0	
Enteric fever: Typhoid ..	4	4	0	0	1	5	4	0	0	
Paratyphoid..	1	0	1B	0	1B	3	1	0	0	
Food-poisoning	217	38	7	0		105	31	16	0	
Infective enteritis or diarrhoea under 2 years					36 49					37 40
Measles*	1,269	67	17	13	14	7,087	889	202	140	233
Meningococcal infection ..	9	0	2	0		11	3	0	0	
Ophthalmia neonatorum..	12	0	1	0		12	2	1	0	
Pneumonia†	77	9	40	2	3	105	19	97	1	
Poliomyelitis, acute: Paralytic ..	2	0	0			1	1	0		
Non-paralytic ..	0	0	0			0	0	0		
Puerperal fever§	76	25	2	0		90	36	2	0	
Scarlet fever ..	239	47	28	5	7	358	48	15	4	11
Tuberculosis: Respiratory ..	210	42	19	7		245	54	35	7	
Non-respiratory ..	40	6	2	3		33	5	9	1	
Whooping-cough	527	86	57	3	18	434	74	76	8	25
DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	1	1		0		1	0		0	
Encephalitis, acute..					1					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	4	0	0	0	4	7	0	1	0	3
Influenza ..	5	1	0	2	0	6	0	0	1	1
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	542	92	19	17	4	628	99	25	22	8
Poliomyelitis, acute..	0	0		0	0	1	1		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	26	6	2	0	4	33	5	5	0	3
Non-respiratory ..				0	0				0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	258	49	15	3	9	297	45	28	4	10
Deaths (excluding stillbirths)	9,535	1506	547	118	120	9,698	1520	560	114	165
LIVE BIRTHS	15,396	2541	937	242	411	16,093	2568	944	249	440
STILLBIRTHS	250	44	12			226	38	15		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.



Codis

when pain is severe

Codis tablets provide soluble aspirin together with codeine and phenacetin. Absorption is rapid and there is less likelihood of gastric irritation during prolonged periods of administration.

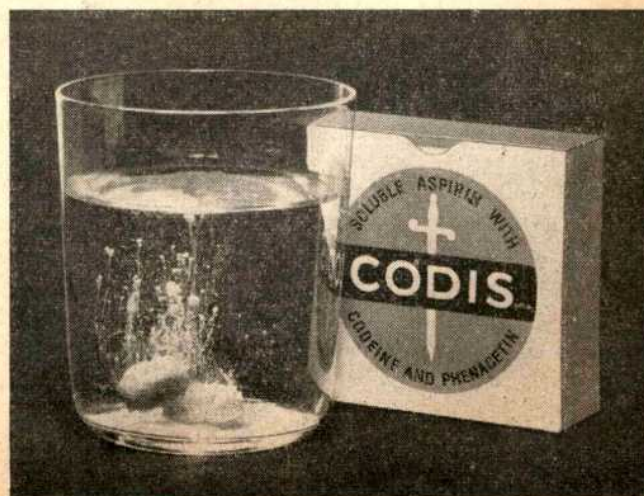
In addition to the rapid analgesic and anti-inflammatory action of soluble aspirin and phenacetin, the codeine component exerts a gentle sedative effect often helpful in those cases of mild insomnia associated with pain.

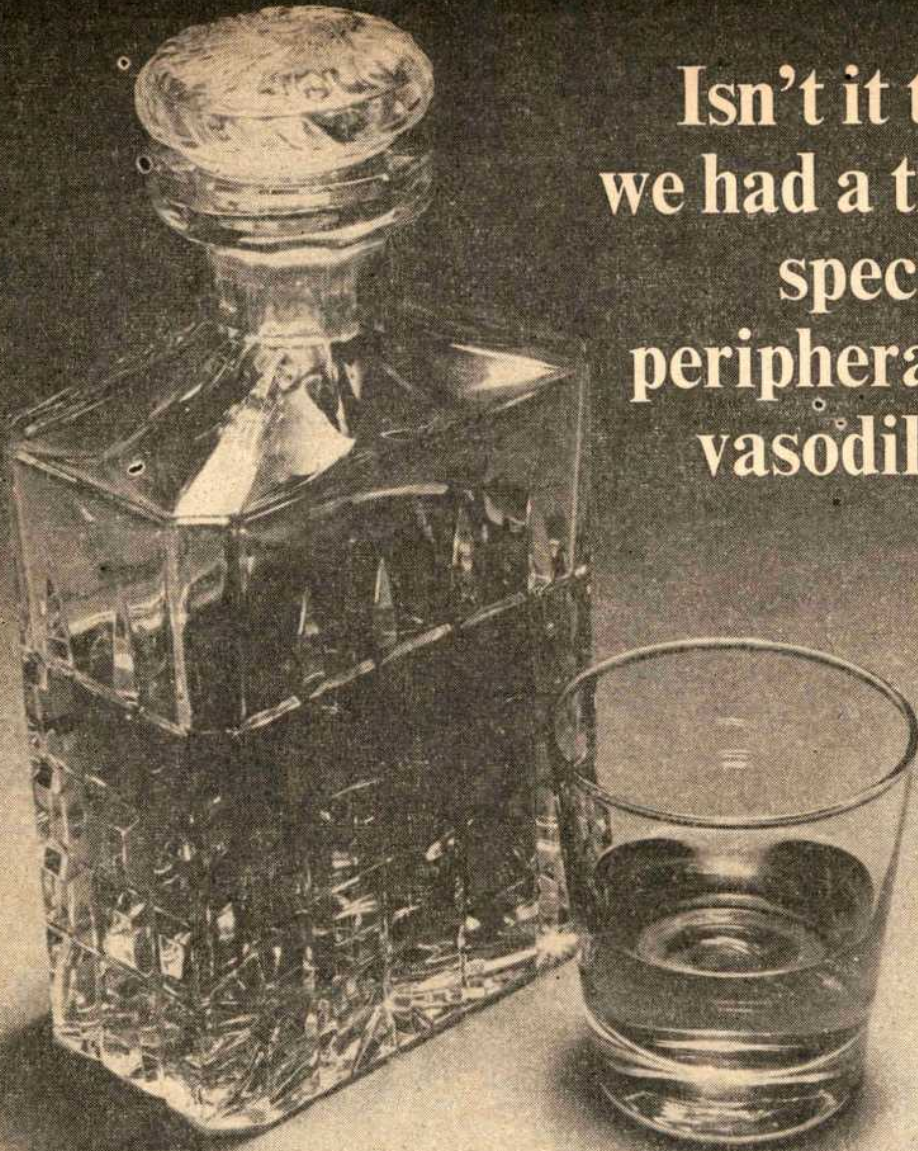
Codis tablets are pleasant to take and, being administered in water, are particularly suitable for invalids and the elderly.

Codis tablets are stable over long periods of time and are presented in protective moisture-proof foil.

Basic N.H.S. price: 500 tablets 25/-.

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A large, ornate glass bottle of Opilon and a glass of water. The bottle is made of clear glass with a faceted design and a stopper. It is partially filled with a dark liquid. Next to it is a simple glass filled with water.

Isn't it time
we had a truly
specific
peripheral
vasodilator?

Opilon

Such peripheral vascular disorders as Raynaud's phenomenon, chilblains, acrocyanosis or excessively cold hands and feet have always been difficult to treat decisively. Now the introduction of OPILON gives the physician specific therapy for such conditions - because OPILON blocks the vasoconstrictor effect of noradrenaline in the arterioles of the skin. Unlike other vasodilators, OPILON does not alter blood flow to skeletal muscle; and because it is solely an alpha-adrenergic receptor blocking agent it cannot directly affect the heart or general circulation. When skin ischaemia is the cause of the complaint, OPILON reliably restores circulation.

OPILON is available as tablets of thymoxamine 40 mg., in bottles of 50 and 250. Basic NHS cost 18/- for 50 tablets, 84/- for 250 tablets. **Dosage:** One 40 mg. tablet four times a day, preferably at 8 a.m., 11 a.m., 2 p.m. and 5 p.m. **Side-effects:** Occasionally mild nausea, diarrhoea, vertigo, headache and facial flushing may be encountered. These are rare, however, and transient. No serious toxic effects have been reported and the development of tolerance has not been observed. **Contra-indications:** None is known. Full information and literature will gladly be sent on request.

Opilon thymoxamine **the unique peripheral vasodilator**

William R. Warner & Co. Ltd., Eastleigh, Hampshire. Tel: Eastleigh 3131.

on the Working of the International Treaties on Narcotic Drugs for 1966.)

Scotland in Second Quarter

The birth rate in Scotland in the second quarter of 1966 was 19 per 1,000 of the population, being 0.3 above the rate for the second quarter of 1966 but 1.1 below the average of the five preceding second quarters. The infant mortality rate was 21 and the neonatal death rate was 14 per 1,000 live births; these rates were both 2 below the rate for the corresponding quarter of 1966.

Fifty-two deaths were attributed to respiratory tuberculosis and 4 to other forms of tuberculosis; these were both 6 fewer than in the preceding second quarter. Malignant neoplasms accounted for 2,961 deaths, 79 more than in the June quarter of 1966; of these deaths 796 were due to cancer of the respiratory system, an increase of 34. Deaths from motor-vehicle accidents numbered 164 and accidents in the home 243; these were 18 and 30, respectively, fewer than in the preceding second quarter.

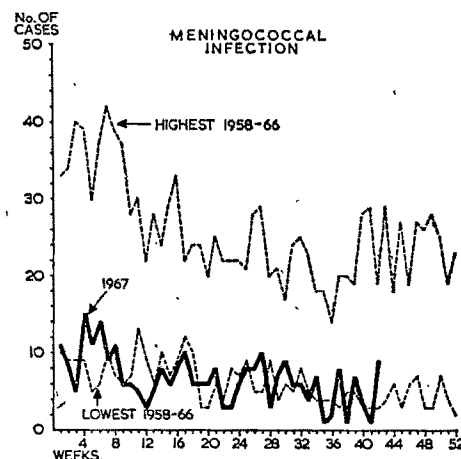
Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

		Week Ending	
		20 Oct.	27 Oct.
Dysentery			
Greater London ...	...	38	40
Lancashire ...	...	27	46
Warwickshire ...	...	20	31
Yorkshire West Riding ...	...	40	53
Glasgow ...	...	42	83
Edinburgh ...	...	19	20
Angus County ...	...	10	10
Stirling Burgh ...	...	6	11
Typhoid Fever			
Southend-on-Sea C.B. ...	...	0	1
Thurrock U.D. (Essex) ...	...	0	1
Kensington and Chelsea (Greater London) ...	...	0	1
Wandsworth (Greater London) ...	...	0	2
Bradford C.B. ...	...	0	1
Edinburgh ...	...	0	1
Clydebank Burgh ...	...	0	1
Rutherglen Burgh ...	...	0	1

Graphs of Infectious Diseases

The graph below shows the uncorrected number of cases of meningococcal infection in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



PARLIAMENT

Minister to Review Structure of N.H.S.

[FROM OUR PARLIAMENTARY CORRESPONDENT]

A full and careful examination of the administrative structure of the medical and related services that was needed "not only for today but looking 10 or 12 years ahead" was announced by the MINISTER OF HEALTH on 6 November.

Over the years, he said, with growing frequency the question had been asked whether the existing structure could be regarded as adequate to meet future needs. While it was wise to avoid making too early adjustments, it would be mistaken to regard as right for all time the structure which came into operation in 1948. It was particularly suitable to meet the crying need at that time, which was to reorganize, expand, and deploy the hospital and specialist services. That phase of initial reorganization was now behind them.

Scope of Inquiry

Some people said that the tripartite structure was unwieldy, and that to have three types of separate authority was not the right way to achieve that degree of integration which a proper service to the individual required. However, the nature of any changes that ought to be made required a most careful examination, and this was what he had now begun.

"I should make it clear," he stated, "that my studies will relate entirely to the administrative pattern. I am not considering the possibility of what would amount to an alternative Health Service, as is sometimes suggested, involving, for instance, a switch in financing from the public to the private sector."

Many and varied ideas had from time to time been put forward for changes. He intended to consider a number of possibilities carefully before making his own tentative

proposals. He would aim in due course, but not for some months, to set out his views, probably in the form of a Green Paper, as a basis for public discussion and wide consultation. Only after this process of consultation would the Government finally make up its mind and introduce legislation, if that was necessary.

A royal commission was studying the whole area of local government in England, and the Seeborn Committee was considering the local authority and allied personal social services. He had told these bodies of his aim to have proposals about the administration of medical and related services ready to be looked at alongside their own recommendations. He had also informed the Royal Commission on Medical Education of his intention.

LORD BALNIEL, for the Opposition, welcomed the proposed review, and asked specifically if the encouragement of private provision was not included. Mr. ROBINSON said his statement had made it clear that the review would be limited to the administrative structure of the Service.

Mr. I. MUKARDO (Poplar, Lab.) asked that the methods and criteria by which members of the various boards and committees were appointed should be considered. Mr. ROBINSON thought this would be within the scope of the structure of the Service.

Mr. E. LUBBOCK (Orpington, Lib.) welcomed the implied recognition that the tripartite structure of the Health Service was unwieldy, and asked for publication along with the Green Paper of the submissions received from interested parties, so that discussion could be as wide as possible. Mr. ROBINSON said he expected most of the submissions would be after publication of the Green Paper, because it was desirable that these should not be definitive but provisional proposals on which discussion could bite. He

agreed that greater integration was desirable if practicable.

Fewer Pay-beds

Mr. P. GRIEVE (Solihull, Con.) asked the Minister of Health on 6 November how many pay-beds were available in hospitals in England and Wales on 1 November 1966, how many were now available, and how many it was anticipated would be available on 1 January next; and for a statement of policy in this matter.

Mr. ROBINSON explained that the numbers of pay-beds available on a given day was not known centrally, and continued: "I have, however, completed my review of pay-beds, which was designed to avoid wastage of beds and make better use of them for National Health Service patients. I have informed hospital boards of my decisions. The number of pay-beds before the review was 5,764. The number now authorized is 4,379, which should meet the present demand for such beds."

Mr. GRIEVE regarded this as part of a concerted policy against pay-beds and said that if the Minister continued this campaign against private medicine he would drive more doctors out of the country. Mr. ROBINSON replied that he had made clear to the profession, and kept them informed of, the purpose and progress of the review. "I have explained to them," he said, "that the object was not to withdraw facilities from private practice but to bring about a situation in which pressure on pay-beds more clearly equals the pressure on non-pay beds."

Dr. J. DUNWOODY (Falmouth and Camborne, Lab.) commented that this meant that the use of more single-bed accommodation was being determined by medical and social reasons, rather than purely commercial ones. He asked for an assurance that this tendency would continue. Mr. ROBINSON: "I hope and believe that will be the case. It will be my policy."

Pledge on Resuscitation

Mr. ST. JOHN-STEVAS (Chelmsford, Con.) asked the Minister of Health whether he would make a statement on the policy of the National Health Service on the resuscitation of elderly patients.

Mr. K. ROBINSON: "The professional advice which I sought as a matter of urgency is that no patient should be excluded from consideration for resuscitation by reason of age or of diagnostic classification alone, without regard to all the individual circumstances. Any form of general instruction is wholly unacceptable. In each individual case the decision to attempt resuscitation must remain the responsibility of the doctor immediately

in charge of the patient.

"This advice has been made known throughout the hospital service."

Points from Parliament

► The interviewing team sponsored by the Ministry of Health (see *B.M.J.*, 30 September, p. 873) has just concluded its interviews with some 140 British doctors now working in North America who would like to return to Britain. They are being advised on their prospects of obtaining re-entry to medicine in Britain. (Minister of Health, 6 November.)

► The Government Social Survey will undertake next year a study of adults living

at home who are substantially and permanently handicapped by limitations in their movements. The survey will show the extent to which they receive and need help from local authority services, and will assist in the development of those services. (Minister of Health, 23 October.)

► In England and Wales in 1965 there were about 2,600 general medical practitioners born outside the United Kingdom and the Irish Republic; there were about 6,150 such doctors working in National Health Service hospitals. (Minister of Health, 24 October.)

► There were 20,027 unrestricted general practitioners, and 20,924 doctors working in National Health Service hospitals in 1965. (Minister of Health, 27 October.)

MEDICAL NEWS

Personal Chair of Physiology

Dr. R. C. JORDAN has been appointed to a personal chair in the department of physiology, University College, Cardiff. Dr. Jordan, who is 57, graduated B.Sc. with honours at Imperial College of Science and Technology, London, in 1930, and subsequently held D.S.I.R. and I.C.I. research appointments there in biochemistry. He was awarded the Ph.D. and diploma of Imperial College in 1933 for a thesis entitled "Metabolism of Fats and Phosphatides in *Phaseolus multiflorus*." After a further two years' bacteriological research on behalf of the Ministry of Works to investigate the role of sulphur-oxidizing organisms in the decay of the stone fabric of the Houses of



Parliament, he was appointed assistant lecturer in biochemistry at University College, Cardiff, and in succession was promoted lecturer in physiology, senior lecturer, and, finally, reader in 1961. From 1935 to 1946 he published, jointly with the late S. E. Jacobs, senior lecturer in bacteriology, Imperial College, a series of papers on the "Dynamics of Disinfection," for which he received the D.Sc.(Lond.) in 1948. About this time Dr. Jordan had his teaching appointment converted to a part-time post to enable him to undertake clinical studies in the Welsh National School of Medicine, Cardiff, and he qualified M.R.C.S., L.R.C.P. five years later. From 1955 to 1961 he was a member of the editorial board of the *Journal of Physiology*. Recently, his research interests have been in the cardiovascular field, and his group has developed new techniques for the quantitative study of spatial vector-cardiographic data and their application to the human subject under a variety of physiological and diseased conditions. Concurrently, investigations have been made in the dog on the influence of electrolyte disturbances and autonomic drugs on the relationship between intravascular pressures and cardiac electrical phenomena.

Medical Research in Scotland

On the recommendation of the Advisory Committee on Medical Research, Mr. WILLIAM ROSS, Secretary of State for Scotland, has approved support of the following medical research projects from National Health Service funds: Professor W. M. MILLAR, department of mental health, Aberdeen University, cytogenetical, biochemical, and clinical study of mental subnormality in a regional population, £9,710 for three years; Dr. W. SIRCUS, Western General Hospital, Edinburgh, clinical pathological study of ulcerative colitis, further grant of £2,100 for one year; Dr. R. J. FALLON, department of pathology, Ruchill Hospital, Glasgow, mycoplasma studies, further grant of £3,400 for three years; Dr. J. B. BROWN and Dr. P. GORDON, Currie, Midlothian, respiratory infections in general practice, £250 for three years; Dr. W. SIRCUS and Dr. I. W. PERCY-ROBB, gastrointestinal unit, Western General Hospital, Edinburgh, investigation on bile salt metabolism in ulcerative colitis, £6,600 for three years; Professor R. G. MITCHELL, department of child health, Aberdeen University, neonatal pulmonary blood flow and its variation in health and disease, £1,650 for three years; Mr. J. S. JEFFREY, Royal Infirmary, Edinburgh, tetanus prophylaxis trial, £600 for six months; Mr. G. MURDOCH, Dundee Limb Fitting Centre, Broughty Ferry, Angus, gait analysis in the amputee, up to £7,700 for three years.

Sub-dean for Postgraduate Studies

University College Hospital Medical School has established a new post of sub-dean for postgraduate studies, and Dr. G. M. STERN has been appointed the first holder of the post. The functions of the sub-dean will be (a) to arrange postgraduate seminars and discussion groups and to co-ordinate and publicize the activities of the various groups that already exist in the hospital and medical school; (b) to give advice to U.C.H. graduates on the taking of higher degrees and diplomas; (c) to assist and advise U.C.H. graduates on the availability of, and how to apply for, preregistration appointments, particularly in hospitals other than U.C.H.; (d) to follow up U.C.H. graduates in their subsequent careers, and to give advice and assistance when needed. Dr. Stern's office is in the administrative block of the medical school (Euston 5861, ext. 33).

New Hospital Buildings at Portsmouth

The Minister of Health, Mr. KENNETH ROBINSON, officially opened last week the St. Mary's Maternity Hospital and a new outpatient department at St. Mary's General Hospital, Portsmouth. The new buildings have cost about £1m. and £250,000, respectively. Referring to recent hospital development, the Minister said that in the five years ending September 1966 building schemes to the value of £223m. had been completed. This represented well over half the total for the entire period of the National Health Service. In this financial year £85m. was expected to be spent on hospital building. The figure last year was £75m. In the Wessex region a start had been made with the construction of a new district general hospital at Basingstoke. There were plans for building others at Southampton and Winchester. While a great deal had to be done to modernize the network of old and out-of-date hospitals, the building programme was being carried out at an accelerating pace.

College of G.P.s Medical Recording Service

The following titles, which may be borrowed by any doctor anywhere, have recently been added to the College of General Practitioners' library of talks recorded on tape; *Medical Negligence*, by Dr. J. LEAHY TAYLOR; *Typhoid—The Clinical Picture*, by Dr. A. MELVYN RAMSAY; *Management of Acute Renal Failure in a General Hospital*, by Dr. J. S. CAMERON; *Haemoglobin*, by Dr. HERMAN LEHMANN; *Old People's Welfare and the General Practitioner*, by Miss EVELYN ROITH; and *Drug Dependence—Recent Developments in Great Britain*, by Dr. P. H. CONNELL. A new series on teaching methods is being added to the library. Details of these talks and a list of more than 300 titles can be obtained from the College of General Practitioners' Medical Recording Service, Kitts Croft, Writtle, Chelmsford, Essex (Writtle 316).

Termination of Pregnancy

The Abortion Act, 1967, provides that any treatment for the termination of pregnancy must be carried out in a hospital vested in the Minister of Health or the Secretary of State for Scotland under the National Health Service Acts or in a place approved by the Minister or Secretary of State. Proprietors of premises who wish to have them approved for the purpose of the Act are invited to write, not later than 24 November, for forms

of application to the Ministry of Health, London S.E.1, or, if the premises are in Scotland, to the Scottish Home and Health Department, Edinburgh.

Hospital Voluntary Service

At the recent annual meeting of the National Association of Leagues of Hospital Friends the Parliamentary Secretary to the Ministry of Health, Mr. JULIAN SNOW, urged the leagues and kindred voluntary organizations to increase their visiting of old people, especially in geriatric and psychiatric hospitals. Projects for fund-raising, he said, should be undertaken only after full consultation with the hospital authority.

Medicine Related to Sport

The Institute of Sports Medicine, formed in 1963, announces that the DUKE OF EDINBURGH has accepted the presidency of the institute and that Mr. NORMAN CAPENER has become chairman in place of Sir ARTHUR PORRITT. As a co-ordinating body the institute is concerned with disseminating information, including the results of original work, initiating and promoting research, and arranging facilities for treatment. An academic board recommends and supervises research projects. The institute's address is 10 Nottingham Place, London W.1.

People in the News

► Dr. ALEXANDER HUTCHISON, medical officer of health, City of Kingston upon Hull, will be the next chairman of the council of the Royal Society of Health. He will take up office on 1 January 1968.

► Dr S. E. FINLAY, assistant medical officer, student health department at Leeds University, is to take charge of the University health service.

► Alderman A. W. BRIGGS has been appointed chairman of the South-east Metropolitan Regional Hospital Board in succession to Sir IVOR JULIAN, who retires on 31 March 1968.

News in Brief

Speaking at the annual dinner of the Royal Society of Health in London last week Mr. R. PRENTICE, Minister of Overseas Development, said that at the end of 1966 the Government was supporting nearly 1,200 doctors and nurses and other health workers overseas. British efforts, he emphasized, must be concentrated mainly on helping developing countries to provide their own trained workers.

Work is scheduled to begin in December on a new £70,000 extension to the Royal Marsden Hospital, London. When completed it will add another 16 beds to the hospital, which commemorates the centenary of the death of its founder, Dr. William Marsden, this month.

The Science Museum, London S.W.7, has set up in its atomic physics gallery a small exhibit to illustrate the nature of radioactivity, and to show how Pierre and Marie Curie discovered radium.

Grants and Awards

The Muscular Dystrophy Group of Great Britain announces that medical research grants for the 12 months beginning 1 October will amount to £126,000, an increase of 38% over the previous year.

Glasgow University has received from the Medical Research Council a grant of £3,300 over three years towards a virological study of sudden death in infancy; also a grant from the Scottish Home and Health Department of £1,300 for a further year's study of medical education on television.

The Drapers Company has contributed £1,000 towards the rebuilding of parts of the London School of Hygiene and Tropical Medicine.

In the year ended 31 July 1966 the Scottish Hospital Endowments Research Trust made grants totalling £126,072. A statement of the types of medical research supported by the Trust during the period and the names of persons who received grants are given in an appendix to the annual report (H.M.S.O., 2s. 6d.).

Recent Publications

The Wellcome Trust: Its Origin and Functions, a booklet outlining the policy under which grants are made and giving details of how applications should be submitted. Copies available from the Secretary, Wellcome Trust, 52 Queen Anne Street, London W.1.

Clinical Trials, a report to the Association of the British Pharmaceutical Industry by Dr. DAVID LONG, chief medical adviser and deputy research director of the Wellcome Foundation Ltd. Copies can be obtained from the office of the association, 162 Regent Street, London W.1.

Association of Clinical Biochemists: Scientific Report No. 3, *Automatic Dispensing Pipettes*. An assessment of 35 commercial instruments. Copies of the report can be obtained, post free, from Mr. J. T. Ireland, Biochemistry Laboratory, Alder Hey Children's Hospital, Liverpool 12, 10s. (7s. 6d. to members).

Report on *Upgrading of Wards*, 12s. 6d., Scottish Hospital Centre, Crewe Road South, Edinburgh 4.

World Health Statistics Annual, volume III, 1963: Health Personnel and Hospital Establishments, £2; volume I 1964: Vital Statistics and Causes of Death, £4. Published by World Health Organization, Geneva.

Hospital Laundry and Related Services, a second report by W. A. J. FARNDAL, Ph.D., senior lecturer in hospital administration, City of Westminster College, London. Copies can be obtained from White's Secretarial Agency, 203 Croydon Road, Beckenham, Kent, price 30s. (postage 1s. 2d.).

A booklet, *Organizations Concerned with Particular Diseases or Handicaps*, is published by the Patients Association, 335 Gray's Inn Road, London W.C.1., 2s. 6d.

Coming Events

Postgraduate Medicine, 1967 (T.V. Programme).—"Advances in Therapy," Scottish Television, 13 November (11.50 p.m.), repeat 15 November (1.10 p.m.). "Puberty," Tyne Tees Television, 14 November (1.15 p.m.), repeat 19 November (10.15 a.m.).

National Fund for Research into Crippling Diseases.—Symposium, "The Disabled Young Adult," 13 November, 9.30 a.m., Royal College of Surgeons of England. Particulars from Mr. D. Whitson, N.F.R.C.D., Vincent House, Vincent Square, London S.W.1 (01-834 7001-2).

Royal College of Surgeons of England: Faculty of Radiologists.—Postgraduate week-end course, 18 November. Fee £1 10s. Applications (with fee) to the Secretary, Faculty of Radiologists, R.C.S., Lincoln's Inn Fields, London W.C.2.

British Association of Manipulative Medicine.—Manipulation in general practice introductory course, part II, "Lumbar and Sacro-iliac Areas," 25-26 November, in London. Details from B.A.M.M., 84 Harley Street, London W.1.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 13 November

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.
INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Professor R. E. Steiner: Densitometry in the Study of Pulmonary Ventilation and Circulation.
INSTITUTE OF LARYNGOLOGY AND OTOLARYNGOLOGY.—5.30 p.m., combined staff consultation clinical meeting.
KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr J. M. Talbot: Recent Advances in Sterilization; 6.30 p.m., Dr. E. G. J. Olsen: Embolism.●
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. W. A. Lishman: Diagnosis and Management of the Acutely Disturbed Patient.
SCOTTISH TELEVISION LTD.—11.45 p.m., *Advances in Therapy*. (Sponsored by Glasgow Postgraduate Medical Board.)

Tuesday, 14 November

B.B.C. 1 TELEVISION.—11.15 p.m. (approx.) medicine today: Low Back Pain. (Sponsored by A.S.M.E.)
BOLTON AND DISTRICT MEDICAL SOCIETY.—At Gymnasium, Bolton Royal Infirmary, 8.15 p.m., clinical meeting.
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. G. F. Joplin: Effects of Y-90-Phenyl Implantation in Man.
HEATHERWOOD HOSPITAL, ASCOT.—At Outpatient Hall, 8.45 p.m., Mr. C. W. Manning: Leg Inequality.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark lecture on perspectives in health planning—I, by Dr. A. Engel (Sweden): Health Planning in a Changing Society.
MANCHESTER MEDICAL SOCIETY: SECTION OF SURGERY.—At Large Anatomy Theatre, Manchester University Medical School, 8 p.m., Mr. A. Hargreaves, Mr. N. C. Keddie: Carcinoma of the Colon and Rectum.
NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., Mr. E. Leighton John: Ulcerative Colitis.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. M. Vitali: Modern Techniques for Amputation and the Rehabilitation of Amputees.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m.,
WEST-END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. J. N. Milnes: clinical demonstration.

Wednesday, 15 November

BRITISH INSTITUTE OF RADIOLOGY.—(1) At Edward Lewis Theatre, Middlesex Hospital Medical School, 10 a.m., meeting: Design of Counting Systems for Dynamic Studies and Uptake Measurements; (2) at Institute of Child Health, 7.15 p.m., conversazione by Professor J. M. Tanner.●
CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital). (1) 12 noon, surgical meeting; (2) 8.30 p.m., Professor J. R. Trounce: Tranquillizers.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. J. Prime: The Atmosphere.
INSTITUTE OF UROLOGY.—5 p.m., Dr. A. B. Francis: Bacteriological Problems in Urology.
KENNEDY INSTITUTE OF RHEUMATOLOGY.—At rear of West London Hospital, 5 p.m., Dr. A. St. J. Dixon: Problem of Polymyalgia Rheumatica and its Differential Diagnosis.
MANCHESTER MEDICAL SOCIETY: SECTION OF PAEDIATRICS.—At Large Anatomy Theatre, Manchester University Medical School, 5 p.m., Dr. J. Blair Hartley: Some Anomalies of the Skull at Birth—significant and insignificant.
OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Mr. W. M. Keynes: Studies in Pancreatitis.
ROYAL FREE HOSPITAL.—5.15 p.m., Dr. J. F. Soothill:
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conferences by Dr. P. J. L. Holt: Rheumatoid Arthritis; Dr. D. L. Gardner: Septicaemia. (2) 2 p.m., Dr. M. Sandler: Catecholamine Secreting Tumours.
ROYAL STATISTICAL SOCIETY.—At Botany Theatre, University College, London W.C., 3 p.m., discussion meeting: Social and Medical Statistics.
SCOTTISH TELEVISION LTD.—1 p.m., *Advances in Therapy*. (Sponsored by Glasgow Postgraduate Medical Board.)
STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. J. Lister: Current Views on the Management of Diabetes Mellitus. (2) 6 p.m., Squadron Leader J. P. Lee-Potter: Schistosomiasis and Leishmaniasis.
WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Professor C. E. Dent: Primary, Secondary, and Tertiary Hyperparathyroidism.

Thursday, 16 November

ABERDEEN UNIVERSITY FACULTY OF MEDICINE.—At Large Lecture Theatre, University Medical Build-

ings, Foresterhill, 5 p.m., Dr. B. D. Acheson: Records, Record-linkage, and Research.
ADDENBROOKE'S HOSPITAL.—At M.R.C. Lecture Theatre, New Addenbrooke's Hospital, 8.30 p.m., Dr. M. D. A. Vickers: Does Halothane Damage the Liver?
BRITISH INSTITUTE OF RADIOLOGY.—6 p.m., discussion group; 7.30 p.m., Mackenzie Davidson memorial lecture by Professor W. V. Mayneord, F.R.S.: Radiation Carcinogenesis.
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. B. Creamer: Paneth Cells.
CAMBRIDGE MEDICAL SOCIETY.—7.30 p.m., visit to Technological Research Station, Spillers Ltd.
CHADWICK TRUST.—At 90 Buckingham Palace Road, London S.W. 5 p.m., paper by Professor A. L. Banks: Public Health—Balance Sheet for the Present Century.
DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Professor J. S. Robinson: Respiratory Failure.
HONYMAN GILLESPIE LECTURE.—At Surgery Lecture Theatre, Edinburgh Royal Infirmary, 5 p.m.,

Professor D. V. Davies: Articular Cartilage.
INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At St. Chelsea Hospital for Women, 2 p.m., Mr. H. B. Lockhart-Mummery: The Pelvic Colon and Rectum.
INSTITUTE OF RELIGION AND MEDICINE: LONDON MEDICAL GROUP.—At London Hospital Medical College, 5.30 p.m., Dr. H. Trowell: Some Problems of the Doctor-Patient Relationship.
LONDON UNIVERSITY.—(1) At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark lecture on perspectives in health planning—II, by Dr. A. Engel (Sweden): Statistics and Health Planning. (2) At Edward Lewis Theatre, Middlesex Hospital Medical School, 5.30 p.m., special university lecture in pharmacology by Professor B. Holmstedt (Stockholm): Use of Gas Chromatography and Mass Spectrometry in Studies of Drugs and Metabolites.
MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Theatre B, Roscoe Building, Brunswick Street, 8 p.m., Professor J. F. Nunn: Factors in the Definition of Minimum Safe Arterial Po₂.

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.—At School of Pharmacy, Brunswick Square, London W.C. 7 p.m., meeting and discussion: The Sainsbury Report. Speakers include Professor A. Kekwick, Dr. G. R. Fryers.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4.15 p.m., Arnott demonstration by Mr. R. G. Nottley: The Ureter.
ROYAL NORTHERN HOSPITAL, London.—5 p.m., Dr. C. W. H. Havard, Dr. P. Turner: Adrenergic Blockade.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 4 p.m., Dr. H. F. West: Cortisol Metabolism in Rheumatoid Disease. (2) 4 p.m., Dr. D. G. Melrose: Hypothermia. (3) 5 p.m., lecture on medical history by Dr. E. S. Clarke: The Anatomical Basis of Medicine—I.
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At London School of Hygiene and Tropical Medicine, 7.30 p.m., laboratory meeting and demonstrations.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Mr. H. Gordon: Intrauterine Transfusion.
WESTMINSTER MEDICAL SCHOOL.—At Meyerstein Lecture Theatre, 5.15 p.m., clinicopathological conference by Dr. F. B. Gibberd.

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Index.
Volume 22, No. 6. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

Friday, 17 November

BROOK GENERAL HOSPITAL.—At Postgraduate Medical Centre, 5.30 p.m., Dr. A. R. Norton: Drug Treatment in Modern Psychiatry.
KINGSTON-UPON-THAMES MEDICAL CENTRE.—1 p.m., psychiatric seminar by Dr. J. S. Bearcroft: Development of Psychiatry in the Kingston Area and Postgraduate Education in Psychiatry related to the opening of the New Psychiatric Unit at Kingston Hospital.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—At Newcastle-upon-Tyne, scientific meeting, morning: Observations on the Aetiology of Certain Gynaecological Cancers; afternoon: Perinatal and other Factors in the Development of Children.
ROYAL COLLEGE OF SURGEONS OF ENGLAND: FACULTY OF RADIOLOGISTS.—4.30 p.m., Skinner lecture by Dr. H. C. Ho (Hong Kong): Nasopharyngeal Carcinoma—Radiodiagnostic and Radiotherapeutic Aspects.
ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION.—At Barnes Hall, Royal Society of Medicine, 2.15 p.m., Maudsley lecture by Professor A. D. B. Clarke: Learning and Human Development.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Mr. M. Paneth: Pulmonary Embolism. (2) 11.30 a.m., Professor H. H. Bentall, Mr. W. P. Cleland: clinicopathological conference (cardiac). (3) 4 p.m., Dr. R. D. Bradley: Investigation of the Circulation in an Intensive-Care Unit.
WEST MIDDLESEX HOSPITAL.—4 p.m., Dr. Chandra Grubb: Vaginal Cytology.

Saturday, 18 November

ROYAL COLLEGE OF GENERAL PRACTITIONERS.—At B.M.A. House, London W.C.1, 11 a.m., James Mackenzie lecture by Dr. Ronald Gibson: Lucerna Pedibus Meis; 2 p.m., annual general meeting.

Sunday, 19 November

CLWYD AND DEESIDE BOARD OF POSTGRADUATE STUDIES.—At Royal Alexandra Hospital, Rhyl, 10 a.m., symposium: Diabetes Mellitus.
GREAT YARMOUTH AND DISTRICT MEDICAL CLUB.—At Northgate Hospital, Great Yarmouth, 10.15 a.m., all-day symposium: The Handicapped Child.
ROYAL COLLEGE OF GENERAL PRACTITIONERS.—At Wellcome Building, Euston Road, London N.W. 9.15 a.m., annual symposium: Combined Operations—Medicine, Science, and Humanity.
ROYAL COLLEGE OF GENERAL PRACTITIONERS: EAST ANGLIAN FACULTY.—At Papworth Hospital, 10 a.m., full-day course for general practitioners: Cardiovascular and Respiratory Conditions of Interest in General Practice.
ROYAL NORTHERN HOSPITAL, London.—10.15 a.m., clinical conference by Dr. D. Geraint James.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Atiology*, London W.C.1. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 18 NOVEMBER 1967

Pointers

Congenital Dislocation of the Hip: Technique of early detection and findings in 14,594 newborn infants described. A clinical classification for more accurate comparison of findings is suggested (p. 377). Leader this page.

Housing and Health: Service families quartered in flats had more respiratory tract infections and psychoneurotic disorders than similar families quartered in houses (p. 382). Leader p. 376.

Mumps and Endocardial Fibroelastosis: An association possible (p. 372).

Child Care: Sheldon report proposes this should become province of general practitioners (p. 374).

Gastric Emptying: Slowed by intravenous gastrin. Acid secretion rate increased and outlasts slowing of emptying (p. 386).

Choice of Stethoscope: Comparison of performance of models in common clinical use (p. 388).

Locating the Placenta: No placenta praevia missed by a colour autoscanner technique (p. 390).

Depot Corticosteroids: Tetracosactrin—a synthetic preparation—maintains its activity twice as long as a gelatin preparation of natural corticotrophin, is easier to inject, but causes more local discomfort (p. 391).

Cushing's Syndrome or Obesity? Fluorimetric estimation of urinary 11-hydroxycorticoids is a relatively simple and rapid procedure for differentiating these two conditions (p. 394).

Case Reports: Tuberous sclerosis and retinopathy (p. 398); stellate ganglion block in total blindness (p. 400); scorbutic megaloblastic anaemia (p. 402).

Postgastrectomy Syndromes: Current Practice article reviews the abdominal complications (p. 403).

Immunization: Review of Sir Graham Wilson's book on its hazards (p. 407).

First Blood Transfusion: Sir Geoffrey Keynes reviews the rival claims of London and Paris (p. 410).

Hospital Organization: Suggestions for shortening waiting-lists, using private beds and local benevolence, and more realistic accounting (p. 411).

Middle-age: Its disabilities reviewed (p. 414).

Artificial Sweeteners: Ministerial assurances on cyclamates (p. 429).

Assistants and Young Practitioners: Want general practitioners to have hospital beds (*Supplement*, p. 53).

Fellowship for Freedom in Medicine: Addressed by Labour M.P. (*Supplement*, p. 55).

Congenital Dislocation of the Hip

One of the most rapid recent advances in medicine has been in the diagnosis and treatment of congenital dislocation of the hip. In 1961 a leading article in the *B.M.J.*¹ stated that late diagnosis was still a major problem and cited the results of treatment of children 3 years old and of a few up to 5 years old. In 58% of cases satisfactory results followed conservative treatment; open reduction had to be performed in 20% of children with this disorder under 3 years old.

Since then a new conception of the nature of congenital dislocation of the hip has replaced the old ideas, which originated in the days of Hippocrates and were elaborated by Dupuytren and others, all of whom thought the condition incurable. In 1936 M. Ortolani² described a test, subsequently modified by other workers, to check the state of the hips of newborn children and to detect congenital dislocation of the hip at birth.³

In an article at page 377 of the *B.M.J.* this week Dr. H. V. L. Finlay, Mr. R. H. Maudsley, and Mr. P. I. Busfield describe this test in detail. Widespread use of it by many hospital workers has convinced most observers that all congenital dislocations are present at birth. The condition is "congenital" only in this sense; it is not a genetic defect in the same class as the developmental errors like harelip, cleft palate, and absent or supernumerary fingers, but is probably an acquired condition occurring in the last few weeks of pregnancy. The figures so far published indicate that there is a noticeable reduction of incidence in children under 4½ lb. (2,000 g.) in weight at birth; and if it were a true developmental error the incidence ought to be the same irrespective of birth weight or its related factor, maturity. Further observations and serial examinations of very young children from birth to one week old show that undue laxity of the hips, from the smallest degree up to complete dislocation, is far more common in newborn children than was believed a few years ago, and that in the first week of life there is a high rate of spontaneous recovery—approaching 60% in fact. These discoveries, together with the opportunities of early treatment that early diagnosis affords, have in a matter of a few years brought the success rate of conservative treatment very close to 100% and reduced the operation rate (adductor tenotomy) to less than 5%.

Here surely is one of the most satisfying things in medicine. The diagnostic test is simple, requires no special skill, no special apparatus, and can be carried out by the doctor or midwife at the mother's bedside immediately the child is born. There is virtually no risk of fracturing a healthy femur if it is accorded the gentleness and care normally extended to newborn babies. In fact there is a far greater risk of the child sustaining a fractured femur during birth, especially a breech birth, than there is in examining the hips. The interpretation of the test is simple. The child is placed in the position described in the article by Dr. Finlay and his colleagues: in a normal hip the femur and the pelvis move together. When the femoral head is slowly moved backwards the pelvis rotates with

it, because the femoral head is in the acetabulum and stays in the acetabulum. In a dislocated hip the femoral head is clearly seen to be moving backwards and forwards on the side of the pelvis; the pelvis does not rotate with it. This movement is accompanied by visible lengthening and shortening of the thigh and by the palpable click described by Ortolani. There is hardly a simpler test in the whole of medicine. On the discovery of such a hip it would seem permissible to wait and then re-examine the child in seven to ten days. If there still appears to be an abnormality the child should be placed on a splint.

Dr. Finlay and colleagues sum up the present position accurately, precisely, and clearly. They make an important point in drawing attention to the apparent variation in incidence in different parts of the country. There may be a true geographical variation, but the apparent incidence in a place will depend to some extent on the skill and experience of the examiner, for the more experienced examiner

will tend to recognize more of the less affected hips. The apparent incidence may also vary owing to lack of uniformity in the definition of the various states of the hip. These authors have produced a comprehensive classification of abnormalities of the hip covering every state of laxity in the newborn baby, including those conditions which are not true congenital dislocations but are teratological and paralytic in origin.

This is a valuable contribution to the already extensive literature on the subject. Examination of the hips for congenital dislocation should become automatic for every doctor who sees newborn or very young babies. The results of treatment after diagnosis at birth are so nearly perfect that crippling from congenital dislocation of the hip should soon recede into medical history.

¹ *Brit. med. J.*, 1961, 1, 1746.

² Ortolani, M., *Pediatrics (Napoli)*, 1937, 45, 129.

³ *Brit. med. J.*, 1966, 2, 1341.

Mumps and Cardiac Embryopathy

Just over 200 years ago Morgagni¹ described a case of "endokardfibrosen." It was probably one of the first reported cases of the cardiac anomaly about which so much was written in later years and for which in 1943 T. Weinberg and A. J. Himelfarb² suggested the name endocardial fibroelastosis. The primary form of endocardial fibroelastosis usually presents with heart failure and cardiomegaly in the first year of life. The aetiology is unknown, but recent evidence suggests that intrauterine infection with mumps may be connected with this syndrome.

A few years ago G. R. Noren and associates³ made the interesting observation that nine children with primary endocardial fibroelastosis showed a delayed-type cutaneous hypersensitivity reaction to mumps virus antigen. More recently J. W. St. Geme, G. R. Noren, and P. Adams⁴ report further observations on this interesting relationship. Fourteen children aged 2 months to 2 years in whom a diagnosis of primary endocardial fibroelastosis had been made were tested by intradermal inoculation with 0.1 ml. formalinized mumps antigen prepared in embryonated hens' eggs. All 14 children developed erythema 10 to 15 mm. in diameter within 24 to 48 hours; one child reacted to both the mumps and the control antigens. Only 2 of the 14 children had detectable mumps neutralizing antibody at the time of the skin test and one of them had been exposed to mumps after birth. In a control group of 25 children of the same age range only 4 developed a skin reaction of 10 mm. or greater; six showed a reaction of 5 to 8 mm., and the remainder either had no reaction or one of 3 to 4 mm. One child reacted to both mumps and control antigens to an equal degree. None of the 25 control children were found to have mumps antibody. Similar tests on the mothers of the children with endocardial fibroelastosis showed that all reacted to the mumps antigen to the usual degree that is expected in those who have contracted natural infection with mumps—that is to say, 15 to 25 mm. Six of these mothers gave a history of exposure to mumps in the first trimester of pregnancy and of having had parotitis as children, whereas none of the mothers of the control group of children did so.

Retrospective inquiries have their disadvantages, but nevertheless these observations cannot be lightly dismissed. Further tests on the children with primary endocardial fibroelastosis gave additional information. Eight of the seronegative children in the endocardial group were tested again after one or more skin tests with mumps antigen in an attempt to detect an anamnestic antibody response, but none gave it. Three of the children were also inoculated with 1.0 ml. of inactivated mumps vaccine. Only one of these developed an antibody response. Punch biopsies from the erythematous skin reactions showed a mononuclear-cell type of response, characteristic of delayed hypersensitivity reactions. Positive transfer of lymphocytes in one of the patients produced a delayed reaction in a previously non-responsive child. Attempts to isolate mumps virus from the hearts of fatal cases were unsuccessful.

Similar studies have been carried out by several other groups of investigators. A co-operative study,⁵ from the Hospital for Sick Children, Toronto, and from Rochester, N.Y., using defined criteria,⁶ produced essentially similar findings on cases of primary endocardial fibroelastosis. Out of 50 children with primary disease aged 0 to 5 years, 42 developed a positive skin reaction of 10 mm. or more of erythema within 24 to 36 hours at the site of inoculation. In the age group 0 to 2 years, which was similar to that studied in the Minneapolis survey, 91% (19 children) were positive. In the control group of 138 children 91% had a negative skin test. J. B. Vosburgh and associates⁷ at the University of Kansas reported positive skin reactions in six out of nine children with primary endocardial fibroelastosis aged 15 to 54 months. But studies conducted from the Children's Hospital Medical Center in Boston have failed to substantiate these findings. W. N. Gersony and associates⁸ could find no evidence of a relationship between endocardial fibroelastosis and mumps on the basis of exposure to mumps in pregnancy, presence of mumps serum antibody, or a positive skin test. However, these authors regarded an erythema of 15 mm. or greater as positive and 10 to 14 mm. as doubtful.

What then is the significance of these findings? Despite contradictory results the relationship between mumps and fibroelastosis cannot be ignored, certainly not on the question

of a millimetre or two of erythema. A verdict of "not proven" would appear to be justified in these circumstances, and this should lead to further investigations. One of the first points to be established is the question of what constitutes a positive reaction. The recommendations of the American Public Health Association and the manufacturers of the antigen state that the minimal area for a positive skin test is 15 mm. and that one of 10 to 14 mm. should be regarded as doubtful. But these recommendations are based on studies of mumps infection in children and adults acquired postnatally. No information is yet available on whether an infant exposed to mumps in utero will react in the same way.

If it is accepted as a working hypothesis that there is some aetiological relationship between maternal mumps and fibroelastosis, how can one explain the findings of a delayed-type hypersensitivity reaction and absence of mumps antibody? The situation is very different from what occurs after foetal infection with rubella and cytomegaloviruses. In both these cases virus persists for long periods and a high titre of neutralizing antibody is produced, but it is not yet known whether infants who have had congenital rubella show a hypersensitivity reaction or not. In trying to visualize a possible mechanism to explain the difference between the effect of rubella and cytomegaloviruses and the possible effect of mumps on the foetus, it may be relevant to note that the former result from primary infections of the mother (certainly this is true of the great majority of cases of rubella), whereas in some of the cases of fibroelastosis a history was obtained of the mother's re-exposure to mumps in pregnancy after an attack of the disease in childhood. It is theoretically possible that a delayed hypersensitivity reaction could develop in the foetus as a result of an interaction, possibly of short duration, between mumps antigen and mumps antibody derived from the mother. Experimental evidence shows that delayed hypersensitivity can be induced without development of circulating antibody. It is also possible to explain this reaction on the basis of cross-reactivity with another myxovirus, such as one of the parainfluenza viruses, but no evidence for this could be obtained.⁴

More clues might be found in a prospective study of mumps in pregnancy, including both primary infections and cases of re-exposure, with a detailed clinical and virological assessment of the offspring. Particular attention would have to be paid to accurate recording of the mumps skin test in terms of millimetres of erythema. But the possibility of a multiple causation of endocardial fibroelastosis must be borne in mind. Recently L. Fruhling and colleagues⁹ produced evidence of Coxsackie B virus infection with recovery of Coxsackie virus from the myocardium of several children with fibroelastosis. More recently still G. C. Brown and T. N. Evans¹⁰ provided serological evidence that Coxsackie virus infection contracted in the first trimester might be causally related to congenital

heart disease. Further work may show the extent to which mumps, Coxsackie, and other viruses are related to congenital malformations.

Hazards of Ambulance Journeys

Though the prime function of an ambulance service is to carry patients, it must also provide special care for the 5% of them who are emergency cases. As emergency treatment has become increasingly successful in saving lives that would previously have been lost, the importance of getting the patient quickly to the therapeutic team is clear. But two closely connected questions arise here. One concerns the therapeutic facilities that should be available to the patient before he reaches hospital, the other the manner of his transport. Recently the report¹ of a working party to the Ministry of Health and Scottish Home and Health Department has made a number of useful recommendations on ambulance design and equipment.

C. R. G. Howard² and K. C. Easton³ among others have called for skilled medical attention to be available at the scene of the accident. Though this cannot always be practicable, there are occasions when it may be—for instance, in country districts with specially enthusiastic and knowledgeable practitioners. (In towns the shorter journey means that calling a doctor may delay the movement of a patient to hospital.) In other circumstances a special team can sometimes be summoned from a suitable hospital,⁴⁻⁶ as when a person is trapped and needs resuscitation. And, again, where accidents are predictable—at motor races, for example—the necessary facilities can be prepared in advance. J. F. Pantridge and J. S. Geddes⁷ have recently reported on the value of a mobile intensive-care unit that can be quickly got to a patient with myocardial infarction.

At present too little information has been published on what happens to patients before they reach hospital. This would seem to be a deficiency worth remedying. Certainly it is difficult to lay down rules for deciding when a patient should be moved from the place of the emergency, how he should be moved, and whither. When special knowledge is lacking, humanity and common sense may suffice, and there is no doubt that ambulance crews in different parts of the country are continually making wise decisions in difficult cases. But better radio communication is needed between ambulances and emergency units—for even experienced men appreciate guidance and those that are less so need it. Moreover, it is valuable if calls for help can be assessed by an experienced doctor.

An ambulance for dealing with emergencies should allow a single patient to be carried in the middle so that attendants

¹ Morgagni, J. B., *De sedibus et causis morborum per anatomen indagatis libri quinque*, 1765, 2nd ed. Padua.

² Weinberg, T., and Himelfarb, A. J., *Bull. Johns Hopk. Hosp.*, 1943, 72, 299.

³ Noren, G. R., Adams, P., and Anderson, R. C., *J. Pediat.*, 1963, 62, 604.

⁴ St. Geme, J. W., Noren, G. R., and Adams, P., *New Engl. J. Med.*, 1966, 275, 339.

⁵ Shone, J. D., Armas, S. M., Manning, J. A., and Keith, J. D., *Pediatrics* 1966, 37, 423.

⁶ Sellers, F. J., Keith, J. D., and Manning, J. A., *Circulation*, 1964, 29, 49.

⁷ Vosburgh, J. B., Diehl, A. M., Liu, C., Lauer, R. M., and Fabiyy, A., *Amer. J. Dis. Child.*, 1965, 109, 69.

⁸ Gersony, W. M., Katz, S. L., and Nadas, A. S., *Pediatrics*, 1966, 37, 430.

⁹ Fruhling, L., Korn, R., Lavillaureix, J., Surjus, A., and Fousseureau, S., *Ann. Anat. Path. (Paris)*, 1962, 7, 227.

¹⁰ Brown, G. C., and Evans, T. N., *J. Amer. med. Ass.*, 1967, 199, 183.

¹ Ministry of Health Report of the Working Party on Ambulance Training and Equipment: Part 2, Equipment and Vehicles 1965-67, 1967. H.M.S.O., London.

² Howard, C. R. G., *J. Coll. gen. Pract.*, 1965, 9, 48.

³ Easton, K. C., *Brit. med. J.*, 1967, 3, 230.

⁴ Hall, M. H., *Lancet*, 1965, 1, 904.

⁵ Collins, J., *Brit. med. J.*, 1966, 2, 578.

⁶ Hall, M. H., and Garden, R. S., *ibid.*, 1967, 3, 170.

⁷ Pantridge, J. F., and Geddes, J. S., *Lancet*, 1967, 2, 271.

⁸ Cullen, C. H., Douglas, W. K., and Danziger, A. M., *Brit. med. J.*, 1967, 3, 438.

⁹ Strange, F. G. St. Clair, *ibid.*, 1967, 3, 560.

¹⁰ Glover, J. R., *ibid.*, 1967, 3, 678.

¹¹ Heald, C. B., *ibid.*, 1967, 3, 678.

¹² Horton, J., *ibid.*, 1967, 3, 678.

¹³ Stewart, A. B., *ibid.*, 1967, 3, 797.

¹⁴ Gurling, K. J., *ibid.*, 1967, 3, 797.

¹⁵ Bothwell, P. W., *Publ. Hlth (Lond.)*, 1960, 74, 459.

have ready access to him from all sides; it should have space for equipment; and it should provide a comfortable ride. Of these requirements the last is more easily stated than achieved. Even for a healthy person it is at least disconcerting to ride recumbent in an ambulance, without the sight of surroundings that would enable him to brace himself when necessary. For sick and injured people such unpleasantness fades into insignificance beside the jolting and swaying of which correspondents have recently written in the *B.M.J.*⁸⁻¹⁴ Even a good road, a modern ambulance, a considerate driver, and a police escort do not guarantee a smooth ride. P. W. Bothwell¹⁵ has long campaigned in the cause of devoting as much care to the suspension of ambulances as to that of racing cars, but manufacturers need some financial incentive, for Britain has only a few hundred new ambulances of all types each year. Meanwhile the Working Party has provided admirable specifications as a guide to local authorities requiring to order new ambulances or to refurbish existing ones.

Escherichia coli Pneumonia

It has long been recognized that antibiotic treatment is altering the bacterial aetiology of nonspecific infections. Those caused by organisms, such as haemolytic streptococci and pneumococci, consistently and highly sensitive to antibiotics are either less common or at least less often assume their severest forms, notably septicaemia. On the other hand, staphylococci and various coliform bacilli, which can be highly resistant to many antibiotics, have come into far greater prominence as causes of life-endangering infections. This has nowhere been made clearer than in the studies of M. Finland and his colleagues¹ in 1959, who showed that septicaemia due largely to Gram-negative species was actually causing a higher mortality than that from old-fashioned forms in the days before either antibiotics or sulphonamides had been introduced.

Many infections of this kind are acquired in hospital, and some are "superinfections" replacing another organism eliminated by the antibiotic used in treatment. This is particularly true of infections of the lung. With the exception of *Klebsiella pneumoniae* (Friedländer's bacillus), which is a rare cause of severe lobar pneumonia, Gram-negative organisms have not been regarded as primary pathogens in the lung, but only as "opportunists." Certainly Gram-negative organisms have not in the past been recognized as causing any pneumonia with distinctive characters. The claim of J. R. Tillotson and A. M. Lerner,² of the Detroit Général (Receiving) Hospital, to have observed a distinctive type of pneumonia caused by *E. coli* must therefore command interest. This hospital serves a predominantly negro population. During a period of 30 months it admitted 1,882 patients with pneumonia: in 81 of these the cause was a Gram-negative bacillus and in 20 this was *E. coli*.

The mean age of these patients was 53, but was higher in the 11 whites than in the negroes; 12 were men. "One or more serious chronic diseases were present in every case"; among many mentioned are diabetes (11), pyelonephritis (11), alcoholism (7), arteriosclerotic vascular disease, anaemia, hypertension, pancreatitis, and peptic ulcer. It thus seems

unlikely that this form of pneumonia can occur in a previously healthy subject. The condition was considered to have developed before admission in 15. The organism, usually found in more than one site, was cultivated from the sputum in 18, from the blood and urine in eight patients each, and from pleural exudate in six. The lesion was a lower lobe bronchopneumonia with a predominantly mononuclear alveolar exudate, often complicated by empyema. Oddly enough, this complication was a favourable prognostic sign: the overall mortality was 60%, but only 37.5% in eight patients with empyema and 75% in those without. Tachycardia was disproportionate to fever and hypotension was common. Herpes labialis was never seen. The infection was considered to have arisen in either the urinary or gastrointestinal tracts, the former in the eight patients with pyelonephritis, and the latter sometimes after gastroenteritis or abdominal operations: aspiration may have been responsible in two. No evidence for these assumptions about origin is offered.

All the patients were treated with antibiotics. The antibiotic used had been shown to be appropriate by laboratory tests in all survivors, but in only two out of the 12 fatal cases. Kanamycin was the most successful; when chloramphenicol and tetracycline were used resistance developed rapidly in repeated cultures from several sources. Tillotson and Lerner suggest that the resistance was due to the operation of transference, but they made no attempt to establish whether this was the explanation. This is perhaps unfortunate, for the finding is unusual, and it is difficult to see how organisms in the blood or urinary tract, where other bacteria would not usually have been present, could have acquired resistance in this way.

There is no reason for supposing that this disease entity is peculiar to the country in which it has been described, though it may well be largely confined to indigent people in whom serious chronic disease has been neglected. Physicians elsewhere may find it rewarding to watch for *E. coli* pneumonia, but if they do so their laboratories should be warned to take more interest than usual in what are commonly dismissed as "coliforms."

Health of the Child

From its inception the National Health Service has been criticized for its tripartite structure. In particular the accusation has often been made that the N.H.S. consists of two sickness services—those provided by the hospitals and by the general practitioners—and that only the services provided by the local authorities can be described as a health service.

In 1964 a subcommittee of the Standing Medical Advisory Committee under the chairmanship of Sir Wilfrid Sheldon was set up "to review the medical functions and medical staffing of child welfare centres and to make recommendations." The subcommittee might have advocated a strengthening of the local authority health services, which would have led to further trichotomy and to increased dissipation of already scarce medical manpower. Instead its report¹ takes a refreshing and realistic look at the subject, and challenges the hospital and general medical services to take more interest in the health of children.

Few doctors doubt that provision for the maintenance of health, prevention of illness, and the early identification and

¹ Finland, M., Jones, W. F., and Barnes, M. W., *J. Amer. med. Ass.*, 1959, 170, 2188.

² Tillotson, J. R., and Lerner, A. M., *New Engl. J. Med.*, 1967, 277, 115.

correction of disease would result in a more healthy society. Moreover, in theory, this should eventually reduce the demand on the curative services. The problem is to decide how the preventive services should be provided. The subcommittee thinks that the general care of infants and children should become the province of general practitioners supported by health visitors, and that the hospitals should provide centres for special assessments and treatment. The medical officer of health should continue to be responsible for the overall supervision of the services for children, and for ensuring that they are adequate.

Many general practitioners have already shown that they can successfully provide in their own premises many of the services described in the report. Several of them have described their experiences in holding infant welfare clinics and health education classes in the surgery, in co-operating with health visitors, and in doing routine school health service examinations. Nevertheless, so far this work has been carried out by enthusiasts, and it can be done only with the aid of an equally enthusiastic and co-operative medical officer of health. Several problems will have to be solved before general practitioners can undertake work in this field. Many are already so burdened with work that they might be unwilling or unable to accept further responsibilities. Not all surgeries have space where clinics could be held, or a room in which a health visitor could work. The holding by general practitioners of clinics, other than in their own premises for their own patients, might be resented by some of their colleagues. Many family doctors would want to have further training in paediatrics and to know more of the skills and training of health visitors and other workers in the health team. The subcommittee was precluded by its terms of reference from making financial recommendations, and thus it forbore to make the obvious point that general practitioners should be paid for this work.

The best way to resolve most of these problems would be for groups of doctors to work from specially designed premises. When one or two members of a group or partnership follow a personal interest jealousies and fears of poaching patients need not arise. The work load might well be eased by more recruitment to general practice from married women and others now employed by local authorities. They might be attracted by the prospect of working part or full time in a group where they could also practise their special skills. Younger doctors would be more inclined to become general practitioners if they knew that they could do good work in good premises.

The Subcommittee underlines the need for changes and improvements in the teaching of child care both for undergraduates and for graduates, and it advocates inclusion of child care in the vocational training of all general practitioners. The Royal College of General Practitioners has advocated at least three, and preferably six, months' vocational training in paediatrics. The subcommittee rightly suggests that principals who wish to undertake the work now carried out for children by local authorities should undertake thorough postgraduate training. At present this would require special payments, as the length of time suggested (six weeks) would not be covered by the existing arrangements under Section 48 of the National Health Act. Payments would also have to be made for locum cover during the absence of the doctors concerned.

¹ *Child Welfare Centres, Report of the Subcommittee, Standing Medical Advisory Committee, Central Health Services Council, Ministry of Health, 1967. H.M.S.O., London. 4s. 3d. net.*

Views are changing on the whole content and organization of general practice. The recommendations of the Sheldon Committee are sensible and they should find general acceptance. Above all they would offer family doctors a chance to enlarge the scope of their work in a field which is properly theirs. It is a chance they should not miss.

Diagnostic Value of Fluorescent Antibodies

The reaction of humoral antibody with its specific antigen is classically detected by precipitation if the antigen is in solution, by agglutination if it is particulate, by lysis if it is cellular, or by the ability of the antigen-antibody complex to fix complement. To detect the distribution of an antigen histologically A. H. Coons and M. H. Kaplan¹ devised and developed a technique for labelling specific antibodies with a fluorescent dye so that histological preparations treated with the conjugate, and thoroughly washed to remove unbound reagent, showed the sites of antigen by their fluorescence on examination with light of appropriate wavelength.

Though the principle of the procedure is simple, in practice the method presents many technical difficulties in the avoidance of false positive reactions. These can be considerably reduced, firstly, by the separation of the immunoglobulin fraction from the serum proteins as a whole by making use of salt fractionation or column chromatography, and secondly by the careful removal of unbound dye, usually by passage of the conjugate through a column of Sephadex G.25. Finally, the tendency of the conjugate to bind to the tissues non-specifically can be largely avoided by absorption with a dried powder of liver or other tissue known to lack the antigen under investigation.

The method is not confined to the study of antigens. By the use of labelled antigens it can as readily be applied to the histological demonstration of specific antibody.² Both these types of procedure in which the specific reagent is itself labelled employ what is known as the direct fluorescent technique. Its major drawback is the necessity for a different labelled reagent for each antigen or antibody under investigation. Much more versatile is the indirect or so-called sandwich technique,³ in which a single reagent can be employed for the study of an indefinite range of antigens and their antibodies. For example, if one wishes to study the distribution of 20 different antigens in a guinea-pig by means of 20 specific antibodies raised in rabbits, it is not necessary to label any of the specific antisera, since their presence in a histological preparation can be as clearly shown by the use of a single labelled antibody to rabbit immunoglobulin prepared in some other species such as goat or sheep. Thus the distribution of type III pneumococcal polysaccharide injected into a guinea-pig is detected by treating appropriately prepared sections firstly with a rabbit antipneumococcal type III antiserum and then by the fluorescent goat antirabbit immunoglobulin antiserum. The rabbit immunoglobulins

¹ Coons, A. H., and Kaplan, M. H., *J. exp. Med.*, 1950, **91**, 1.

² ———, Leduc, E. H., and Connolly, J. M., *ibid.*, 1955, **102**, 49.

³ Weller, T. H., and Coons, A. H., *Proc. Soc. exp. Biol. (N.Y.)*, 1954, **86**, 789.

⁴ Cherry, W. B., Goldman, M., and Carski, T. R., *Fluorescent Antibody Techniques in the Diagnosis of Communicable Diseases*. 1960. Atlanta.

⁵ Fife, E. H., Bryan, B. M., Sanders, R. W., and Muschel, L. H., *Amer. J. clin. Path.*, 1961, **36**, 105.

⁶ Glynn, L. E., and Holborow, E. J., *Autoimmunity and Disease*. 1965. Oxford.

bound by the type III polysaccharide will then in their turn bind the fluorescein-labelled goat antirabbit globulin. Any antigen therefore against which a rabbit antiserum is available can be demonstrated by a single fluorescent preparation of goat or sheep antirabbit immunoglobulin antiserum.

Of the many applications of the fluorescent-antibody technique now in use some of the most useful are in the identification of micro-organisms and the detection of specific antibodies in suspected cases of infection.⁴ In syphilis, for example, the treponema fluorescent antibody test is proving of great value,⁵ comparable to the immobilization test. All that is required is an acetone-fixed preparation of the Nichols strain of *Treponema pallidum* and a fluorescent antihuman immunoglobulin serum. If the patient's serum under test contains antibodies to the treponema, the application of the fluorescent antiserum will reveal the organisms by the characteristic fluorescence of the conjugated dye. An ever-widening field of application is also to be found in the study of autoimmunity and autoimmune disease.⁶

The successful use on a large scale of fluorescent-antibody methods in clinical pathology will depend, however, on a commercially available supply of reliable, standardized preparations of fluorescent antibodies. At least one such preparation now appears to have been developed for the purpose of rapidly identifying viral diseases.

Living in Flats

The problem of housing Britain's expanding population is bound to intensify in the next two decades. Indeed, many people are now asking how best to provide acceptable dwellings while retaining sufficient land for industry, agriculture, recreation, and communications. Consequently it would seem that a higher proportion of flats is likely to be built than has been customary in the past.

It is generally believed that families living in high flats are exposed to certain medico-social hazards. More recently, as local housing authorities outside the big cities increasingly turn from traditional houses to flats of three or four stories, it is being suggested that life in low flats can also present its problems. Now Wing-Commander D. M. Fanning in a paper at page 382 of this issue of the *B.M.J.* has performed a useful service by making an ingenious study of a substantial number of armed Forces families living in such flats. He provided an adequate control group, and he was able to eliminate the major variables. Measurements of the comparative incidence of illness are more difficult to choose. The number of consultations a patient has during a particular illness may depend on many factors, not all relevant to its severity, and objective assessment of severity was not practicable in the circumstances of Wing-Commander Fanning's survey. The choice of "first consultation rate" was thus

probably wise, though this too has its deficiencies as a measure.

The figures showed that flat-dwellers had 57% more morbidity (as measured by the seeking of medical advice) than dwellers in houses. Hospital admissions were much the same in the two groups, but referrals to specialists showed the same disparity as first consultations. One might infer from this that while the incidence of serious disease was unaffected the flat-dwellers tended to present rather more complicated clinical pictures. The flat-dwellers' higher rate of sickness was most marked in diseases of the allergic endocrine-metabolic group, the nervous system and sense organs, the respiratory system, the genito-urinary system, the mental and psychoneurotic group, and the skin and cellular tissue group. The only significant groups in which the house-dwellers showed a higher morbidity were disorders of bones and organs of movement, and accidents.

The largest of all the groups was respiratory illness, with among the flat-dwellers three times as many patients as any other. Fanning reasonably suggests that lack of open-air exercise might contribute to this type of illness. This would be consistent with the finding that there was a small but steady increase in the incidence of respiratory disorders as the height of the flat increased. The young children, especially those aged 5-9 years, were the most frequent sufferers, and in this context it would have been interesting to have an analysis of the types of disorder. Could the disparity have been related to emotional stress? Fanning's discussion of social factors makes it clear that a substantial number of the conditions which lead to emotional stress—notably monotony, boredom and isolation, and difficulty in looking after the children—were present, and he may well be right in his surmise that the comparatively small number of patients with psychoneurotic disorders were only the tip of an iceberg. In these last, also, the incidence was greater among people living in the higher flats.

One difficulty about using first consultation as a measure of sickness is that what has been called the "surrender point" cannot be excluded. The decision to seek medical advice is a deliberate one. The patient, or the parent of the child patient, is sufficiently disturbed by the symptoms of the disease to acknowledge illness and to accept the inconvenience, effort, and worry which that acknowledgement may entail. The more active and interesting a person's life, the less a particular symptom is likely to obtrude. The bored, the isolated, and the irritated may not be more ill but simply *feel* more so. Does this explain at least part of the greater morbidity among dwellers in flats than in houses?

From the immediate clinical point of view this may not be very important. What patients seek from the doctor is first and foremost relief from their symptoms. It may, however, be important in long-term prevention, when the community has to decide between providing fewer flats, providing better flats, and preparing flat-dwellers for a new type of living.

Papers and Originals

Dislocatable Hip and Dislocated Hip in the Newborn Infant

H. V. L. FINLAY,* M.B., F.R.C.P.ED., M.R.C.P.; R. H. MAUDSLEY,† M.B., F.R.C.S.; P. I. BUSFIELD,† F.R.C.S.

Brit. med. J., 1967, 4, 377-381

Congenital dislocation of the hip produces, if untreated, an obvious and tragic disability. The results of treatment are profoundly affected by the age at which the condition is first diagnosed. In recent years increasing emphasis has been placed on routine examination of newborn infants in order to detect those conditions of the hip that might precede established dislocation. It is claimed that if such hips were splinted in abduction for the first few weeks of life established dislocation would be largely or entirely prevented. These claims were vigorously prophesied by Roser in 1879, though his own wide experience of dislocated hips was confined to infants over the age of 1 year. We began a study of the problem in 1961, and now report the findings.

Ortolani (1937) focused attention on the fact that instability of a child's hip joint could be detected on clinical examination, though Roser (1879) had noted that there were older infants with loose hip joints which could be dislocated by adducting the thighs and which could be reduced again by abduction. Andrén and Borglin (1960) thought that this instability might result from laxity of the hip capsule produced by maternal hormones, as they had found that analysis of urine from newborn infants with congenital dislocation of the hip indicated a disorder of oestrogen metabolism. Andrén (1960) also showed that the pubic symphysis may share in this laxity.

Starting in 1952, von Rosen (1962, 1963), of Malmö, found 68 cases of clinically diagnosed "congenital hip-joint dislocation" among a total of 31,200 newborn infants—an incidence of 2.2 per 1,000. Of those, 53 were girls and 15 were boys. He showed that the routine splinting of such hips in abduction for some weeks resulted in normal joints. He further claimed that, as a consequence of such splinting, established cases of congenital hip dislocation were no longer appearing in the community where he worked.

Coleman (1956), in Salt Lake City, examined the hips of 3,500 newborn infants during a period of 10 months, and found 30 babies with "congenital dysplasia" of the hip on physical examination alone, by showing either a "jerk of exit" or persistent and unequivocal limitation of abduction of the flexed hip.

Palmén (1957, 1961), in Sweden, reported the application of the Ortolani test to 12,394 newborn infants he had examined from 1950 to 1960. From 1956 onwards this test was complemented with a "subluxation provocation." In all, 70 cases with positive signs were diagnosed and were treated immediately with fixation in abduction on a wooden board. In most cases the infants were examined on one occasion between the first and fourth days of life. At a re-examination in 1961, out of 39 infants abnormal at birth, who were by then at least 3 years old, one had dysplastic changes and two showed the results of capital necrosis. Palmén had instigated in 1953 the routine examination of the hips of all newborn infants

at the majority of obstetric clinics in Sweden having paediatric consultants. Up to and including 1960 the survey had covered approximately 415,500 newborn infants, representing 49.5% of all children born alive in Sweden during this period.

Later Barlow (1962, 1963, 1966), of Salford, was able to confirm von Rosen's work. He started his series in 1957. Examining the babies within a week of birth, he found 357 abnormal hips out of a total of 19,625 infants. Of these, 168 were frankly dislocated hips and the remaining 189 dislocatable. Only six of the abnormal hips in the series occurred among the infants weighing less than 5 lb. (2,270 g.) at birth. Barlow also claimed that of the children whose hips were regarded as normal when examined at birth only three had later been found to have a dislocated hip.

Among 6,000 newborn infants examined from 1958 to 1962 Stanisavljevic (1964) found a positive Ortolani sign in 29. Ten had bilateral and 19 unilateral signs. Four of these babies were not treated for 6 to 10 months after birth, and none improved spontaneously. Twenty were treated with Frejka pillows immediately after birth until the age of 3 months, and at 6-8 months the hips of all these babies were found to be normal on clinical and radiographic examination.

Writing from Tel-Aviv, Weissman and Salama (1966) reported that the Ortolani sign was present in 45 out of 16,841 infants born alive during the three years 1962-4. The average and practically constant incidence for the whole period was 2.7 per 1,000.

Present Investigation

In the Duchess of Kent Maternity Wing at Hillingdon Hospital in the summer of 1961 we began a survey of all the newborn live infants, who were examined to determine the state of the hip joints. A separate survey sheet was filled in for each infant. All the initial examinations were carried out by members of the paediatric team, so that there was some uniformity in the assessment. Virtually all the initial examinations took place within 36 hours of birth.

Method of Examination

The examination was performed in a manner similar to the method described by Barlow (1961). The infant was examined lying supine in the cot. The bedclothes were always spread completely flat. The hands were warmed and the infant was approached gently in an effort to obtain general muscular relaxation. The position of the head of the femur was first carefully noted with the infant at rest and before the hip was passively moved. The infant's knee was acutely flexed, and this enabled the head of the femur to be grasped between the examiner's thumb anteriorly and his fingers posteriorly. An attempt was now made to move each femoral head in turn gently forwards into or backwards out of the acetabulum. After

* Paediatric Unit, Hillingdon Hospital, Uxbridge, Middlesex.

† Orthopaedic Unit, Hillingdon Hospital, Uxbridge, Middlesex.

the peculiar clonking sensation of the femoral head clearly jolting in and out of the acetabulum had once been experienced by the examiner, this sign of instability of the hip joint became quite unmistakable and case-finding much more reliable.

The child's femora were then gently abducted simultaneously. During the first two days of life maximum abduction usually approaches 90° from the vertical, and this degree normally decreases slightly over the next few days. Abduction is markedly impaired in the case of an established dislocation of the hip of the teratological type. It is also impaired in cases of dislocated hip with lax capsule, but the act of abduction itself readily tends to reduce such a joint. Thus the abduction test in the newborn infant has severe limitations diagnostically, and it must be sensitively carried out.

It must be stressed that in all these manoeuvres the head of the femur was grasped in the manner described and the knees were not held at all. This safely reduces the leverage effect, when combined with gentle handling and lack of hurry. It is common during the first few hours after birth to find that, with the baby lying supine, this manoeuvre may initiate regurgitation of stomach contents with choking, so that mucus suction may be necessary.

Classification

The widely differing statistics from different observers may be partly due to race, climate, and other factors, but are also due to the differing criteria of what constitutes "dislocation." Some are based on Ortolani's test or its modifications. Some, such as "dysplasia," are based on radiological criteria.

Dexterity in examination may detect a larger percentage of dislocatable hips. Each hip of an infant may fall into differing groups at the time of examination, and, owing to progressive changes taking place over the first few days of life, a hip joint may fall into one group one day and into another on the next day. The terms "slack hip," "lax hip," or "unstable hip" may not mean precisely the same entity to different observers.

The following classification of the clinical state of the hip joint in the newborn infant is suggested as a means of comparing accurately the findings in different centres.

Newborn Infant's Hip—A Classification

Normal Hip : Group A

Group A1 : Stable and Abducts Fully.—The hip joint is stable and abducts fully.

Group A2 : Stable with Lack of Abduction but no Dislocation.—The hip joint is stable, but shows a moderate limitation of abduction. The radiograph is normal and the adductor tightness apparently bears no relation to dislocation in these cases. Stanisavljevic (1964) found nine such infants with limited abduction in a series of 395 newborn babies. Without treatment, at the age of 14 months a clinical and x-ray follow-up showed no abnormality.

Group A3 : Crepitant or with Ligamentous Click.—The hip joint is stable but on attempting to dislocate the head backwards out of the acetabulum a clicking noise may be heard, or a slight crepitant, crunching, or grating sensation felt by the examiner. This has been termed "the crepitation of ligamentous origin" (Parkkulainen and Solonen, 1959), and arises from a flattened or oval-sectioned ligamentum teres rotating under the femoral head or from other tendons moving over each other in the region of the greater trochanter (Barlow, 1966). Such cases are so common that they must be regarded as within normal limits. Unfortunately infants in this group

may erroneously be thought to have the "clicking sign," and for this reason the term should be abandoned.

Group A4 : Lax but not Dislocatable.—There is more laxity of the capsule than usual, with increased mobility of the femoral head, which, however, cannot be completely moved out of the acetabulum. We have splinted four such cases, probably unnecessarily. Such hips we now regard as within normal limits. It is clear that this intermediate group—deliberately placed within the normal group—represents a minor degree of the same condition found in the dislocatable group. Certain infants may have one hip in this group while the other may be dislocatable or dislocated.

Unstable Hip : Group B

Group B1 : Dislocatable but in Normal Position at Rest.—This hip lies in a normal position at rest, but is dislocatable. The femoral head can readily be dislocated out of the acetabulum by pressing the femoral head backwards so that the characteristic clonk is felt. Full abduction can always be obtained. Infants in this group during the first day or two after birth may then pass into the lax but not dislocatable group A4. If untreated, probably the majority would remain in the normal position.

Group B2 : Dislocated at Rest but can be Reduced.—The hip lies in the dislocated position at rest, but can be reduced, readily in most instances, by pressing the femoral head forwards. On gently abducting the femur the range of abduction is limited up to the point when reduction is made to occur and then full abduction can be attained. The joint capsule is lax and the femoral head can readily be dislocated backwards again. If untreated, there is a considerable risk of the dislocation persisting. The dislocatable and this dislocated group again represent differing severities of the same condition.

Pathological Hip : Group C

Group C1 : Dislocated but Not Reducible by Palpation and Not Associated with Other Congenital Abnormalities.—This group corresponds to the older infants with established, untreated dislocation. Partly because the infants in our series were examined so soon after birth we encountered no neonatal example of this type, but in one case of dislocated hip of unstable type we were able to reduce the joint only with some difficulty.

Group C2 : Teratological Dislocation.—There are gross lack of abduction and the classical signs of dislocation of the hip. The femoral head cannot be readily replaced in the acetabulum, and such cases cannot be controlled by the Barlow or modified von Rosen type of splint. There is an association with arthrogryposis or other congenital abnormalities. As well as being clinically distinct, the majority in this group are also likely to be entirely separate aetiologically. These cases have been termed "teratological" by several writers.

Group C3 : Dislocation Associated with Meningomyelocele.—The hip joint is dislocated in association with a meningo-myelocele. These cases merit a separate group as they present in a distinct way, and the hip-joint dislocation is usually the least of the child's disabilities.

Radiographs

Andrén and von Rosen (1958) showed that, if radiographs of the hip joint were taken with the femora internally rotated and abducted to at least 45°, dislocation of the unfossified head could be demonstrated by the alignment of the femoral shaft in the newborn infant with an unstable hip. This technique has been used and commended by Jacobs (1966), who reported

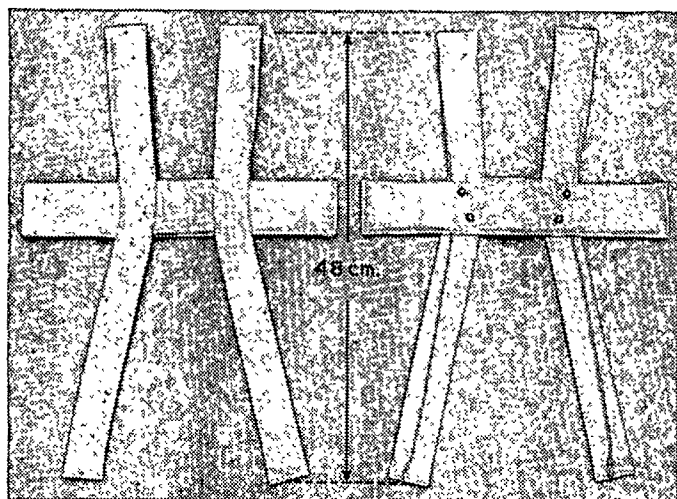
the radiographic findings in a Birmingham series. Only during the early part of the investigation did we routinely take radiographs of children whose hip joints were thought to be abnormal in the newborn period, since we soon appreciated that the diagnosis in the unstable groups was basically a clinical one and radiographs had not added to our information in these groups. Palmén (1961) also regarded as unnecessary the x-ray examination of these cases before beginning treatment. Radiographs have proved most helpful in other groups. We have more recently preferred to avoid exposure to radiation in the unstable groups except for follow-up control.

Even during the follow-up examinations interpretation of the radiographs has sometimes proved difficult, especially during the months until the femoral head has become clearly ossified. A slight degree of pelvic tilt or rotation can produce a misleading radiological view of the hip joint.

Treatment

The first cases of unstable hip which we discovered were treated initially by full hip abduction, using several layers of napkins secured by a pin at each side until a Frejka pillow or suitable splint was provided. This thick napkin method proved unsatisfactory, as it did not have a sustained effect, and, indeed, gave a false sense of security.

For the last three years of the series the von Rosen splint in a modified form (see Illustration) was routinely applied within four days of birth, and we now have three sizes available even for the neonate. Various slight modifications have been made from time to time. The metal framework of duralumin must satisfy the twin needs of strength and correct malleability. The rubber covering formerly used has now been replaced by a white washable vynide covering which is less irritating to the skin of some infants. The seams of this covering have been specially sited away from pressure points. By angulating the crossbar so that it has a shallow vertical groove in the midline, pressure on the spine can be avoided. The shoulder pieces of the splint must be set at an optimum angle, while the leg extensions must not abrade the medial skin of the thigh above each knee.



Modified type of von Rosen splint used in present series

This splint is reasonably well tolerated and has enabled us to maintain satisfactory abduction. Inevitably both hips are affected by the splint. The child is not removed from the splint, except for adjustments, for a period of three months. In a few of our cases, particularly the small premature infants, the application of the splint had to be postponed owing to poor general condition after birth.

We now regard all the infants in our group A as requiring no treatment.

Results of Present Neonatal Study

During the latter part of 1961 the results of routine hip examinations in our unit were difficult to determine because of uncertainty in examination techniques.

In the five-year period 1962–6 a total of 14,594 infants were born alive in the unit. The hips of all were examined, except in the few instances when death occurred very soon after birth. Apart from two cases of dislocated hip of teratological type (born in 1964 and 1965 respectively), and all cases of meningocele, a total of 60 children were discovered who had a clearly dislocatable or dislocated hip (Table I). Of these 60, 13 were male and 47 female. In 21 instances the hips were bilaterally affected, but in several of these one hip was dislocatable while the other was dislocated at rest. In six infants the right hip only was affected, and in 33 the left hip only. Breech presentation and/or a history of version accounted for 13 (22%) out of the 60 cases. The overall breech delivery rate in the unit was 4%.

TABLE I.—Infants with Dislocatable or Dislocated Hips of Unstable Type, 1962–6

Year	Total Live Births	Total with Dislocatable or Dislocated Hips of Unstable Type	Male	Female	Right Only	Left Only	Bilateral	Birth Weight above 5½ lb. (2,500 g.)	Birth Weight 5½ lb. (2,500 g.) or Less	Breech or History of Version
1962	2,791	8	0	8	1	5	2	8	0	1
1963	2,975	10	4	6	2	7	1	8	2	2
1964	3,047	12	3	9	1	4	7	12	0	4
1965	2,786	14	3	11	2	8	4	13	1	2
1966	2,995	16	3	13	0	9	7	14	2	4
Total	14,594	60	13	47	6	33	21	55	5	13

The series includes three singleton siblings, all from the same Indian family—in each instance the initial examiner was not at the time aware of the family history. The mother of another affected infant had been operated on at the age of 2 years for congenital dislocation of the hip.

The more detailed findings on initial examination of the 30 cases seen during the last two years of the study are set out in Table II. In 15 of these infants one or both hips were dislocated; in 20 infants one or both hips were dislocatable. During the last two years these 30 cases represent an incidence of 1 in 193 infants—that is, 5 per 1,000 live births.

TABLE II.—Findings on Neonatal Examination of 30 Cases of Dislocatable or Dislocated Hips Seen in 1965–6

Both dislocated	..	..	2
Right dislocated and left dislocatable	..	..	2
Left dislocated and right dislocatable	..	..	3
Right dislocated and left stable	..	..	1
Left dislocated and right stable	..	..	7
Both dislocatable	..	..	4
Right dislocatable and left lax but not dislocatable	..	..	1
Right dislocatable and left stable	..	..	0
Left dislocatable and right lax but not dislocatable	..	..	1
Left dislocatable and right stable	..	..	9

We have excluded from the series those newborn babies with abnormal hips who were not actually born in the unit.

Follow-up Study

Of the 60 cases in the series, two died during the neonatal period and two failed to attend as outpatients.

The remaining 56 were followed up in the orthopaedic clinic, either at our hospital or, in the case of eight babies, at some stage at other hospitals. In four children born during 1962–3 dislocation was not prevented, and these required further attention—two of these were premature infants with birth weights of 4 lb. 2 oz. and 3 lb. 6 oz. (1,870 g. and 1,530 g.) respectively.

At the end of the series all the patients still living locally were asked to attend for a detailed follow-up survey, and 37 were seen. Those born in 1966 who attended were over the age of 6 months when examined. The radiographs were studied particularly for evidence of dysplasia or necrosis of the femoral head. In one child born in 1963, and aged 3½ years when examined, the affected hip showed no clinical or radiological evidence of dislocation, but there was an irregularity of the trabecular pattern of the upper femoral metaphysis.

In two cases the question of dislocation remained radiologically doubtful for several months, but the hips were radiologically normal on final follow-up examination.

The overall results of the follow-up, which includes information received from other hospitals, are summarized in Table III.

TABLE III.—Overall Follow-up Study of 60 Infants with Dislocatable or Dislocated Hips of Unstable Type

Year	Total	Died in Neonatal Period	Not Available for Follow-up Beyond the Neonatal Period	Dislocation Persisted and Further Treatment Required	Satisfactory and Followed up but not Seen Beyond Age 6 Months	No Clinical or Radiological Evidence of Dislocation on Follow-up Beyond Age 6 Months
1962	8	1	0	1	1	5
1963	10	0	0	3	0	7
1964	12	1	1	0	2	8
1965	14	0	0	0	1	13
1966	16	0	1	0	1	14
Total	60	2	2	4	5	47

Six months after the last child in our series was born we obtained the active co-operation of 134 family doctors who replied to our letters of inquiry about cases of hip dislocation, and whose practices lay partly or wholly in the area surrounding the hospital. This inquiry brought to light one female infant, born in our unit in 1962, whose hips were passed as normal when examined on the day after birth. At the age of 11 months a diagnosis of benign congenital hypotonia was made at another hospital. At the age of 2 years and 9 months the left hip was found to be frankly dislocated, and an open reduction was later successfully carried out.

So far we have been unable to trace any patients with established dislocation of the hip unassociated with other disease who had been born in our unit during the period 1962–6 and whose hips had been passed as normal on neonatal examination.

Discussion

Careful examination of the hip joints in all newborn infants is already being widely carried out in this country. The results are of great interest, but it is important to assess their value critically, as there are still those who are sceptical. From a purely statistical point of view it is unfortunate that the natural incidence of established congenital dislocation of the hip is so low. Firm conclusions are difficult to reach unless large numbers of newborn infants are available for study. The differing criteria of various clinicians have in the past made comparison difficult.

Such routine examinations would be justified if it could be shown that the majority, if not all, of the potential cases of congenital dislocation of the hip were included within the unstable groups with either dislocatable or dislocated hips—a conclusion strongly suggested by our inquiries and follow-up studies.

It is also most desirable that a large number of babies should not be subjected to unnecessary splinting, for, though the splint is kept on for an average of only three months, it creates considerable parental anxiety and concern as well as some discomfort for the infant. There is a potential risk of inhalation of feeds, and breast-feeding may be made more difficult.

In addition there is the question whether such apparently simple routine treatment may cause damage to the joint. Allen

(1962) reviewed the radiographs and records of 150 children who had been seen during a period of 10 years with an original diagnosis of "hip dysplasia," based on the finding of an acetabular angle greater than 30° as seen radiologically. No dislocation was demonstrated at any time in these patients. Some were left untreated, some were treated with Frejka pillows, and others were manipulated and then held in 90° abduction casts or apparatus. Radiological evidence of ischaemic necrosis had developed subsequently in 14 children—each of these had been treated with a 90° cast except one who was in a 90° apparatus without plaster. Allen pointed to the danger of making a cripple out of a normal child. This has not been our experience. It is only fair to add that Denis Browne (1961) thought that so-called fragmentation of the head of the femur or avascular necrosis were terms used to describe a purely temporary effect which occurs fairly often in cases treated by controlled movement.

It is not easy to assess accurately the number of established cases which would have resulted in our series if no treatment had been given. That certain races have a higher incidence of congenital dislocation of the hip than others is well known. There were 148 cases among children born in Birmingham in the years 1942–52. This gives an incidence of 0.65 per 1,000 live births. Though this may be slightly below the true value it is probably acceptable as an estimate of incidence among children who survived infancy (Record and Edwards, 1958). Many would accept an incidence of 0.7–1 per 1,000 for Great Britain up until 10 years ago.

Out of the total number of infants examined 10.5% were the children of Indian immigrants. Out of the 60 cases of unstable hip of either dislocatable or dislocated type eight were Indian, but this figure includes three siblings all in the same Indian family. We can assume that within the 14,594 infants born during the period under our study there would finally have resulted at least 12 cases of established dislocation of the hip (including those of teratological type). This means that possibly three or four children were being subjected to unnecessary splinting for every one child who was saved from the development of established dislocation.

Over the last two years of the series, when the neonatal incidence was 5 per 1,000, four out of every five children were in retrospect unnecessarily splinted. What is needed is some means of differentiating those cases with unstable hips in the neonatal period which are most at risk. It is tempting to suggest a policy of "wait and see"—to re-examine abnormal hips at the age of 1 week and splint only those that are still abnormal. The history of our unsuccessful cases does not encourage us in this view.

Sayle-Creer and Barlow (1960) made a careful distinction between dislocatable hips and dislocated hips, though to some extent it may be fortuitous, depending largely on the position of the legs, whether the hip is in or out of joint at the time of the neonatal examination. We have encountered several infants with a dislocatable hip within 24 hours of birth who within two days showed such a rapid lessening of joint laxity that they fell into the lax but not dislocatable group. It might be logical to splint those in the dislocatable group for a shorter period—for example, two months—than those in the already dislocated group—for example, three months.

As there is a tendency for unstable hip joints to become progressively more stable during the first 10 days of life, the earlier the infants are examined in a series the higher will be the incidence of unstable hips discovered. It is stressed that in our series virtually all the infants were first examined within 36 hours of birth, and the majority within 24 hours. Barlow (1962), reporting the first 9,000 newborn infants in his series examined at a weekly clinic, found that the half that were under 3½ days old produced 100 babies with 112 abnormal hips. In the half who were 3½ to 7 days old he found only 39 with 47 abnormal hips.

The tendency of the neonatal hip joint to become progressively more stable is one of several reasons for considering that groups A4, B1, B2, and C1 indicate advancing degrees of joint capsule laxity. In almost all infants the degree of joint laxity already present apparently decreases from the hour of birth. On theoretical grounds, mild laxity would be expected to disappear with the joint in correct position, but pronounced initial laxity would carry a greater risk of the joint remaining in the dislocated position. This accords with the fact that the earlier cases with pronounced instability are splinted with the hip joint in its correct position the better are the results.

The possibility should be borne in mind that repeated clinical examination may itself produce changes in the joint. We have personally examined a few of the infants with a readily dislocatable hip, and then carried out re-examination within a few hours, only to find in some an almost stable joint showing a moderate degree of palpable periarticular thickening. This suggests that the manipulation involved in testing the joint may on occasion produce a local reactive oedema. When this occurs it is important that the joint should not be left in the dislocated position—a valid reason for applying a splint without delay once the diagnosis is made.

The part played by the position of the child in utero is emphasized by the number with breech presentation, and also by the significantly small proportion of cases showing involvement of the right hip alone.

It is of interest to compare our findings in a series at risk with those of Record and Edwards (1958), who studied a large series of cases of established dislocation of the hip in the city of Birmingham. The sex ratio in their series was 85% female—in the present series it was 78%; including their bilateral cases, the left hip was affected in 80% of the cases—in the present series 90%; 17% were associated with breech deliveries—in the present series 22%. Only 4.2% of their series had associated defects of the nervous system. The incidence among their children born in the winter was double that of children born in the summer, and the risk of a subsequent child being affected was about 5%. Such a series would also include those presenting neonatally as teratological in type, with various other malformations. Von Rosen (1963) in fact excluded two such cases from his neonatal series.

The term "congenital hip dysplasia" was introduced by Hilgenreiner, of Prague, in 1925. A review of the literature shows that in the past this label has embraced many infants whose hips we would regard as entirely within normal limits.

The series published by Coleman (1956), Palmén (1961), Barlow (1963), and Stanisavljevic (1964) are of particular value, as the newborn infants in each series were personally examined by the same individual. In our own experience there is no doubt that our case-finding of abnormal hips would have been higher if carried out in this way, instead of by a trained team with careful checking by one of us of abnormalities found. Nevertheless, our figures give some idea of what may be attained by the routine examination of the hips as standard practice by a paediatric team in a neonatal unit.

We have excluded from our series cases of congenital dislocation of the hip associated with meningocele. For the purpose of comparing findings in the newborn infants with those in established untreated cases, it is wise to exclude also those in the special teratological group, though the latter are usually included in published series referring to older children.

Summary

In the five-year period 1962–6 a total of 14,594 infants were born alive in a single maternity department. Except in the few instances when death occurred very soon after birth, the hips of all were examined within 36 hours of birth. The condition of the hip joint was specifically noted on a survey

sheet in each case. All the examinations were carried out as a routine by a member of the paediatric team. Excluding two cases of dislocation of the teratological type and all cases of meningocele, 60 infants with clearly dislocatable or dislocated hips were discovered. The female preponderance was nearly 4 to 1. Approximately one-third were bilaterally affected, and in the remainder the left hip was 5.5 times more often involved than the right. In 22% of the cases there had been a breech delivery. During the last two years of the study the incidence of neonates with dislocatable or dislocated hips of unstable type was 5 per 1,000, and in half of these infants the hip was dislocated.

A clinical classification of the state of the hip joint in the newborn infant is suggested, with reasonably clear-cut groups as a mean of comparing accurately the findings in different centres.

The technique of clinical examination of the hip joints within 36 hours of birth is given in detail, and should be a routine procedure, as it can lead to the prevention of established dislocation, at least in the great majority. At present this involves the splinting of approximately four cases which would spontaneously stabilize for every one case which would finally remain dislocated. The implications of this are discussed. Splinting of the hips in abduction should be carefully confined to infants who are at real risk, and in these the splint should be applied within four days of birth if possible. In our series a von Rosen type splint proved satisfactory, and it was kept on the infant for an average period of three months.

Details are given of the follow-up investigation carried out on the children with abnormal hips. Two infants died in the neonatal period and two were not available for follow-up. Owing to inadequate or late splinting in the earlier cases of the series, four cases of dislocation were not prevented, and these required further attention.

We wish to thank all members of the paediatric team who assisted in this survey, and we greatly appreciate the co-operation of the local family doctors.

We are grateful to Dr. S. M. Tucker for the inclusion of several of the 1966 cases, and to those orthopaedic surgeons who have kindly sent us follow-up information about infants who have subsequently come under their care. Our thanks are also due to Miss S. G. Ward and Miss T. E. Turner for their secretarial assistance.

The von Rosen type splint was supplied by Mr. J. Drew, 443 Uxbridge Road, Ealing, London W.5.

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Families in Flats

D. M. FANNING,* O.B.E., M.B., B.S., D.P.H.

Brit. med. J., 1967, 4, 382-386

The fact that poor housing affects the health of the community has been understood since the time of Chadwick, but the ways in which housing can affect health, and the nature of the ill-health which may be caused by unsatisfactory housing, have changed. Over the past 25 years the health of people living in new towns and on new housing estates has been shown in several instances to be poorer than might have been expected, in spite of the improvements which have occurred in their sanitary environment.

Much of the blame for this has been ascribed to social factors, such as those described by Young and Willmott (1962) in their account of the movement of families from Bethnal Green to a new estate outside London, thus breaking their family links. Brotherston and Chave (1956) described a higher rate of attendance on their general practitioners by people who lived on a new housing estate than might have been expected; and Martin, Brotherston, and Chave (1957) found that the incidence of neurosis on a new housing estate was 77% in excess of the national average. Taylor and Chave (1964) described how on a new housing estate they found that there was a lowered threshold for consulting a doctor, which resulted in a higher rate of overt neurosis.

The effect of the adverse environment of new housing estates is well documented, but that of another phenomenon of modern housing development—namely, the building of blocks of multi-storeyed flats in large numbers—is not. Hird (1966) found an increase in illness in flats. He stated that in flat dwellers he found twice as many upper respiratory infections in children below the age of 10 as there were in house dwellers, and that he had twice as many consultations in which symptoms of emotional disturbance predominated.

It would appear that people who live in new housing estates and in new blocks of flats are often poorer in health than those who live in older and hygienically less satisfactory types of accommodation, even though the design and appointment of the new dwellings are thought to be greatly superior to the old. The morbidity which occurred among the families of some members of the armed Forces living in modern flats and houses in Germany was examined in order to compare the health of those who lived in the flats with those who occupied houses.

Scope of Survey

The records of 558 families were examined in detail over a period of 10 weeks from 30 August to 6 November 1965, including the practice records concerning attendances, referral for specialist opinion, and domicile of the patient. The families were chosen because they lived in two well-defined and comparable areas—one an estate of houses, similar in design and layout to a modern local authority estate, and the other an estate which was composed of three- and four-storey blocks of flats, also comparable with a similar arrangement in England. The period was relatively short, but was kept so in order to minimize the number of families who moved during the study. In fact, during the 10 weeks eight families moved away, and were replaced by another eight whose size, age, and sex distribution

were sufficiently similar not to affect the composition of the population.

All medical attendances were known to the practice, as it was in the circumstances the only one available, and all contact with the local hospital was arranged through it. The community was self-contained and self-sufficient, with all the amenities that are found on a well-developed housing estate in England, all services such as schools, churches, shops, buses, and entertainment being readily available. A time was chosen when attendances were neither markedly more nor less than usual, and there was no epidemic of infectious disease current. Attendances for the whole practice during 1965 included 11,187 consultations with a general practitioner from a population which averaged 2,480, a consultation rate of 4.51 per registered patient in the year. In the section which was studied there were 1,409 consultations with a general practitioner from the 1,608 patients over the 10-week period, which was equivalent to an annual rate of 4.56.

The section of the practice which was chosen had the following attributes: (1) They were all families of non-commissioned ranks; that is, in the same social class and income group. Though they were unclassified in the 1966 General Register Office Classification of Occupations, they were placed in class III in the 1950 classification. (2) Only those who were in a flat or a house by chance rather than by choice were included. The usual system was one of allocation of the next available dwelling to the family at the top of the waiting-list, but there were some exceptions to this, and these were excluded from the study. (3) Social facilities were comparable; that is, buses, schools, shops, and medical services were equally available. (4) They all came under the care of the same practice. This applied to the wives and children, but not to the men, who were therefore not included in the study. (5) They were all within walking distance of a doctor's surgery.

The age distribution of the two groups, which is shown in Table I, was sufficiently alike to permit comparison. The mean number of children per family in flats was 1.9 and in houses 1.8.

TABLE I.—Age Distribution of Populations in Flats and Houses

Age Group:	0-4	5-9	10-19	20-29	30-39	40+	Total
No. living in flats ..	374	250	143	232	128	36	1,163
" " " houses	121	85	77	77	50	35	445

The houses were of modern design, soundly built, and two-storeyed, in short terraces with a common front and individual back gardens, with two or three bedrooms, and centrally heated throughout. The flats were in blocks of three or four storeys, well laid-out in an open space with grass surrounds, with two or three bedrooms, and also centrally heated. Group A, living in 398 flats, comprised 1,163 women and children, and group B, living in 160 houses, 445 women and children.

Measurement of Morbidity

Most studies of illness in general practice use the total number of consultations with the doctor as a measurement of morbidity. It is felt that as the number of times that a doctor may see a

* Wing Commander, Royal Air Force.

patient with any particular illness may vary with his personal preference, clinical methods, experience, or work load, or with factors imposed by the patient, a more precise measurement of morbidity is obtained by using a "first consultation rate," as described in the Registrar General's subcommittee report on measurement of morbidity (1954). This measurement is that of the number of first consultations for an illness or disease during a defined period, related to the average number of persons exposed to risk during that period. As, particularly in the case of respiratory infections, any patient may attend with more than one illness during a specified period, the number of patients consulting a general practitioner during the 10-week period of the survey has also been recorded. Both these measurements have been used to compare the women and children who lived in flats with those who lived in houses. The number exposed to risk is taken as the population at the beginning of the survey.

Differences in Types of Illness

The total number of first attendances, referrals to specialists, and admissions to hospital is shown in Table II.

TABLE II.—Attendances by Families From Flats and Houses Over the 10-Week Period

	Group A: Flats			Group B: Houses		
	No. of Patients Attending	No. of First Attendances	Rate per 1,000 in Group	No. of Patients Attending	No. of First Attendances	Rate per 1,000 in Group
First attendance by G.P. for any reason ..	672	696	598.5	162	170	382.0
Referred to specialist ..	81	81	69.6	19	19	42.7
Admitted to hospital ..	25	25	21.5	11	11	24.7

The differences in the rates of first attendance by the general practitioners show an increase of morbidity of 57% in those families who lived in flats compared with those who lived in houses, and the difference in the rates at which they were referred for specialist opinion was 63%. The proportion admitted to hospital was nearly the same in both groups, and this may indicate that though the amount of illness in the flats was greater than that in the houses, the degree of seriousness was not.

The nature of the increased morbidity was established by classifying the diagnoses made according to the World Health Organization *International Classification of Diseases*, and this is shown in Table III. The most frequent diagnosis in both groups was of disease of the respiratory system; 35.1% of all illnesses seen in patients from flats, and 26.5% in those from houses, fell into this category. The difference between the incidence in the two groups is significant at the level of $P < 0.01$ if a χ^2 test is applied. The predominant illness was infection of the upper respiratory tract, but it is interesting to note that a diagnosis of bronchitis or of pneumonia was made in 14 instances in patients who lived in houses, and 66 times in those who lived in flats, which represents incidences of 31.5 and 56.7 per 1,000 respectively, the difference between which is significant at the level of $P < 0.05$. A similar difference ($P < 0.05$) was seen in the incidence of disorders of the nervous system and sense organs, which were partly related to the respiratory diseases, as they included cases presenting as acute otitis media which were precipitated by nasopharyngeal infection.

Genitourinary disorders were more than twice as common in women who lived in flats as they were in those in houses, the most frequent form being a menstrual irregularity. The doctors concerned were all of the opinion that they were associated with the incidence of psychoneurotic disorders,

which were twice as frequent in flats as they were in houses, and the differences in incidence in each case are significant at the level of $P < 0.05$.

There was one significant difference where the incidence of a group of disorders was higher in the families in houses than it was in those who lived in flats—namely, those which fell

TABLE III.—Comparison of Rates of First Attendance by General Practitioners on Both Groups, According to the Diagnoses Made

Disease Group	Group A: Flats			Group B: Houses		
	No. of Patients Consulting	No. of First Attendances	Rate per 1,000 in Group	No. of Patients Consulting	No. of First Attendances	Rate per 1,000 in Group
I. Infective and parasitic ..	18	18	15.5	6	6	13.5
III. Allergic, endocrine, and metabolic ..	23	23	19.8	3	3	6.7
IV. Blood disorders ..	4	4	3.4	4	4	8.9
V. Mental and psychoneurotic ..	42	42	36.1	8	8	17.9
VI. Nervous system and sense organs ..	48	48	41.3	7	7	15.7
VII. Circulatory system ..	6	6	5.2	1	1	2.2
VIII. Respiratory system ..	227	244	209.8	38	45	101.1
IX. Digestive system ..	77	77	66.2	27	27	60.7
X. Genitourinary system ..	61	61	52.5	10	10	22.5
XI. Complications of pregnancy ..	5	5	4.3	2	2	4.5
XII. Skin and cellular tissue ..	31	32	27.5	7	7	15.7
XIII. Bones and organs of movement ..	11	11	9.5	11	11	24.7
XVI. Unknown and undiagnosed ..	65	71	61.0	12	13	29.2
XVIII. Accidents ..	26	26	22.4	16	16	35.9
XVIII. Non-sickness ..	28	28	24.1	10	10	22.5
Total ..	672	696	598.5	162	170	382.0

into the group of disorders of the bones and organs of movement, which were more than twice as frequent in women in houses, and under which heading were collected a variety of diagnoses, the most frequent being the low-back-strain syndrome ($P < 0.05$).

Differences Between Age Groups

Some age groups showed a greater difference in the incidence of sickness between flats and houses than others, and this is shown in Table IV.

TABLE IV.—Differences in Rates of First Consultation With the General Practitioners Between Those Living in Flats and Those in Houses, by Age Groups

Age Group	Group A: Flats			Group B: Houses		
	No. of Patients Consulting	No. of First Consultations	Rate per 1,000 in Age Group	No. of Patients Consulting	No. of First Consultations	Rate per 1,000 in Age Group
0-4	232	250	668.4	47	53	438.0
5-9	123	125	500.0	24	26	305.9
10-19	58	59	412.6	18	19	233.8
20-29	165	166	715.5	39	39	506.5
30-39	74	75	585.9	22	22	440.0
40+	20	21	583.3	12	12	342.9
Total ..	672	696	598.5	162	170	382.0

With the children there was a higher sickness rate in those under 5 years in both groups than in their older siblings, as might be expected, but there was a marked difference between those in all age groups who lived in flats and those who lived in houses. With the women, the greatest difference between flat- and house-dwellers was in those of 40 years and over, and in those in their twenties, with a much smaller difference between those in their thirties. The major difference in sickness

rates between the children from the flats and those from houses was seen in the incidence of respiratory disorders in those under the age of 10. This difference narrowed in those aged from 10 to 19, but increased again slightly in the young mothers of 20 to 29, as is shown in Table V.

TABLE V.—*Differences in Rates of First Consultation With the General Practitioners for Disorders of the Respiratory Tract Between Those Living in Flats and Those in Houses, by Age Group*

Age Group	Group A: Flats		Group B: Houses	
	No. of First Attendances	Rate per 1,000 in Age Group	No. of First Attendances	Rate per 1,000 in Age Group
0-4	134	358.3	26	214.9
5-9	60	240.0	8	94.1
10-19	16	111.9	4	51.9
20-29	22	94.8	3	38.9
30-39	9	70.3	3	60.0
40+	3	83.3	1	28.6

The principal differences in the incidence of psychoneurotic disorders were seen in the women aged between 20 and 29, and, so far as can be judged from the small numbers in the population surveyed, in those over 40. This is shown in Table VI.

TABLE VI.—*Differences in Rates of First Consultation With the General Practitioners by Women for Psychoneurotic Disorders Between Those Living in Flats and Those in Houses, by Age Group*

Age Group	Group A: Flats		Group B: Houses	
	No. of First Attendances	Rate per 1,000 in Age Group	No. of First Attendances	Rate per 1,000 in Age Group
20-29	24	103.4	3	38.9
30-39	8	62.5	3	60.0
40+	3	83.3	0	0

The conclusions to be drawn from these figures are that there was an increase in general morbidity in the families who lived in flats as compared with those who lived in houses, and that this increase was most pronounced in children under the age of 10, who had more respiratory disorders, in those women between the ages of 20 and 29, who had more respiratory and psychoneurotic disorders, and probably in those women aged 40 and over, who also had more psychoneurotic disorders.

The differences which were recorded over this period were not unusual ones, as the rates of surgery attendances and domiciliary visits during the 10 weeks were not unusually high or low for either of the groups concerned, so it seems reasonable to conclude that those families who lived in flats were not as healthy as those who lived in houses. The amount of ill-health in flats appeared to be considerable, but the degree less so. Though there was one death during the period—that of an infant living in a flat who succumbed to a fulminating virus pneumonia—if the degree of illness is judged by the number who had to be admitted to hospital this was proportionately the same in both groups (Table II).

Respiratory Infections

The classical reasons for an increased rate of respiratory infection—namely, overcrowding and poor ventilation—were not present by the accepted standards. These flats were of a good size, with two or three bedrooms, and centrally heated throughout, allowing free use of all the floor space in comfort; nevertheless, the floor space in modern flats usually approximates more closely to the minimum standards laid down for dwellings, bedrooms tend to be smaller than they are in houses, and the whole design is more compact than in a house, bringing the occupants into closer contact.

Apart from floor space, the main difference between a house and a flat is the ease of access to the open air in the

former, and this may well have been a major reason for the increased rate of respiratory infections among flat-dwellers. A child returning home from school to a house will probably go out to play in the garden, but one coming back to a flat tends to remain there. Though play areas were provided in the communal surrounds of the flats, and were used to some extent, one never saw as many children using the swings and slides even on a fine day, as might have been expected from the number of children in the neighbourhood. On the other hand, large numbers of children in the back gardens or playing on the communal lawn in front of houses were a far more usual sight. Mothers who live up several flights of stairs tend to use them as little as possible, and are naturally reluctant to let small children too far out of their sight, and the children themselves are often unwilling to stray too far from their mothers. A further indication that people tend to be less active and more confined when they live in a flat is the significantly higher rate of musculoskeletal disorders found during the period under review in the group living in houses.

If confinement to the flat is a factor in precipitating respiratory infections one would expect to find a higher incidence in those living above ground level than in those who were on the ground floor and therefore probably more likely to go out, and this was found to be the case, as is shown in Table VII.

TABLE VII.—*Incidence of First Attendance by the General Practitioners on Families Living in Flats for Respiratory Disorders, by Height of Residence*

Level of Flat	First Attendances for Respiratory Disorders	Population at that Level	Rate per 1,000 at that Level
Ground floor	68	351	193.7
First	71	49	203.4
Second	74	37	219.6
Third	31	126	246.0
Total	244	1,163	209.8

It will be seen that there was a small but steady increase in the incidence of respiratory disorders as the height of the flat increased, though the flats were of the same design and size on each floor. The smaller population living on the third floor is due to the fact that most of the blocks were only three storeys high.

Neuroses

Though few in number by comparison with respiratory ailments, the incidence of psychoneurotic disorders as judged by their first presentation to the general practitioners was nearly three times as high in women in their twenties who lived in flats as it was in those living in houses. The numbers recorded in both groups were probably lower than the true incidence, as an attendance was put into this category only when a firm diagnosis of psychoneurotic illness could be made. Many others which would probably fall into this category were recorded under the heading of "vague symptoms and no diagnosis," as this miscellaneous group included the occasions when a wife might come herself or even bring a child with some superficially trivial problem, just so that she could talk with a neutral person such as the doctor.

The degree of illness was not usually serious, and most of the cases could be and were treated by the general practitioners concerned, backed up by the health visitor. During the 10-week period five patients who lived in flats were referred to the psychiatrist, and three who lived in houses. There was one psychiatric admission to hospital, and this was of a woman who lived in a house. Nevertheless, these illnesses, however mild, are often prolonged and disabling, and tend to become recurrent. It was felt that those patients who presented with psychiatric symptoms were only the tip of the iceberg, and a high proportion of undisclosed and undiagnosed mental illness

probably went unnoticed, and that part of the overall increase in the incidence of disorders in other categories, particularly gynaecological disorders, reflected underlying tensions and anxieties.

The causes were probably many, but there is no doubt that monotony and boredom played a considerable part. The flats were well appointed and designed to save labour, and women occasionally complained to their doctors about this, saying that the housework took so little time that there was nothing left to do. Again, because shopping facilities were close at hand, even a daily expedition took little time. It was possible to take a bus to another and bigger shopping centre, but, as with going for walks locally, this activity soon palled, and all that was left was confinement within the flat and introspection. If there were children below school age in the family this confinement became even more necessary, as they had to be watched all day. There was no small garden into which they could be released in safety, and they themselves eventually provided another irritant in their mothers' lives.

The most striking contrast between life in flats and that in houses was the lack of communication between families living in flats compared with those in houses, and this was probably the principal cause of the isolation and loneliness of the wives in the flats. Apart from the discussions in the surgery when this was revealed, it was noticed by the doctors and by the health visitor in the daily round, when one could observe the contrast during domiciliary visits. It was not uncommon to find neighbours visiting and talking when one visited a house, and if a wife was ill in bed the door would often be opened by a neighbour who had come in to help. This was not nearly so frequent in the flats, where it was more usual to find a wife coping by herself, or whose husband had had to stay away from work to help.

This phenomenon of isolation has previously been described as occurring on new housing estates, as in Young and Willmott's (1962) families who moved from Bethnal Green, and arises from the destruction of the matrilocal family structure, where mothers and their married daughters living near each other communicate frequently and form an extended family which is interdependent and which constitutes a self-sufficient social unit. Why, though, should this affect people who live in flats more than those who live in houses? Perhaps because in houses the children, instead of helping to confine their mothers indoors as they do in a flat, form a link between the women by bringing their mothers together when they play in their gregarious bands around the front doors. Stepping outside the front door or talking over the back-garden fence requires much less effort than climbing the stairs of a block of flats, and the gardens are neutral territory which do not involve the positive social act of going to call on someone in a flat. Thus the initial shyness of a woman who may be susceptible to mental illness may be broken and the illness prevented.

Some support for this can be found if the incidence of psychoneurosis is examined in relation to the height of the flat, and in Table VIII the women who made first attendances on the general practitioners at which a diagnosis of psychoneurotic disorder was made are divided according to the height

of the flat in which they lived. This shows that the incidence of psychoneuroses in women was twice as high if they lived on the top floor as it was in those who lived on the ground floor, and that there was a steady increase in incidence as the height of the residence increased.

Further support for this explanation of the situation is found in the observation that women in their thirties did not seem to suffer from mental illness if they lived in a flat any more than if they lived in a house. These were the women whose children were at school and therefore did not confine them to the flat. They were also those who went out to work, as many did in full- or part-time jobs in shops and offices, thus making social contacts and avoiding isolation.

The women aged 40 and over seemed to suffer because they were less tolerant of a new situation than the younger wives. They had been used to living in houses previously, and many could not adapt themselves to flat life.

With women of all ages it may have been that this increase in morbidity and intolerance of flat life would not have occurred but for the fact that their basic cultural pattern had already been disturbed, and that living in flats in a community which had a more acceptable social pattern would have been better tolerated.

Discussion

The health of this community might be expected to be relatively good, as they had committed themselves to a turbulent domestic life where they were expected to travel around the United Kingdom and overseas as the men's occupation required, and there was the possibility of an element of selection in this respect. They were, however, subject to stresses and lived under conditions which were very similar to those found in a new housing estate in England. The break in their family links was voluntary in that all the men had chosen the armed Services as their career, accepting the disturbance of family ties that must follow. This makes direct comparison with the health of a population on a new housing estate or in a new town in England difficult, but the increase in morbidity of the families who lived in flats does indicate that a health problem can exist and the nature of the illnesses which such a situation may precipitate.

With the two most important types of illness which arose in these families—namely, respiratory infections and psychoneuroses—though they may not be regarded as very serious at the time, they may both lead eventually to chronic disability. Recurrent respiratory infections in children will cause underlying structural damage and eventually chronic bronchitis and bronchiectasis, a pathological pattern already notorious in England. Even mild neurotic illnesses tend to be prolonged and difficult to treat successfully, and are apt to recur. The pattern of social withdrawal and confinement to the dwelling of young mothers and children is one which invites chronic ill-health, and is against all the tenets of good hygiene.

The problems of living in flats are recognized by some of the planners of new housing, but it is important that they, and more particularly doctors who work in general practice and in the field of public health, should attempt to evaluate them on a wider scale than has yet been done, and that public and private authorities who are responsible for building homes should be made aware of them. In particular, more research is needed into the problems of morbidity of families who have had a double social disturbance by being removed from their places of origin and also placed in a flat.

Summary

Two groups of families of members of the armed Services stationed in Germany were compared, one group living in

TABLE VIII.—Incidence of First Attendance by the General Practitioners on Females Aged 15 and Over for Psychoneurotic Disorders, by Height of Flat

Level of Flat	Females Aged 15 and Over		
	First Attendances for Psychoneurotic Disorders	Population	Rate per 1,000
Ground floor	8	127	63.0
First "	8	120	66.7
Second "	14	128	109.4
Third "	7	55	127.3
Total	37	430	86.0

flats and the other in houses. It was found that the morbidity of those families who lived in flats was 57% greater than of those who lived in houses, and that the greatest differences were seen in the incidence of respiratory infections in young women and children, and of psychoneurotic disorders in women.

The reasons for the differences in respiratory infections were felt to be the relatively small space available in a flat compared with that in a house, and confinement of the family within the flat. This confinement, and the resulting social isolation, were thought to be the reasons for the increase in psychoneuroses in the women.

The families concerned had had a double social disturbance in that their family ties had been severed and they were also subject to the restricting environment of life in a flat, and it is suggested that in view of the large number of flats which are being built, and the tendency towards family mobility,

further investigation is needed into the effects of flat life on health.

I am grateful to the Director, General of Medical Services, Royal Air Force, for permission to publish this paper.

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Effect of Gastrin II on Gastric Emptying and Secretion During a Test Meal

J. N. HUNT,* M.D., D.S.C., M.R.C.P.; N. RAMSBOTTOM,* M.B., B.S.

Brit. med. J., 1967, 4, 386-390

Hypersecretion of gastrin by an islet cell tumour of the pancreas is believed to be the cause of the Zollinger-Ellison syndrome (Zollinger and Ellison, 1955; Gregory, Tracy, French, and Sircus, 1960). Patients with this condition have extreme gastric hypersecretion and peptic ulceration. In one case described by Lawrie, Williamson, and Hunt (1962) there was also very rapid gastric emptying. This feature seemed to be explained when Smith and Hogg (1966) found that injected gastrin stimulated gastric motility as judged by measurements of intraluminal pressure. We therefore expected that an increase in the rate of gastric emptying would result from intravenous infusion of gastrin, but this was not so.

Procedure

The plan of the experiments is set out in Fig. 1. Three test meals were given in succession with a 10-minute interval between them. For the 10 minutes before and during the second meal a continuous intravenous infusion of gastrin was given. The stomach was washed out with 250 ml. of water before each meal in order to remove any residual secretion. Each of the three tests of gastric emptying, which lasted 10 minutes, was separated from the subsequent test by 10 minutes. The meals consisted of 750 ml. of 100 mN sodium citrate containing 30 ml. of a saturated solution of phenol red per litre as marker. They were instilled down a tube into the stomach in about 75 seconds. This meal was chosen because it empties very rapidly; also it is buffered by the presence of the citrate ion, so minimizing the possible slowing action of secreted acid. Immediately after recovery of the first meal injection of gastrin into the running intravenous infusion was begun and continued for 20 minutes. Hog gastrin II was used in doses ranging from 0.125 to 3 μ g./min.

The recovered gastric contents were analysed according to the method of Hunt (1954, 1959). The volumes of original meal present in the recoveries were calculated as the product of the volume recovered and the ratio of its phenol red con-

centration to that of the original meal. The parietal secretion was calculated and expressed as millilitres of 160 mN HCl. The two of us, 75-kg. men aged 50 and 27, were the subjects for this investigation.

Results

The meal which was given during the infusion of gastrin left the stomach more slowly than the preceding or the succeeding meal. The minimal effective dose of gastrin in subject N.R.

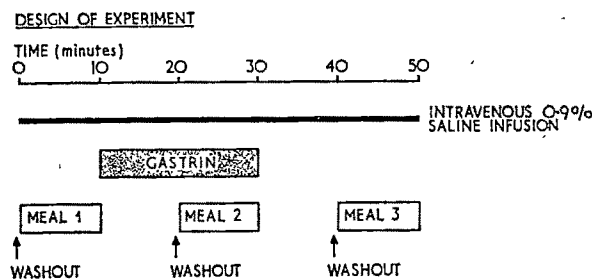


FIG. 1.—Plan of experiment.

was 0.5 μ g./min. (Fig. 2) and, in subject J.H. 2 μ g./min. (Fig. 3). In both subjects the threshold for stimulating secretion of acid in the second meal was less than that required to slow emptying—0.125 μ g. in N.R. and 0.5 μ g. in J.H. (Figs. 4 and 5). With most doses the slowing of emptying had worn off in the 10 minutes between stopping the infusion of gastrin and giving the third meal. On the other hand, with the larger doses, 0.75 μ g. in N.R. and 2 μ g. in J.H., the secretion of acid in response to the third meal was greater than that in response to the second, though there was no injection of gastrin during the third meal.

* Department of Physiology, Guy's Hospital Medical School, London S.E.1.

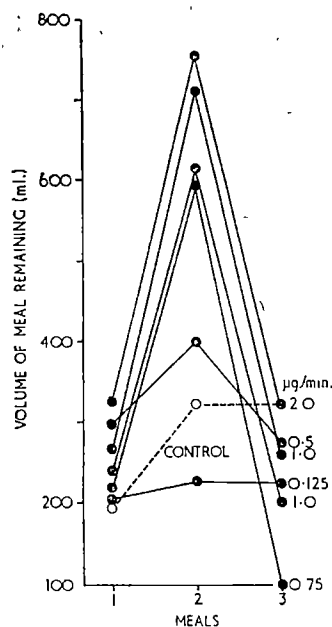


FIG. 2

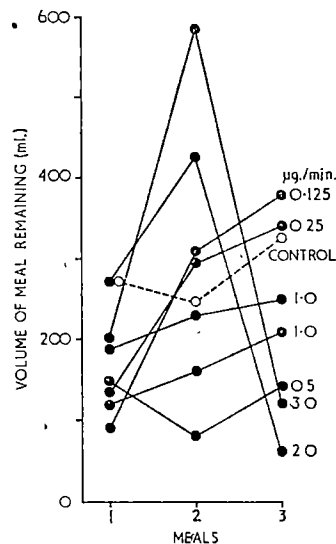


FIG. 3

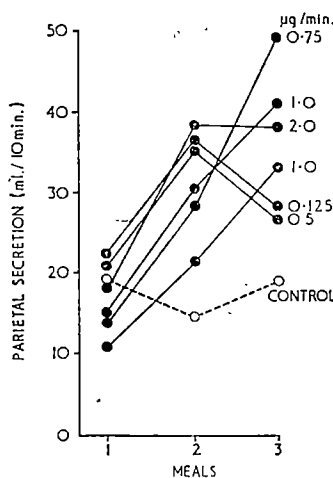


FIG. 4

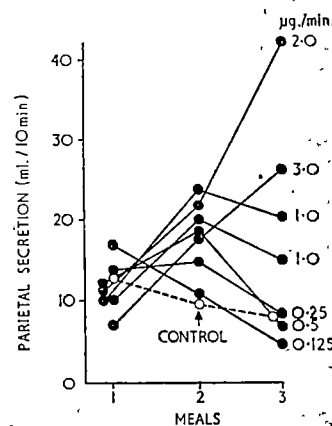


FIG. 5

FIG. 2.—Relation between dose of injected gastrin and volume of test meal remaining, N.R. FIG. 3.—Relation between dose of injected gastrin and volume of test meal remaining, J. H. FIG. 4.—Relation between dose of injected gastrin and volume of parietal secretion, N.R. FIG. 5.—Relation between dose of injected gastrin and volume of parietal secretion, J. H.

Discussion

It was believed that the hormones of the alimentary tract—for example, cholecystokinin, pancreozymin, and gastrin—had specific actions on their target organs. Originally gastrin was thought to act only on the parietal cell (Uvnäs, 1948), but more recently it has also been found to affect pepsin production and the secretion of protein by the pancreas (Emås and Grossman, 1967; Preshaw and Grossman, 1965). There is now evidence that gastrin also increases motility of the alimentary tract (Gregory and Tracy, 1964; Smith and Hogg, 1966). Because of the rapid gastric emptying seen in a patient with the Zollinger-Ellison syndrome, we expected infused gastrin to increase the rate of emptying. However, 0.5 $\mu\text{g./min.}$ (0.007 $\mu\text{g./kg./min.}$) in N. R. and 2 $\mu\text{g./min.}$ (0.03 $\mu\text{g./kg./min.}$) in J. H. slowed the emptying of the stomach. These doses were submaximal for the secretion of acid, since the next higher dose gave a greater secretion of acid and a greater slowing of gastric emptying.

Acid in test meals slows gastric emptying (Shay and Gershon-Cohen, 1934 ; Hunt and Pathak, 1960). However, the slowing of gastric emptying by gastrin was not caused in this way. For example, 0.75 μ g. of gastrin per minute in N.R. increased the recovery of test meal from 200 to 600 ml. The volume of parietal component secreted during this second meal was 28 ml., and the titratable acid was 5.6 mEq/l. of gastric contents. For the third meal the recovery of test meal was only 100 ml., yet the secretion of parietal component was 50 ml. and the titratable acidity of the gastric contents was 16 mEq/l. The secretion of parietal component before gastrin was given was 14 ml., with a titratable acidity of the gastric contents of 3.6 mEq/l. There was in this experiment, and in most of the others, a clear dissociation between gastric emptying and the titratable acidity of the gastric contents. Thus the slowing of emptying by gastrin was not caused by increased acidity of the gastric contents.

Gastrin and its pentapeptide analogue (I.C.I. 50.123) were found to increase the motility of the alimentary tract as indicated by changes in intraluminal pressure (Gregory and Tracy, 1964; Smith and Hogg, 1966). The slowing of gastric emptying by gastrin may result from a general increase in the tone of the gut. When this happens those parts of the alimentary tract with the smaller diameter are at a mechanical

advantage because of the operation of the law of Laplace (Brody and Quigley, 1948). Thus contraction of the duodenum may prevent the stomach from emptying. This appears to be the mechanism by which morphine slows gastric emptying (Folley and Osler-Abbott, 1942).

The difference between the rapid evolution of the maximal slowing of emptying and the slow approach to maximal secretion is worth comment. Presumably the motor response to gastrin depends on the plasma concentration. The delay in secretory response to gastrin may be analogous to the delay in response to aldosterone, which delay is currently ascribed to the induction of an enzyme (Sharp and Leaf, 1966). This would fit in with the work of Blair (personal communication), who found that, with a single intravenous dose of gastrin, by the time the peak of acid secretion was reached the concentration of gastrin in the plasma was only 3% of the initial level.

Summary

The effect of gastrin II on gastric emptying and secretion was examined in two men. The rate of gastric emptying was slowed in proportion to the dose given. The increased rate of gastric secretion of acid long outlasted the slowing of gastric emptying.

We should like to thank Professor R. A. Gregory, who kindly supplied us with the gastrin for this experiment.

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Which Stethoscope?

C. S. HAMPTON,*† M.B., CH.B.; A. CHALONER,*‡ M.B., CH.B.

Brit. med. J., 1967, 4, 388-390

The choice of a stethoscope is largely irrational. The newly fledged medical student is either likely to follow his professor's choice or buy the latest slim-line model. However, it would seem that an instrument which is an extension of the clinician's sensory system should be chosen on some rational basis.

Previous papers on this subject have described tests of stethoscope components rather than complete instruments. This would seem to be of limited value, as the acoustic properties of the complete instrument need bear no direct relation to that of its components.

Recently several stethoscopes have been manufactured which have tended to be lighter, more compact, more pleasing in

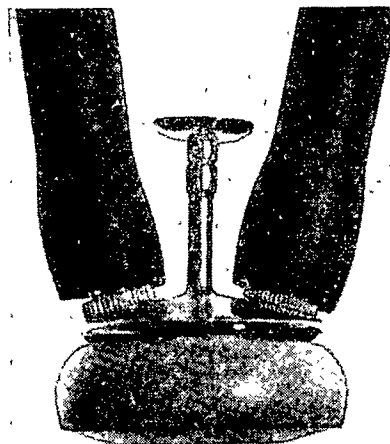


FIG. 1.—Guy's chestpiece used as "basic."

appearance, and more expensive. In this paper we have attempted to compare the performance of the newer stethoscopes with older and cheaper models.

Materials

The materials used in this experiment were:

(1) Peter's SPD5 audiometer connected to a vibrator unit (bone conduction).

TABLE I.—*Stethoscope Dimensions*

Stethoscope	Tubing Length and Internal Diameter	Binaural Length and Internal Diameter	Chestpiece Area of Skin Covered (sq. cm.)	Internal Volume (ml.)	Price £ s. d.
Basic stethoscope	2 × 40 cm.	2 × 22 cm.	3.8	22.9	1 12 6
Guy's chestpiece	4.5 mm.	4.5 mm.	3.8	9.1	4 15 0
Leatham stethoscope	2 × 20 cm.	2 × 21.5 cm.	11.0	25.7	
{ Little bell	3.0 mm.	3.0 mm.	7.0	8.1	
{ Big bell			6.0	13.5	
{ Diaphragm			13.8	10.8	
Littmann	35 cm.	2 × 21 cm.	4.5	25.7	6 0 0
{ Bell	4.5 mm.	3.0 mm.	10.0	7.1	
{ Diaphragm			5.0	7.8	
Sprague-Bowles	2 × 38 cm.	2 × 22 cm.	15.9	4.4	3 6 0
{ Bell	4.5 mm.	4.5 mm.			
{ Diaphragm					
Allen type V	36 cm.	2 × 25 cm.			6 0 0
{ Bell	3.0 mm.	3.0 mm.			
{ Diaphragm					
Wooden monaural	17 cm. Diameter variable		2.3		

The internal volumes were measured by filling the stethoscopes with mercury and measuring the volume of the mercury with a burette.

* Tubing shorter than original length.

(2) Normal human chest.

(3) *Stethoscopes*.—The stethoscope chosen as "basic" had the Guy's rubber-ended chestpiece as shown in Fig. 1. Compared with this basic were: (i) Sprague (Reiger) Bowles bell and diaphragm; (ii) Leatham large and small bells and diaphragm; (iii) Littmann bell and diaphragm; (iv) Allen bell and diaphragm; and (v) wooden monaural stethoscope. Dimensions and prices of these stethoscopes are given in Table I.

The auscultator was the same observer throughout.

Method

A Peter's SPD5 audiometer with a bone conduction vibrator was used as a source of sound. The audiometer vibrator was placed in the suprasternal notch of a live human subject. The auscultator listened for the sound by holding the chestpiece of the stethoscope on a point 7.5 cm. from the anterior midline in the fifth right intercostal space of the subject. With the lowest frequencies the position of the chestpiece was in the right first interspace 5 cm. from the midline, as in the more caudal position no signal was received. This arrangement allowed the emitted vibration to be conducted through the chest of the subject without either the subject being aware of the vibration or the auscultator receiving any sound by direct air conduction.

At each session, lasting about an hour, one frequency only was considered; the whole range of stethoscope chestpieces was tested for this one frequency. Output and frequency controls of the audiometer were recalibrated at the beginning of each session. Tones interrupted three times per second were used to facilitate interpretation; the audiometer was operated by the auscultator. Thirteen frequencies spaced at approximately equal intervals along the logarithmic scale between 0 and 1,000 c/s were chosen, as the usual auscultatory sounds lie within this range (Rappaport and Sprague, 1941).

On the Peter's SPD5 audiometer the only frequencies already calibrated between 0 and 1,000 c/s were 250, 750, and 1,000 c/s. The other frequencies chosen arbitrarily for this experiment were subsequently calibrated by means of the beat frequency technique. The apparatus used was a radiometer beat frequency oscillator HO 32 connected to a 10-in. (25-cm.) loudspeaker. A stethoscope was used to compare the frequencies emitted by the audiometer vibrator and the loudspeaker, the vibrator being placed between the stethoscope chestpiece and the loudspeaker. It was found by this technique that the 250 c/s reading on the audiometer was in fact 240 c/s. The other frequencies used are given with the results in Table II.

Ten readings for the basic stethoscope were made; the lowest intensity which could be interpreted was read in decibels from the audiometer scale—this being taken as the threshold. The same chest position was used and comparison was made with the various stethoscopes, there being 10 readings for each chestpiece bell or diaphragm. Twice during the session a further 10 basic readings were taken, making a total of 30 basic readings

* Demonstrators, Department of Physiology, St. Andrews University, St. Andrews, Fife.

† Late Medical Registrar, the County Hospital, Dorchester, Dorset. Present address: Renal Unit, Leeds General Infirmary, Leeds 1.

‡ Now Medical Officer (Research), R.A.F. Institute of Aviation Medicine, Farnborough, Hants.

for each frequency tested. The procedure was followed for each of the 13 frequencies.

Results

It was found that on deep inspiration the threshold was raised by about 5 db; however, during our experiment the subject was at rest and breathing was shallow. Under these conditions the threshold did not vary appreciably with respiration.

Accurate positioning of the chestpiece on the chest wall was essential for consistent thresholds at the lower frequencies.

Thresholds varied by up to 5 db with changing pressure of application by the auscultator on the chestpiece. The threshold values in this paper were obtained by using the optimal pressure for each stethoscope chestpiece at each frequency.

The lowest frequency measured by our technique was 73 c/s, owing to the low output of the bone conduction vibrator at lower frequencies.

The auscultator noted that the subjective quality of sounds heard via different stethoscopes varied.

The results are set out in Table II. Each figure in this Table is the mean of 10 threshold determinations, 30 in the case of the basic stethoscope. Column C gives the standard deviation of 30 basic thresholds; from these figures some idea of the consistency of the thresholds may be obtained. Application of the method of analysis of variance and Student's *t* test yielded the figures for column D.

Statistical significance of the results can be assessed by adding or subtracting the figure in column D from the basic results shown in column B. These limits must then be compared with the results shown under each stethoscope heading at the same frequency. Subsequent columns give figures which are the mean of 10 thresholds for the stethoscopes tested. The thresholds were measured repeatedly and statistical methods were applied in an attempt to compensate for threshold inconsistencies.

Fig. 2 summarizes the data in Table II. High and low frequencies were considered separately because of the oft-quoted axiom that low frequencies are best heard with bells and high frequencies with diaphragms.

Discussion

Dawson (1964) states that heart and chest sounds fall into the following frequency ranges:

Low heart sounds (presystolic and some systolic murmurs; basal and mitral diastolic murmurs; auricular and first, second, and third heart sounds; gallop rhythms) ...	20-115 c/s
Medium and high heart sounds (systolic and diastolic murmurs) ...	200-660 c/s
Pericardial rubs ...	140-660 c/s
Amphoric breathing ...	240-660 c/s
Bronchial breathing ...	240-1,000 c/s
Crepitations ...	750 c/s upwards
Vesicular breathing ...	150-1,000 c/s
Breath sounds heard in trachea, bronchi, bronchioles ...	800 c/s upwards
Foetal heart sounds ...	16 c/s upwards

TABLE II.—Thresholds (db) for Various Stethoscopes

A Frequency (c/s)	B "Basic" Mean of 30 Readings	C S.D. of 30 Readings	D Required Variation from Basic Mean at 5% Level of Signi- ficance	Sprague-Bowles		Littman		Leatham			Allen		Wooden Monaural
				Bell	Dia.	Dia.	Bell	Dia.	Big Bell	Little Bell	Dia.	Bell	
73.3	53.4	0.9	0.6	56.8±	50.4*	52.9±	54.0†	57.3±	52.0*	52.0*	55.5±	47.6*	Over 62±
90.0	53.3	0.7	0.4	57.3±	55.8±	57.3±	56.2±	55.4±	52.8*	48.7*	57.7±	55.4±	" 60±
120.0	56.6	0.5	0.4	57.5±	54.8*	57.6±	57.0±	56.8±	57.2±	53.2*	58.2±	58.4±	" 60±
161.6	44.8	1.3	0.7	49.4±	49.4±	44.0*	46.2±	52.3±	46.9±	48.3±	44.1†	40.5*	51.9±
207.4	34.2	0.6	0.6	32.4*	40.8±	35.0±	34.6†	42.3±	35.6±	27.0*	36.1±	32.5*	38.8±
(250) 239.4	34.0	1.0	0.9	33.9†	33.9†	34.2†	34.7†	36.7±	31.3*	30.5*	37.8±	37.9±	34.7±
299.2	49.9	1.3	1.2	53.4±	45.2*	45.0*	49.8†	53.7±	45.0*	54.1±	47.8†	50.0*	54.6±
347	36.7	0.5	0.8	37.5†	35.9†	42.4±	33.3*	41.7±	38.5±	40.2±	41.8±	34.3*	59.4±
437	36.9	0.6	0.4	30.8*	30.5*	39.8±	33.5*	39.5±	35.4*	34.1*	42.5±	29.5*	44.4±
(500) 497	34.4	0.5	0.4	35.4±	27.3*	30.3*	27.0*	30.7*	35.4±	24.2*	27.3*	29.9*	30.6*
595	22.6	0.5	0.3	23.8±	17.4*	20.4*	22.4†	22.0*	17.6*	22.5†	19.8*	19.7*	29.0±
(750) 758	25.6	0.6	0.4	36.1±	35.2±	32.3±	27.6±	10.4*	22.6*	12.5*	34.5±	18.7*	35.5±
(1000) 1006	24.1	0.8	0.6	24.5†	20.1*	22.8*	14.7*	18.6*	18.4*	15.6*	19.8*	20.1*	28.3±

The figures given for the required variation from basic mean at the 5% level of significance were obtained by using the method of analysis of variance and Student's *t* test. Each figure is the mean of 10 readings (30 in the case of the basic stethoscope).

S.D. = Standard deviation. * Significantly better than basic. † Not significantly different from basic. ‡ Significantly worse than basic.

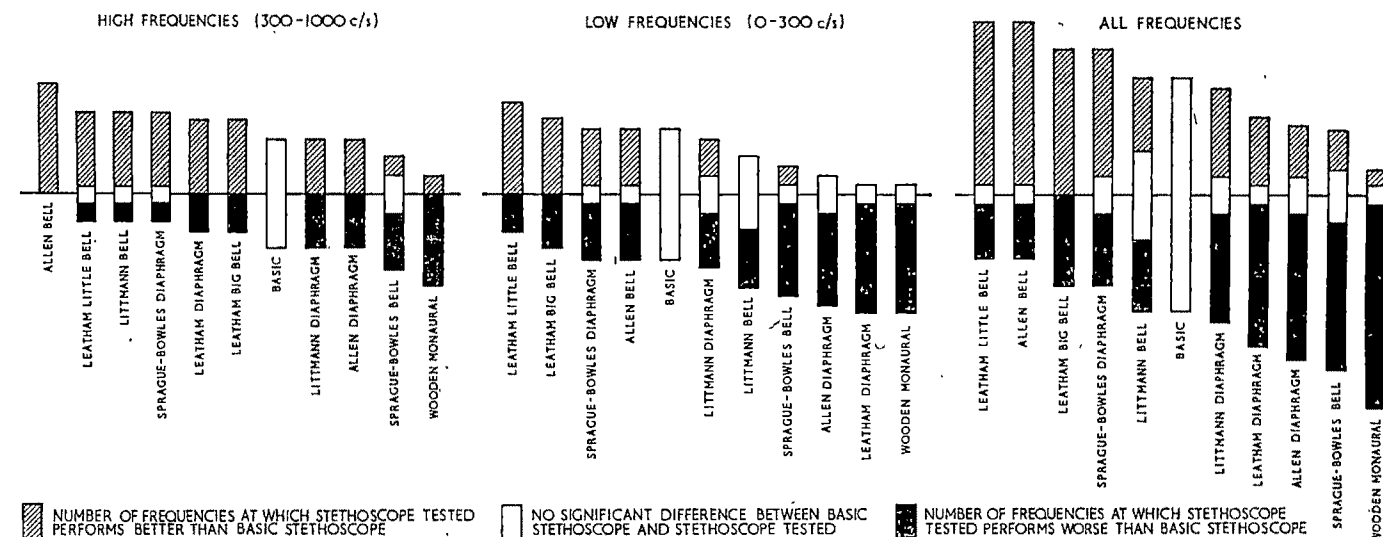


FIG. 2—Summary of data given in Table II.

It would appear that any frequency falling between 20 and 1,000 c/s is of relevance to some clinical situation.

The stethoscopes used in this experiment were chosen as being most representative of those in general use, the exception being, of course, the wooden monaural.

An initial attempt to reproduce the experimental conditions of Rappaport and Sprague (1941) was unsuccessful, as it proved impossible to obtain an effective soundproof seal between the chest wall and a loudspeaker baffle.

Some previously enunciated principles of stethoscope design may now be examined in the light of our results.

(1) "It is apparent that the larger the area of the stethoscope piece in contact with the chest, the greater the amount of sound collected" (Macfarlan, 1938). The Leatham big bell has a performance somewhat inferior to that of the little bell; the skin area enclosed by the Sprague-Bowles bell is greater than that of the basic stethoscope, yet the performance of the Sprague-Bowles bell is inferior, though the two stethoscopes have similar tubing and binaural dimensions.

(2) A good stethoscope needs both a bell and a diaphragm chestpiece (B.M.J., 1962). The Sprague-Bowles diaphragm is superior to the bell in both the higher and lower frequencies. The Littmann diaphragm performs better than the bell in the lower frequencies; the converse applies at the higher frequencies. Both the Allen and the Leatham bell seem to be superior to their respective diaphragms at both higher and lower frequencies.

(3) A stethoscope should have a small internal volume (Barss *et al.*, 1926; Rappaport and Sprague, 1951). In general our results seem to support this principle. The Leatham and the Allen both use small-bore tubing (diameter 0.3 cm.) and have small internal volumes.

In general these results differ from those of Barss *et al.*, (1926) and Rappaport and Sprague (1941, 1951). Barss *et al.* concluded that increasing the area of the chestpiece leads to greater efficiency. Their conclusions were based on an experiment involving the passage of sound from a source, through air, to the chestpiece; these conditions are very different from

those obtaining in the clinical use of the stethoscope. Rappaport and Sprague compared stethoscope components rather than complete stethoscopes. The acoustic properties of any component are very different from those of a stethoscope incorporating that component.

It is suggested that in stethoscope design most of the previously accepted principles should be ignored and an empirical approach should be used. Stethoscopes of small internal volume might be modified step by step, discarding modifications leading to an inferior performance and incorporating those leading to improved performances.

The conditions of testing should correspond as closely as possible to those in clinical use.

Summary

A comparison has been made of the efficiency of various stethoscopes in common clinical use by simulating natural conditions as far as possible. Of the stethoscopes tested by this method the Leatham little bell and the Allen bell gave the best overall performances. The current prices in the U.K. of the various stethoscopes are listed. It is suggested that an empirical approach to stethoscope design is adopted, though, in general, stethoscopes with small internal volume and small endpiece skin contact gave the better performances.

We would like to thank Dr. J. H. Taylor, who originally suggested that we should attempt a *Which?* report on stethoscopes, and Professor A. E. Ritchie for his help and advice. Mr. P. D. L. Constable gave invaluable help with the statistics.

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Location of Placenta by Means of a Colour Autoscan Technique

W. THOMPSON,* M.B., B.Sc., M.R.C.O.G.; T. K. BELL,† B.Sc., A.Inst.P.; J. H. M. PINKERTON,* M.D., F.R.C.O.G.

Brit. med. J., 1967, 4, 390-391

Location of the placenta by radioactive scanning techniques has considerable advantages over existing x-ray methods and is being used with increasing frequency (Hibbard, 1966). When tracer doses of isotopes tagged to human albumin are employed the radiation risk to the foetus is greatly reduced (McGee and Duron, 1960). In 1966, at the Royal Victoria Hospital, Belfast, a colour autoscan apparatus became available that could be adopted for use in placentography. This paper describes the use of this apparatus and the results so far obtained in 62 cases.

Method and Equipment

Lugol's iodine solution, 0.3 ml. three times daily for 24 hours before and seven days after the test, was given to block the maternal and foetal thyroid (Cavanagh *et al.*, 1961).

Human serum albumin labelled with ¹³¹I, obtained from the Radiochemical Centre, Amersham, was diluted in saline and

5 microcuries administered intravenously to each patient. Five to 10 minutes were allowed for the radioactive compound to mix throughout the vascular department. The patient was then placed supine on the couch of a total body scanner (Isotope Developments Ltd., Reading) beneath a fixed scintillation counter in axial alignment with another similar counter below the couch. Each counter contained a 3-in. (7.5-cm.) diameter sodium iodide crystal in a 3-in. diameter lead collimator. The couch was mechanically moved backwards and forwards between the counters along parallel lines separated by a distance of 1 cm. until the whole abdominal area was scanned.

The radiations detected by each counter are converted to electrical pulses, added together, and operate a striker and the six-colour ribbon beneath it. Distribution of the radioactivity is displayed on a sheet of paper in the form of coloured dashes, indicating regions of high and low concentrations. This double counter system gives higher counting rates, better distinction, and a shorter operating-time—approximately 20 minutes—as compared with the single counter placed above the patient used in earlier work in this series.

* Department of Gynaecology, the Queen's University, Belfast.

† Department of Medical Physics, Royal Victoria Hospital, Belfast.

At the end of the scan the individual counting rates from each detector viewing the "hot" region indicate whether the placenta was anterior or posterior.

Results

The indications for placentography were a suspicion of placenta praevia in 58 patients who presented with antepartum haemorrhage (52) or a persistent unstable lie at 37 weeks (6) (see Table), and the need to define the placenta before amniocentesis in four. The usual gestation period at which the test was performed was 32–33 weeks, but satisfactory results were obtained as early as 30 weeks. In four patients placenta praevia diagnosed on scanning was not confirmed clinically. These false-positive results were due mainly to overcautious assessment of the scans early in the series, and with experience it has been possible to increase the accuracy of prediction. Of 42 patients with antepartum haemorrhage 32 were allowed home for intervals of two to six weeks after placentography had indicated that the placenta was in the upper uterine segment; no foetal loss resulted.

Summary of Results

Placental Site	Autoscan Report	Correct at Delivery	Accuracy
Upper uterine segment	42	42	100%
Lower " " "	16	12*	75%
Total	58	54	93%

* Four false-positive results.

Discussion

Clinical Applications.—The accuracy of the method described is 93%, and is comparable to that of other reported isotope techniques; its main clinical value is the exclusion of placenta praevia before allowing the patient home for part or all of the remainder of the antenatal period, and it is important in this connexion to note that in no patient was a placenta praevia missed. In this way we calculate that the equivalent of three out of 100 hospital beds a year are released for other purposes. No attempt was made to estimate the degree of placenta praevia, as all cases carry the risk of further possible severe haemor-

rhage, and are therefore kept in hospital until after delivery. The other application of the procedure is before amniocentesis, when there is clinical evidence of an anteriorly placed placenta. Here the scan is useful in the selection of a suitable puncture site.

Choice of Isotope.—Albumin tagged with ^{131}I was chosen as the most suitable tracer material, because it has been successfully used elsewhere for placental location (Weinberg *et al.*, 1957; Heagy and Swartz, 1961; Durfee and Howieson, 1962), its biological characteristics are fully known, its production is reliable, it is relatively cheap, and it is readily obtained commercially. Isotopes such as ^{132}I and technetium 99m have the advantage of a much shorter half-life, so that larger quantities of radioactive material can be used, resulting in higher counting rates and better discrimination. If, however, the facilities required for routine production of albumin tagged with these isotopes are not available ^{131}I albumin has been shown to give satisfactory results.

Summary

A technique of isotope placental location is described which uses ^{131}I and a colour autoscan apparatus. The use of a two-collimator modification has been found to increase the definition of this method, so that the readily available albumin-tagged ^{131}I gave satisfactory results.

The accuracy of the method was 93%; no placenta praevia remained undetected.

We are indebted to the consultant staff of the Royal Maternity Hospital, Belfast, for permitting us to include their patients in this study. Our thanks are also due to Dr. R. Ferguson and Dr. W. B. Sproule for their help.

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Adrenocorticotrophic Action of Long-acting Tetracosactrin Compared with Corticotrophin-gel

G. M. BESSER,* M.D., B.SC., M.R.C.P.; P. W. P. BUTLER,* M.B., B.S., M.R.C.P.
 F. S. PLUMPTON,† B.M., B.CH., F.F.A. R.C.S.

Brit. med. J., 1967, **4**, 391–394

Tetracosactrin (β^{1-24} corticotrophin, Synacthen) is a synthetic polypeptide containing the first 24 amino-acids found in naturally occurring corticotrophin (A.C.T.H.). It has a high degree of corticotrophic activity (Landon *et al.*, 1964) and is used to test adrenocortical responsiveness (Wood *et al.*, 1965). However, since its action lasts only three to four hours after an intramuscular dose (Landon *et al.*, 1964), unmodified tetracosactrin can have little place in therapy. A long-acting version of this compound might offer practical advantages over naturally occurring corticotrophin, particularly in patients who develop hypersensitivity reactions or antibodies to natural corticotrophin, since its amino-acid sequence is identical with that of

the active portion of human corticotrophin and the preparation does not contain any animal contamination. Tetracosactrin has now been modified by adsorption on to an inorganic zinc complex to prolong its action. This paper reports a comparison of its adrenocorticotrophic properties and length of action compared with corticotrophin-gel of animal origin in normal subjects and in patients previously treated with oral corticosteroids or corticotrophin.

Methods and Subjects

Subjects.—All subjects were volunteers without evidence of endocrine, renal, or liver disease. There were 18 non-steroid-treated subjects, of whom eight were ambulant medical staff,

* Medical Professorial Unit, St. Bartholomew's Hospital, London E.C.1.
 † Department of Anaesthesia, St. Bartholomew's Hospital, London E.C.1.

four were inpatients who did not require corticosteroid therapy, and six were patients in whom corticosteroid therapy was indicated by the severity of their underlying disease. In the steroid-treated group there were six patients treated with prednisolone for more than three months (range 4 to 12 months) and six treated for less than three months (1 to 10 weeks). The dose varied from 10 to 60 mg./day. The six corticotrophin-treated subjects had received 40–80 units of corticotrophin-gel daily for one to three weeks, and the injections were stopped 48 hours before the test.

Trial Design and Analysis.—There were three treatments—1 and 2 mg. of depot-tetracosactrin, and 80 units of corticotrophin-gel (Armour) of a single batch number (MB 0802). The treatments were given intramuscularly at 72-hour intervals between 9 and 10 a.m. and the order of administration was randomized and balanced among the subjects by means of orthogonal latin square designs. Plasma cortisol estimations were performed at 0, 2, 4, 8, 12, 24, 32, 48, and 72 hours after drug administration. The changes in plasma cortisol were initially analysed by the method of analysis of variance (Snedecor, 1956), and the differences between the means at each time were tested by Hartley's (1955) modification of Student's *t* test.

Plasma Cortisol Assay.—Plasma 11-hydroxycorticosteroids were measured by the fluorimetric method of Mattingly (1962). This measures principally cortisol (hydrocortisone), as well as small amounts of circulating corticosterone and some other unknown fluorescent substances. The combination is referred to as "plasma cortisol" in this paper.

Results

Initially results from the patients requiring corticosteroid therapy were analysed separately from those from the other normal subjects, as they were somewhat stressed and might have given different responses. Their results were subsequently combined, since there were no significant differences between the responses of the two subgroups and their variances were homogeneous. This whole group is referred to as "normal subjects." The two groups of corticosteroid-treated patients were also combined in the final analysis, as their responses and variances were not significantly different.

Normal Subjects (Fig. 1)

The mean plasma cortisol levels after the three treatments were not significantly different at 0, 2, and 4 hours, rising to over three times the resting concentration during this time. After 80 units of corticotrophin-gel the mean level rose further to a maximum of 69 $\mu\text{g./100 ml.}$ at eight hours, and then fell off rapidly to reach basal levels by 24 hours. After 1 mg. of depot-tetracosactrin the maximum mean plasma cortisol

occurred at four hours and was then 6 $\mu\text{g./100 ml.}$ less than the maximum after 80 units of corticotrophin-gel, but this difference was not significant. Compared with the response to the gel, the mean concentration fell more slowly after the 1-mg. dose and reached basal values at between 32 and 48

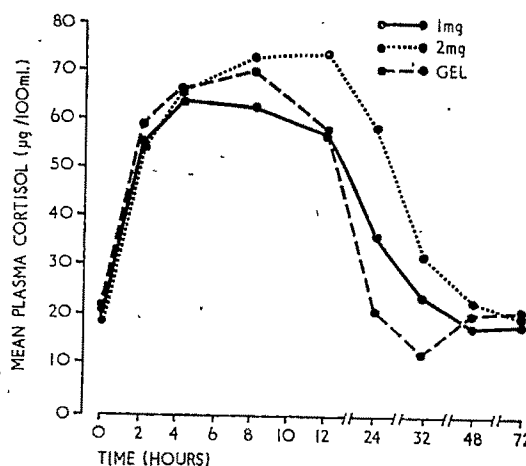


FIG. 1.—Mean plasma cortisol concentrations in 18 normal subjects after 80 units of corticotrophin-gel and 1 and 2 mg. of depot-tetracosactrin.

hours. The cortisol concentrations were significantly higher after 1 mg. than after the gel at 24 and 32 hours (see Table). After 2 mg. the maximum level was greater than after the gel or 1 mg. and remained higher from 4 to 48 hours, by which time it had just reached basal levels (23 $\mu\text{g./100 ml.}$). The differences from the levels after the gel were significant at 12, 24, and 32 hours and from the 1 mg. dose at 8, 12, 24, and 32 hours (see Table).

Corticosteroid-treated Patients (Fig. 2)

The general pattern of effects was similar in this group. However, the maximum plasma cortisol levels achieved were virtually the same on all three treatments and were about 30 $\mu\text{g./100 ml.}$ (40%) lower than in the normal subjects. Since these subjects' adrenal cortices were to a greater or less extent suppressed by the prednisolone treatment, the starting levels were low, but all three treatments provided a potent stimulus to the suppressed glands. In only 2 of the 12 subjects did the first treatment fail to raise the plasma cortisol above 25 $\mu\text{g./100 ml.}$, and in these this level was achieved after the second treatment in one and after the third in the other. The mean plasma cortisol concentration after the 80 units of corticotrophin-gel at 24 hours (27.5 $\mu\text{g./100 ml.}$) was only just above the upper limit for the normal range at 9 a.m. (6–26 $\mu\text{g./100 ml.}$), whereas after the 1-mg. dose of the depot-tetra-

Probability Values for the Significance of the Differences Between the Mean Plasma-cortisol Levels after 80 Units Corticotrophin-gel and 1 and 2 mg. Depot-tetracosactrin in (a) 18 Normal Subjects and (b) 12 Corticosteroid-treated Patients

(a) Normal Subjects									
Time (hours):	0	2	4	8	12	24	32	48	72
Gel v. 1 mg.	..	NS	NS	NS	NS	<0.01	<0.01	NS	NS
Gel v. 2 "	..	"	"	"	<0.01	<0.001	<0.001	"	"
1 mg. v. 2 "	..	"	"	<0.05	<0.01	<0.001	<0.05	"	"
S.E. of mean	..	1.42	2.16	2.46	2.78	3.47	2.56	1.75	0.90
(b) Corticosteroid Patients									
Time (hours):	0	2	4	8	12	24	32	48	72
Gel v. 1 mg.	..	NS	NS	NS	NS	NS	NS	NS	NS
Gel v. 2 "	..	"	"	"	"	<0.05	<0.01	<0.01	"
1 mg. v. 2 "	..	"	"	"	"	NS	<0.05	<0.01	"
S.E. of mean	..	1.43	3.82	4.69	4.50	3.69	3.72	3.23	1.66

NS = Difference not significant.

cosactrin it did not fall to this level until 32 hours, and after the 2-mg. dose until 48 hours. However, the concentrations after corticotrophin-gel and the 1-mg. dose were not signifi-

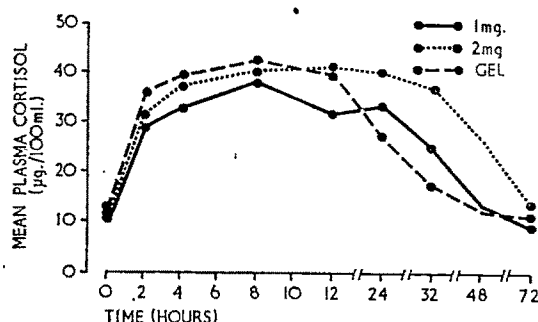


FIG. 2.—Mean plasma cortisol concentrations in 12 corticosteroid-treated patients after 80 units corticotrophin-gel and 1 and 2 mg. depot-tetracosactrin.

cantly different at any time, though they were significantly greater after the 2-mg. dose compared with the gel at 24, 32, and 48 hours, and compared with the 1-mg. dose at 32 and 48 hours (see Table).

Corticotrophin-treated Patients (Fig. 3)

In these six patients the pattern of results was similar to that of the normal subjects except that the maximum levels of cortisol achieved were some 10 µg./100 ml. higher. In this small group the effect of the 1-mg. dose appeared to fall off more quickly than in the other groups, reaching 26 µg./100 ml. at 24 hours.

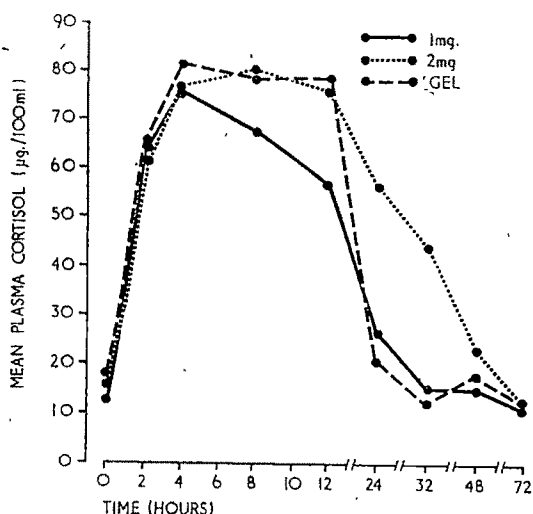


FIG. 3.—Mean plasma cortisol concentrations in six corticotrophin-treated patients after 80 units corticotrophin-gel and 1 and 2 mg. depot-tetracosactrin.

Clinical Features

The depot-tetracosactrin is an aqueous suspension of 1 mg. of powder in 1 ml. and was simple to give, unlike the corticotrophin-gel, which was viscous and required preliminary warming. Thirteen out of 36 subjects complained of local discomfort after the depot-tetracosactrin, particularly when this was given into the deltoid muscle rather than into the thigh or buttock. Of these subjects, three also had discomfort after the gel.

Though not specifically investigated, it was apparent that in those subjects with asthma and rheumatoid arthritis given the depot-tetracosactrin for therapy symptoms were relieved within two to three hours and the clinical effect of 1 mg. lasted about 32 hours.

Discussion

The depot-tetracosactrin powerfully stimulated the adrenal cortex under normal conditions and also when suppressed by exogenous corticosteroids or stimulated by a previous course of corticotrophin. Since there were no differences between the 1-mg. dose, the 2-mg. dose, and the 80 units of corticotrophin-gel over the first four hours, it may be presumed that the gland was maximally stimulated over this time by each treatment. In terms of the maximum plasma cortisol concentration achieved, 1 mg. of the new drug was not significantly different from 80 units of corticotrophin-gel. The depot-tetracosactrin, however, maintained the plasma cortisol level for longer, and it may be concluded that to maintain a continuously elevated plasma cortisol 1 mg. of the synthetic agent need be given only once daily while the corticotrophin-gel in this dose must be given twice daily. Since the cortisol concentrations after 2 mg. were considerably, and significantly, higher than after 1 mg. up to 32 hours, alternate daily administration might be sufficient at this dose.

It is established that A.C.T.H. of animal origin may produce severe and sometimes fatal hypersensitivity reactions (Wilson, 1951; Hill and Swinburn, 1954; Inderbitzin, 1954; Pearson, 1959; Rajka, 1961; Forssman *et al.*, 1963; Rosenblum and Rosenblum, 1964), though this must be a rare event with modern purified preparations. Jenny *et al.* (1963), Landon *et al.* (1964), and El-Shaboury (1965) challenged known corticotrophin-hypersensitive patients with the short-acting, unmodified tetracosactrin without producing hypersensitivity reactions, yet there was an adequate adrenocortical response in each case. However, the action of unmodified tetracosactrin is too short for practical therapy. The depot-preparation has a useful time course of action of 32 to 48 hours, and it is probable that at least a proportion of natural corticotrophin-hypersensitive patients could be treated with it.

Since stress-induced growth hormone release is inhibited by oral corticosteroids but not by corticotrophin (Frantz and Rabkin, 1964; Hartog *et al.*, 1964; Friedman and Stimmeler, 1966), corticotrophin therapy may be indicated rather than oral corticosteroids in children; there is evidence that "steroid-stunting" is less likely to occur (Friedman and Strang, 1966; Friedman and Greenwood, 1967). Similarly, A.C.T.H. release in response to stress is less likely to be suppressed after corticotrophin therapy than after oral corticosteroids (Savage *et al.*, 1962; Friedman and Greenwood, 1967). A complicating factor is the development of antibodies to the species-specific portion of the corticotrophin molecule in a high proportion of patients (Friedman and Greenwood, 1967) and sometimes acquired resistance to its adrenocorticotrophic action may develop (West, 1960, 1962). It is possible that corticotrophin of animal origin is more antigenic in man than the short-chain synthetic preparation containing the first 24 amino-acids of human corticotrophin in their natural sequence. The availability of a depot preparation of this synthetic tetracosactrin allows its antigenic potency to be tested in man, since it can be administered therapeutically on a long-term basis.

Bioassay initially showed that 1 mg. of tetracosactrin was equivalent to 106 units of animal corticotrophin (Schuler *et al.*, 1963). This study has suggested that the modified depot preparation of this polypeptide is somewhat less potent, 1 mg. being approximately equal to 80 units of corticotrophin.

Summary

The adrenocorticotrophic action of a long-acting version of the synthetic polypeptide tetracosactrin has been compared in two doses (1 and 2 mg.) with 80 units of a gelatin preparation of natural corticotrophin in 18 normal subjects, 12 corticosteroid-treated patients, and six corticotrophin-treated patients over 72 hours. In terms of the mean maximum plasma cortisol

concentrations attained 1 mg. of depot-tetracosactrin was approximately equivalent to 80 units of corticotrophin-gel. Mean plasma cortisol levels had returned to normal by 24 hours after the corticotrophin-gel, and by 48 hours after both doses of the depot tetracosactrin. To maintain a continuously elevated plasma cortisol corticotrophin-gel in this dose must be given twice daily and 1 mg. of the depot-tetracosactrin once daily; after 2 mg. alternate daily administration might be sufficient. All three preparations gave maximal adrenal cortical stimulation over the first four hours. The depot-tetracosactrin was simpler to give than the corticotrophin-gel. Local discomfort was more common after the synthetic preparation.

We are grateful to Professor E. F. Scowen and Dr. P. V. Cole for their interest and to the physicians of St. Bartholomew's Hospital and St. Leonard's Hospital for permission to study patients under their care. CIBA Laboratories kindly provided the depot-tetracosactrin, which is at present available only for clinical trial. We are particularly indebted to Miss Catherine Duncan for the statistical analysis.

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Simple Screening Test for Cushing's Syndrome

D. MATTINGLY,* M.B., M.R.C.P.; CHRISTINE TYLER,† B.SC., PH.D.

Brit. med. J., 1967, 4, 394-397

Cushing's syndrome is now generally recognized to be due to the prolonged excessive secretion of cortisol (hydrocortisone), and all of the main clinical features of this disorder have been accidentally reproduced at one time or another in patients on corticosteroid therapy. Gross cases may present no difficulty in diagnosis, but in recent years it has become apparent that these are in a minority, since adrenal hyperfunction is often present in patients with few signs and symptoms suggestive of classical Cushing's syndrome (Ross *et al.*, 1966). Obesity is almost invariably present, but is of little diagnostic value because of its high incidence in the population as a whole, particularly in women between the ages of 20 and 50 years, who are the most likely to be suffering from Cushing's syndrome. Nevertheless, obesity is of some help in drawing attention to the possibility of this disease, and the suspicion of adrenocortical overactivity may be reinforced if the obesity is of central distribution and accompanied by hypertension, menstrual irregularities, hirsutism, or diabetes mellitus.

Clinical acumen, however, is insufficient to establish the diagnosis of this disease, and confirmation depends on showing that cortisol production is in excess of normal. The most reliable means of doing this is to measure the cortisol secretion rate by isotope dilution (Cope and Black, 1958; Brooks *et al.*, 1963; Cope and Pearson, 1965; Ross *et al.*, 1966). This technique has proved invaluable in equivocal cases, but is too highly specialized for routine clinical use. The same objection applies to the estimation of urinary cortisol excretion by chromatography, another procedure which has high diagnostic value (Cope and Black, 1959; Brooks *et al.*, 1963; Rosner *et al.*, 1963). At present most laboratories are only equipped to estimate urinary 17-oxogenic steroids or 17-hydroxycorticoids.

It is now clear, however, that these levels often fall within the accepted normal range in patients with undoubted Cushing's syndrome, and so are an unreliable index of cortisol production in this disease. Indeed, Cope and Pearson (1965) have shown that there is no correlation between the cortisol secretion rate and 17-oxogenic steroid excretion over the normal range and the region just above it where so many of the equivocal values lie.

In order to recognize Cushing's syndrome in patients who are not yet grossly diseased, a test is needed the results of which more accurately reflect the cortisol secretion rate, and which is simple enough to be carried out routinely for screening purposes. In 1964 a simple fluorimetric method was described for estimating unconjugated 11-hydroxycorticoids in urine (Mattingly *et al.*, 1964). These urinary 11-hydroxycorticoid estimations showed a better correlation with the cortisol secretion rate over the required range than did the 17-oxogenic steroids. Elevated levels were found in a number of patients with Cushing's syndrome, and it was suggested that this method might be of value in screening patients for this disease. The present paper extends these observations to include 34 patients with Cushing's syndrome, and compares their urinary 11-hydroxycorticoid excretion with that of control subjects and patients with "simple" obesity.

Materials and Methods

The ages of the subjects ranged from 13 to 72 years. They were divided into three groups:

- (1) A control group consisting of 50 females and 59 males made up of normal subjects and of convalescent hospital patients. The latter were not acutely ill and were under no obvious stress at the

* Director, Postgraduate Medical Institute, University of Exeter.

† Research Assistant, Postgraduate Medical Institute, University of Exeter.

time of urine collection. Patients with endocrine, liver, or renal diseases were excluded.

(2) A group of 62 female and 13 male patients who were obviously obese but had no other manifestation of Cushing's syndrome.

(3) A group of 27 female and 7 male patients with Cushing's syndrome. The series consisted of 25 patients with adrenal hyperplasia, 4 with adrenal tumours, and 5 with adrenal hyperplasia associated with "non-endocrine" tumours. The diagnosis was confirmed independently in 20 cases by estimation of the cortisol secretion rate (Mattingly *et al.*, 1964) and by inspection of the adrenal glands at operation or necropsy in the remainder. In all cases plasma 11-hydroxycorticoid levels were measured by fluorimetry (Mattingly, 1962). The normal diurnal variation of these levels was absent or greatly reduced in all 34 patients, and in 33 cases the plasma 11-hydroxycorticoid levels and urinary corticosteroids failed to suppress normally during dexamethasone administration (Mattingly, 1963; Cope, 1966).

Urine Collections.—Collections of urine over 24-hour periods from normal subjects and outpatients were made with no interruption of their daily lives. In ward patients a normal ward routine was followed, but care was taken to ensure that the patients were not subjected to any stressful procedure during the collection period. Subjects were instructed to empty their bladders before defaecation to avoid losses at this time. Urine was collected in Winchester bottles without any added preservative. The bottles had been washed with either chromic acid or the detergent Decon 75 (Medical-Pharmaceutical Developments Ltd.). This latter substance, unlike most other detergents, does not fluoresce and so does not interfere with the steroid estimations (V. H. T. James, personal communication). Since it is more convenient to use than chromic acid it was used exclusively in the latter stages of the work. If the analyses were not undertaken immediately a 20-ml.

aliquot of the urine was deep-frozen within a few hours of the completion of collection.

Determination of 11-Hydroxycorticoids.—The fluorimetric method of Mattingly *et al.* (1964) was used throughout, using 2 ml. samples of urine. Latterly, the detergent Decon 75 was used to wash glassware in place of the less convenient chromic acid. In all cases the alkali wash consisted of 2 ml. of 1N sodium hydroxide. The fluorescence was read on a direct-reading fluorimeter (model 27A, Electronic Instruments Ltd.), with excitation at 430 m μ and emission at 540 m μ . The precision and accuracy of the method were good. The coefficient of variation over the normal range was 8%, and the mean recovery of added cortisol in amounts ranging from 0.1 to 5 μ g. was 97.2%. Results are expressed throughout in terms of cortisol.

Determination of 17-Oxogenic Steroids.—These were measured in the routine biochemistry laboratory by the method of Gibson and Norymberski (1954) or of Appleby *et al.* (1955). The same 24-hour urine samples were used as those for the determination of 11-hydroxycorticoids, but 17-oxogenic steroid estimations were not carried out on all of them.

Results

Control Group.—In 50 females between the ages of 14 and 67 the urinary excretion of 11-hydroxycorticoids ranged from 78 to 311 μ g./24 hours, with a mean of 174 ± 53 (S.D.) μ g./24 hours (Fig. 1). In 59 males between the ages of 17 and 70 years the figures were somewhat higher, and ranged from 108 to 396 μ g./24 hours, with a mean of 229 ± 66 (S.D.)

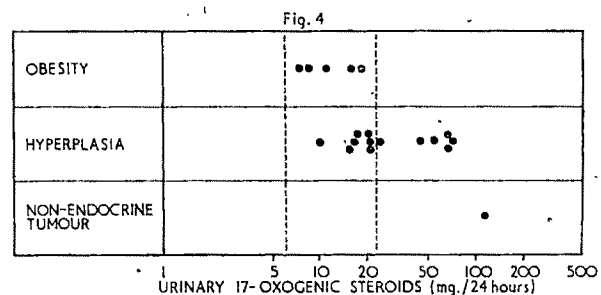
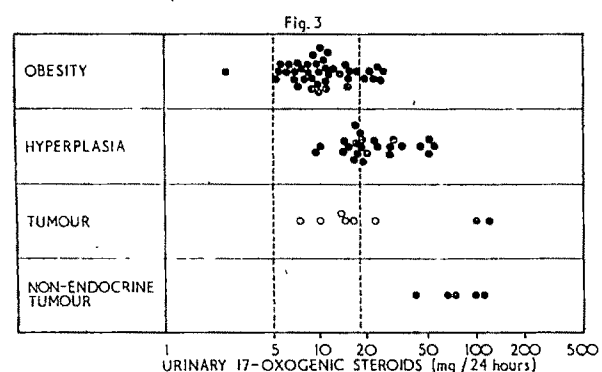
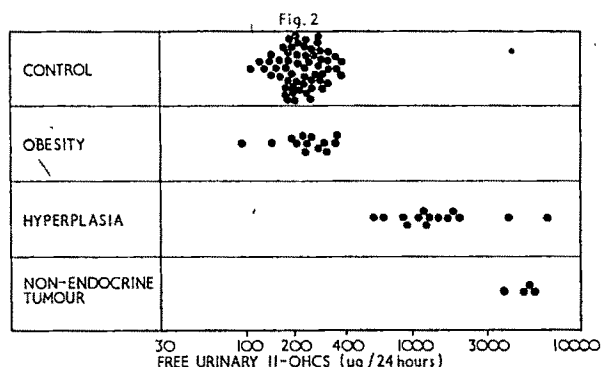
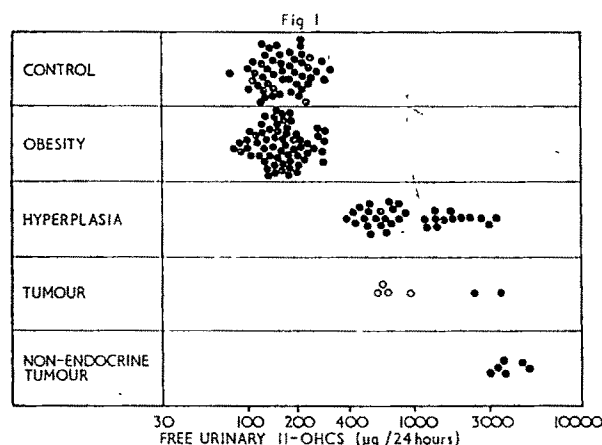


FIG. 1.—Levels of free 11-hydroxycorticoids in the urine of female subjects. Each dot represents one estimation, and in some cases of Cushing's syndrome more than one estimation was done on each patient. In the tumour section the open circles indicate patients with adenoma and the solid circles those with carcinoma. FIG. 2.—Levels of free 11-hydroxycorticoids in the urine of male subjects. Each dot represents one estimation, and in some cases of Cushing's syndrome more than one estimation was done on each patient. FIG. 3.—Levels of 17-oxogenic steroids in the urine of female subjects. Each dot represents one estimation, and in some cases of Cushing's syndrome more than one estimation was done on each patient. In the tumour section the open circles indicate patients with adenoma and the solid circles those with carcinoma. The vertical broken lines show the normal range. FIG. 4.—Levels of 17-oxogenic steroids in the urine of male subjects. Each dot represents one estimation, and in some cases of Cushing's syndrome more than one estimation was done on each patient. The vertical broken lines show the normal range.

$\mu\text{g./24 hours}$ (Fig. 2). In this small series the level of urinary 11-hydroxycorticoids did not appear to be related to the age of the subject.

Obese Group.—The excretion of 11-hydroxycorticoids was similar to that in the control group, and the ages of the subjects were comparable to those of the controls. In females the amounts ranged from 74 to 294 $\mu\text{g./24 hours}$, with a mean of 166 ± 53 (S.D.) $\mu\text{g./24 hours}$ (Fig. 1), and in males the range was from 92 to 352 $\mu\text{g./24 hours}$, with a mean of 245 ± 77 (S.D.) $\mu\text{g./24 hours}$ (Fig. 2). The urinary excretion of 17-oxogenic steroids was measured in most of these patients. In females it ranged from 3.4 to 24.8 mg./24 hours; 6 of the 41 estimations were above the accepted upper normal limit of 18 mg./24 hours (Fig. 3), as quoted by Brooks *et al.* (1963). One estimation fell below the accepted lower normal limit of 5 mg./24 hours, but the urine volume was low, and this result may have been due to the collection being incomplete. In the relatively small number of males the values all fell within the normal range of 6 to 22 mg./24 hours. The actual range found was from 7.0 to 18.4 mg./24 hours (Fig. 4).

Patients with Cushing's Syndrome.—The 11-hydroxycorticoid excretion was raised above normal levels in all 34 patients. In the 27 female patients the excretion ranged from 399 to 5,570 $\mu\text{g./24 hours}$, while in the seven male patients the levels ranged from 611 to 7,000 $\mu\text{g./24 hours}$ (Figs. 1 and 2). Particularly high values were found in patients with an adrenal carcinoma and in patients with hyperplasia associated with a non-endocrine tumour. There was a considerable day-to-day fluctuation in the urinary 11-hydroxycorticoid excretion in patients with adrenal hyperplasia. For example, one female patient showed levels on four separate occasions of 1,440, 638, 815, and 3,700 $\mu\text{g./24 hours}$. The excretion of 17-oxogenic steroids in both female and male patients showed a considerable overlap with the normal ranges. In a number of patients more than one estimation was made on different 24-hour urine collections. Only 29 out of the total of 51 estimations were above the upper limits of normal (Figs. 3 and 4). High levels were invariably found, however, in patients with an adrenal carcinoma and in patients with hyperplasia associated with a non-endocrine tumour.

Discussion

These results show that by measuring the urinary output of free 11-hydroxycorticoids a clear distinction can be made between patients with established Cushing's syndrome and those with simple obesity. This method therefore provides a relatively simple screening test, which can be used to decide whether patients with suspected Cushing's syndrome should be further investigated. Our results confirm the findings of previous workers that the urinary 17-oxogenic steroid excretion is often within the normal range in patients with Cushing's syndrome (Cope and Black, 1959; Brooks *et al.*, 1963; Cope and Pearson, 1965; Ernest, 1966; Ross *et al.*, 1966), and that, in addition, the levels in some obese patients are elevated (Cohen, 1958; Simkin, 1961; Baird, 1963; Gogate and Prunty, 1963).

The incidence of Cushing's syndrome and obesity is higher in women than in men, and this is reflected in the relative proportions of the sexes in this study. Furthermore, the normal ranges of urinary steroids differ between men and women so that it is necessary to consider the data separately.

In the control group the mean value for the free 11-hydroxycorticoids in women was 174 $\mu\text{g./24 hours}$, ranging from 78 to 311 $\mu\text{g./24 hours}$. In men the mean value was 229 $\mu\text{g./24 hours}$, the range being 108 to 396 $\mu\text{g./24 hours}$. These levels are very similar to those found by De Moor *et al.* (1962), who, using a comparable method of estimation, found a mean value for females of 179 $\mu\text{g./24 hours}$, and for males of 201 $\mu\text{g./24 hours}$. On the other hand, Gantt *et al.* (1964) have reported levels that are substantially lower than those quoted above.

Their mean level was 86.8 $\mu\text{g./24 hours}$ in 17 healthy adults between the ages of 20 and 40 years, with a range of 31 to 150 $\mu\text{g./24 hours}$. Their method involved a more complex schedule for washing the methylene dichloride extracts, and in our hands led to a reduction in the recovery of added cortisol from 95% to 80%, and to a 40% loss in the fluorescence of a urine specimen estimated by both methods. Presumably some of the more polar steroids which are estimated with cortisol in our method are removed by this technique.

The reliance which can be placed on the results of any scientific work depends mainly on the validity of the methods used to produce those results. Criticisms can be levelled against this fluorescence method for the estimation of 11-hydroxycorticoids, but its virtues far outweigh its disadvantages. It is accurate and precise, and is quick and easy to carry out. Six estimations can be completed in less than two hours. In contrast to the 17-oxogenic steroid estimation the presence of glucose in the urine does not interfere with this method.

The justification for its use as a measure of adrenocortical activity lies in the good correlation between this method and the isotopic estimation of the cortisol secretion rate, but it should be emphasized that this fluorescence method was originally proposed as a measure of free 11-hydroxycorticoids in the urine, and not of cortisol alone (Mattingly *et al.*, 1964). There is little doubt that other steroids are measured besides cortisol, and these include corticosterone and 20-hydroxycortisol. Indeed, cortisol may comprise only a small proportion of the total fluorescence in some urines. Espiner (1965), using paper chromatography and an internal isotope standard to correct for losses, found that the amount of free cortisol accounted for only 8 to 73% of the fluorescence measured in different urine samples. In addition there is a small amount of nonspecific substances included in the estimation. The total fluorescence increases with time if the urine is not deep-frozen within 24 hours of completing the collection, and the increase is greatest in infected urines.

Drugs administered to patients do not appear to interfere with these estimations, with the exception of spironolactone and mepacrine. Mepacrine may continue to be excreted for many days after cessation of administration (Freitas e Costa *et al.*, 1965); we found the same phenomenon in one patient on spironolactone who is not included in this series. It is well known that oestrogens raise the plasma levels of 11-hydroxycorticoids, and that high levels are found in women taking oral contraceptives (Metcalf and Beaven, 1963). It might be expected that this would affect the amount of free 11-hydroxycorticoids found in the urine, but the increase of plasma 11-hydroxycorticoids is due to an increase in the protein-bound cortisol which is not filtered through the renal glomeruli. In a small number of healthy women taking contraceptive pills, who are not included in our control group, the urinary excretion of 11-hydroxycorticoids at the end of the three-week cycle fell within the normal range at a time when their plasma 11-hydroxycorticoids were elevated. Nevertheless, if high urinary levels are found in patients taking contraceptive pills it is recommended that the treatment be stopped and a repeat estimation done a month later. Katz *et al.* (1962) found that an unconjugated 11-hydroxycorticoid—namely, 6- β -hydroxycortisol—was increased in the urine after oestrogen administration. This particular steroid is not measured by the fluorimetric technique used here, but their findings suggest that oestrogens produce an alteration of cortisol metabolism, and it is possible that this might result in an increased excretion of other unconjugated 11-hydroxycorticoids in the urine.

It is easy when introducing a new diagnostic test to use an elliptical argument in deciding its value; a suspected case shows a positive result in the new test, therefore the diagnosis is confirmed in that case, and therefore the test is useful in diagnosing such cases. This pitfall has, we hope, been avoided here. In all the cases of Cushing's syndrome the diagnosis was

confirmed by independent means. A raised midnight plasma 11-hydroxycorticoid level was found in all cases, and in 33 out of the 34 patients the morning plasma 11-hydroxycorticoid levels failed to suppress normally during the administration of 2 mg. of dexamethasone daily for 48 hours (Mattingly, 1963; Cope, 1966). Raised cortisol secretion rates were found in the 20 patients in whom this investigation was carried out, including the one patient who suppressed normally on dexamethasone. In the remaining 14 patients the diagnosis was ultimately confirmed at operation or necropsy. It was not practicable to carry out these investigations on all the patients with "simple" obesity, but a random sample of 20 obese patients showed normal midnight plasma 11-hydroxycorticoid levels and normal suppression during dexamethasone administration.

There is considerable controversy over whether adrenocortical activity is significantly increased in "simple" obesity. It has been shown in numerous studies that urinary corticosteroid excretion may be raised and that the mean cortisol secretion rate may be higher than normal, a few patients showing grossly elevated levels (Gogate and Prunty, 1963; Migeon *et al.*, 1963; Schteingart *et al.*, 1963; Dunkelman *et al.*, 1964; Copinschi *et al.*, 1966). It is possible, however, that the latter cases were atypical cases of Cushing's syndrome which could not be recognized from the clinical findings. Our results do not support the view that there is a marked deviation of cortisol secretion from normal in obese subjects, since their urinary 11-hydroxycorticoid levels are very similar to those in the control group.

The control group consisted of healthy adults and convalescent hospital patients not suffering from endocrine, liver, or renal disorders that might affect the excretion of steroids in the urine. Care was taken to ensure that these subjects were not stressed during the urine collection period, since both emotional and physical stress will temporarily increase adrenocortical activity and result in a raised urinary 11-hydroxycorticoid excretion. It should be remembered that this study has been based on the urinary 11-hydroxycorticoid excretion in adults and teenagers, and it is probable that the normal ranges will be lower in younger children. For practical purposes, however, this is of little importance, since Cushing's syndrome is rare in this age group.

Summary

Urinary 11-hydroxycorticoids were measured in 34 patients with established Cushing's syndrome, and the results compared with those found in 75 obese patients and in a control group of 109 subjects made up of healthy volunteers and convalescent hospital patients. Raised levels were found in all

the cases of Cushing's syndrome while normal levels were found in the obese group. Urinary 17-oxogenic steroids, on the other hand, showed a considerable overlap between these groups, and normal levels were not infrequently found in patients with Cushing's syndrome.

The fluorimetric estimation of urinary 11-hydroxycorticoids is a relatively simple and rapid procedure, suitable for routine clinical use. It provides a reliable screening test for patients with suspected Cushing's syndrome.

We are grateful to the Medical Research Council for financial support, and to Dr. K. Fotherby and Miss M. M. McCready for the 17-oxogenic steroid estimations. We are also indebted to our colleagues at the Hammersmith Hospital and the Royal Devon and Exeter Hospital for allowing us to study patients under their care.

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Case of Tuberous Sclerosis and Haemorrhagic Retinopathy (with Fundus Photographs)

A. M. DYER,* M.B., CH.B., D.O.; R. HILL,† G.M., M.B., CH.B., M.R.C.P.GLASG.

R. M. ROWAN,‡ M.B., CH.B., M.R.C.P.GLASG.; W. O. G. TAYLOR,§ M.B., CH.B., D.O.M.S., F.R.C.P.GLASG.

Brit. med. J., 1967, 4, 398-399

Tuberous sclerosis is a genetically determined disorder (Duke-Elder, 1940) characterized by mental deficiency, epilepsy, skin fibromata, and maldevelopment. Patients may not always present with the complete form of the disorder. It is said that the disease is usually fatal, the majority of patients dying before the age of 24. The patient in the following case is 38.

Case Report

The patient, who was born in 1928, was said to have been well up to 1945, when she began to develop fainting attacks or fits. In August of that year she attended Ayr County Hospital, where it was noted that she was nervous and that her fits seemed to be related to menstruation. A provisional diagnosis of petit mal was made and $\frac{1}{2}$ gr. (32 mg.) of phenobarbitone was ordered. Subsequently the use of thyroid was also advised. The late Dr. J. N. Tennent also saw her repeatedly at this time. He reported normal vision and no refractive error, but "considerable swelling of the right optic disc; rather cystic-like on nasal side." The fields of vision showed a possible defect in the right upper nasal quadrant. X-ray film of the skull, however, showed possible enlargement of sella, though this was not confirmed on repeat. Six weeks after the initial observation it was thought that *both* optic discs were swollen, the right more pronounced, and in April 1946 Dr. Tennent noted a "tapioca grain appearance" of the right disc. In September 1949 stabilization of the fits on phenytoin sodium and phenobarbitone was carried out, and in October she was admitted to Ballochmyle Hospital for investigation. The abnormal findings were confined to the electroencephalogram, which was carried out at Killearn Hospital. The report stated: "Gross dysrhythmia with low voltage from all leads. This indicates marked cerebral dysrhythmia—attacks epileptic." Several fits occurred under observation, and a psychiatrist reported "major and minor fits preceded menses," and, the following week, "Intelligence below average but not defective. No gross emotional disorder." On his advice she was given phenytoin 400 mg. daily in divided doses, benzedrine 5 mg. at midday, and phenobarbitone 1 gr. (65 mg.) morning and night. These reduced but did not eliminate the fits.

In March 1956 she had a nocturnal fit, after which she was completely aphasic for 10 days. In May she complained of defective vision and was referred to the medical outpatient department of Heathfield Hospital. The complaint appeared to be glare; there was a history of several attacks of status epilepticus, and for the first time a facial rash was mentioned. There was no abnormality in the fundi, but an iron-deficiency anaemia was found and treatment with primidone suggested, because of the mixture of petit and grand mal, in addition to iron therapy.

At review the anaemia had improved but the patient failed to come into hospital for fuller investigation.

In 1961 she developed a persistent cough, and from January 1964 she felt weak and unwell and developed gradually increasing oedema. She was admitted to the medical ward at Heathfield Hospital on 24 February 1964.

On examination the positive findings were marked clubbing of fingers and oedema of hands and feet, slow speech, and rather poor intelligence. X-ray film of chest showed an area of consolidation in the right lower lobe and recent bronchopneumonia was suggested. Sputum culture showed pneumococci. X-ray examination of the skull revealed no abnormal calcification in the cerebral hemispheres. The blood picture showed severe anaemia, and a sternal marrow puncture was therefore performed. The latter showed appearances compatible with the diagnosis of megaloblastic anaemia, and treatment initially by blood transfusion and then iron by mouth with injections of folic acid was given. By 14 July 1964 her haemoglobin had risen (from 4.1 to 15.4 g./100 ml.). Phenytoin was continued.

Fundus examination on 25 February revealed haemorrhages and exudates in the left eye with drusen of the optic nerve head and one exudate. It was suggested that this indicated a vascular retinopathy and tuberous sclerosis. This diagnosis was later confirmed (Figs. 1 and 3).

On 20 November 1964 (Fig. 2) all haemorrhages and exudates had cleared, though the drusen in the other eye naturally remained unchanged (Fig. 3). Her visual acuity with correction was 6/5 right and left when last seen on 13 October 1966.

Discussion

It is tempting to conclude from the wording of J. N. Tennent's report in 1946 that he had in mind the actual diagnosis made in 1964. His detailed description of the appearance of the discs shows that there was no great change in them

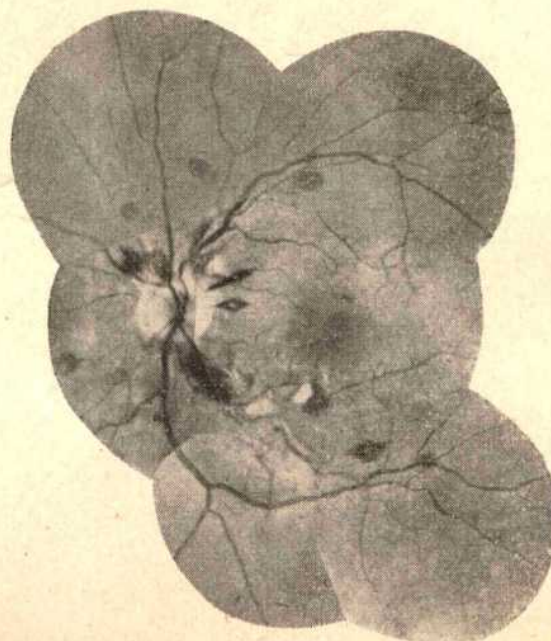


FIG. 1.—Left fundus on 28 February 1964, showing numerous retinal haemorrhages, mainly in the nerve fibre layer, and some "exudates."

* Ophthalmic Registrar, Heathfield Hospital, Ayr. Present address: Medicine Hat, Alberta, Canada.

† Consultant Physician, Heathfield Hospital, Ayr.

‡ Medical Registrar, Heathfield Hospital, Ayr. Present address: Area Laboratory, Ballochmyle Hospital, Mauchline, Ayrshire.

§ Consultant Ophthalmologist, Heathfield Hospital, Ayr.

over this long time, though the number of drusen (R—14, all nasal; L—2 nasal, 1 superior temporal) may have increased (see Reese, 1940).

The term "drusen" is a confusing one. There are several conditions in which this term is used (Duke-Elder, 1940), but as applied to the optic disc the word was first employed in German literature as *Drusenbildungen* ("granular formations," apparently a mineralogical term (Fuchs, 1951)). Parsons anglicized the word to drusen in an excellent comprehensive review of the subject (Morton and Parsons, 1903), but up to the time of his paper only two cases had been diagnosed ophthalmoscopically before pathological examination.

Nodules occur in the retina in tuberous sclerosis (Van der Hoeve, 1920, 1923), including the disc, but the specific type known as drusen of the optic disc was not connected with this disease until Reese made the suggestion in 1940.

The megaloblastic anaemia was presumably the result of a folic acid block from the diphenylhydantoin (see Goodman and Gilman, 1965). This type of megaloblastic anaemia is uncommon (Williams, 1963). It appears to require long-continued use of the drugs (Badenoch, 1954; Berlyne *et al.*, 1955)—as was the case here.

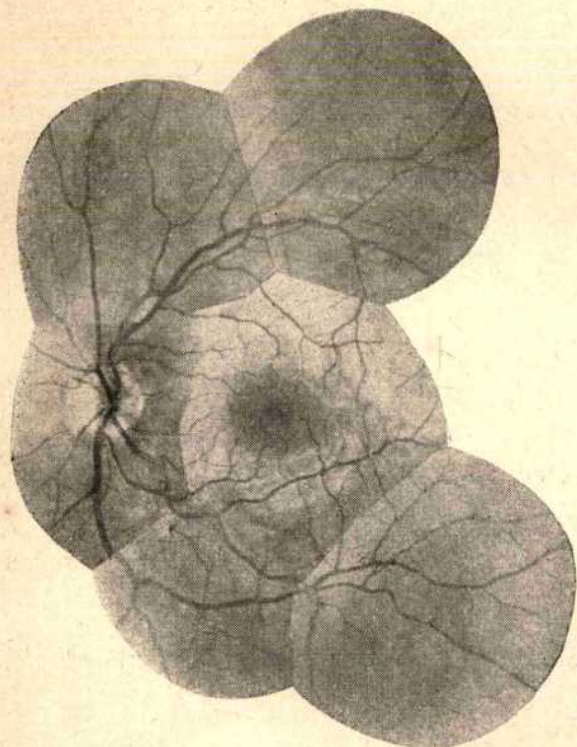


FIG. 2.—Left fundus on 20 November 1964, showing complete clearing of the haemorrhages. One drusen can be seen at the upper temporal margin of the disc.

As can be seen from the fundus photographs, with treatment of the anaemia the haemorrhages in the left eye cleared rapidly, with restoration of the visual acuity (Figs. 1 and 2).

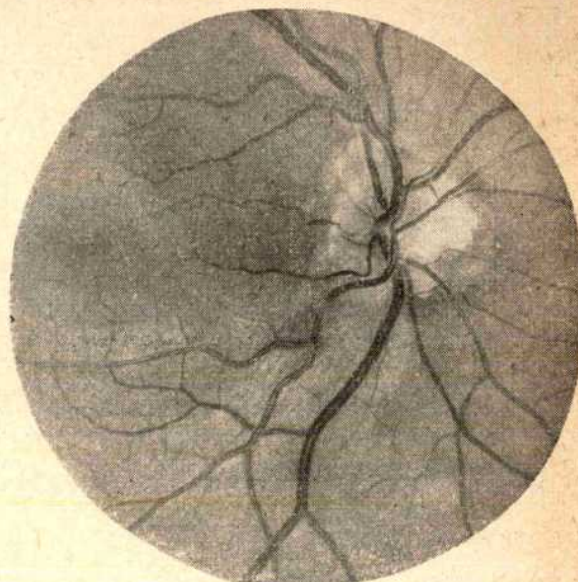


FIG. 3.—Right fundus on 20 November 1964, showing numerous drusen on the nasal side of the disc.

Summary

A case is described of probable tuberous sclerosis, or Bourneville's disease, in a woman who presented at the age of 16 with major and minor epileptic seizures. She also showed adenoma sebaceum and drusen of the optic disc, low intelligence, temper tantrums, and hysteria. The fits were partially controlled by phenytoin, benzedrine, and phenobarbitone from the age of 21, but subsequently she developed megaloblastic anaemia which required treatment with folic acid.

We must express our thanks to the Department of Ophthalmology, Glasgow University, for the fundus photographs.

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Medical Memoranda

Stellate Ganglion Block in Treatment of Total Blindness Due to Quinine

Brit. med. J., 1967, 4, 400-401

Stellate ganglion block has been successful in the treatment of a variety of conditions where disorder of the sympathetic supply to the head, neck, and upper extremity is a causative factor.

CASE REPORT

The patient, a single girl aged 17, thinking herself pregnant (erroneously as it happened) took 8 g. (125 gr.) of quinine hydrochloride in 24 hours (Day 1).

When seen on Day 3 there was no perception of light in either eye. The pupils were widely dilated and did not react to light.

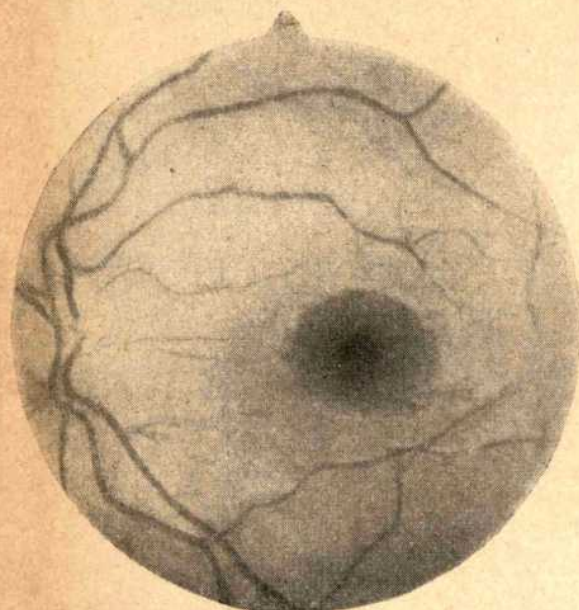


FIG. 1.—Fundal photograph on Day 4 shows macular oedema, normal discs and vessels.

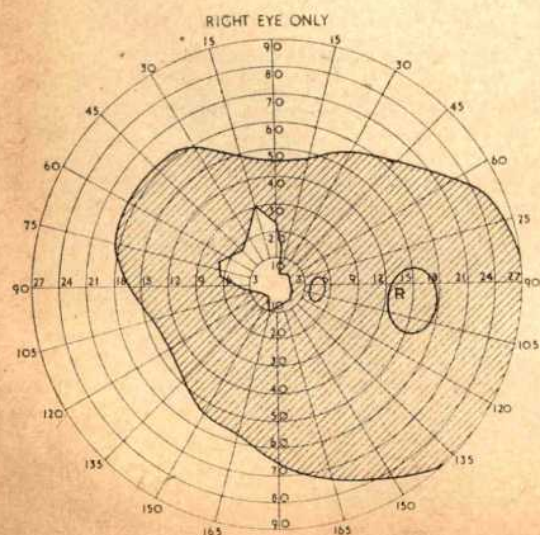


FIG. 2.—Visual field on Day 4 showing marked contraction.

The retinal arteries were not constricted. The optic discs were of normal colour, but the margins were blurred and there was macular oedema. Gastric lavage was performed. A bilateral retrobulbar injection of 100 mg. of acetylcholine was given followed by tolazoline hydrochloride 50 mg. and nicotinic acid 100 mg. four-hourly.

She was still completely blind that evening. The duty anaesthetist was consulted and stellate ganglion block decided on. The right side was blocked with 5 ml. of 1% lignocaine with 1:160,000 adrenaline, the anterior paratracheal approach (Davies, 1952) being used. Within a minute a positive Horner's syndrome was noticed and the patient could perceive light in the right eye. After about 10 minutes the left side was blocked with an identical result.

It was decided to repeat the stellate ganglion block at any time that the patient felt her vision was deteriorating, and it was performed on 19 separate occasions in seven days.

Day 4.—The fundi had not changed since admission (Fig. 1). Vision was 6/9 with the right eye and 6/6 with the left, but the visual fields were markedly contracted (Fig. 2).

Day 6.—Clearance of quinine was virtually complete (Fig. 3).

Day 9.—The visual fields continued to enlarge, but oedema of the retina and blurring of the disc margins persisted. Dichlorophenamide (Daramide) 125 mg. t.d.s. and potassium chloride 0.5 g.

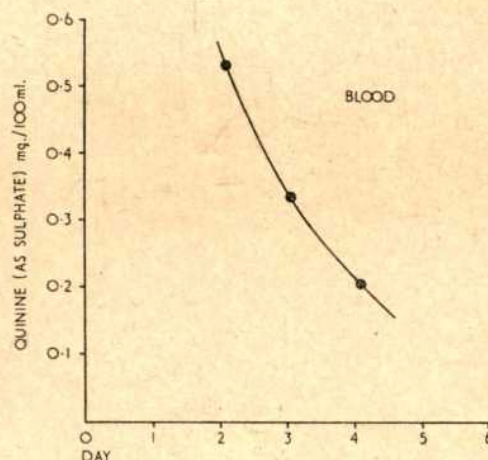


FIG. 3.—Concentration of quinine as sulphate in the blood.

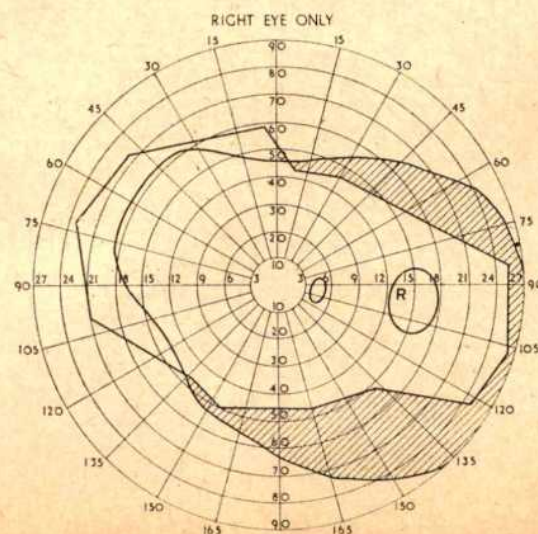


FIG. 4.—Visual field on Day 93. This shows some persistent restriction of the peripheral field.

daily was given to reduce retinal oedema. The patient noticed marked deterioration of vision at dusk.

Day 13.—Discharged from hospital. Pallor of both optic discs had developed with further constriction of the retinal arteries.

Day 19.—Vision almost normal and retinal oedema less marked.

Day 27.—Retinal oedema more restricted. Vessels were narrower and the disc was becoming a little pale.

Day 93.—Vision was subjectively normal, except for some difficulty in adaptation on entering a lighted room, but some constriction of the peripheral fields persisted (Fig. 4). A further fundal photograph is shown (Fig. 5). Hearing was assessed by an audiogram and was normal.

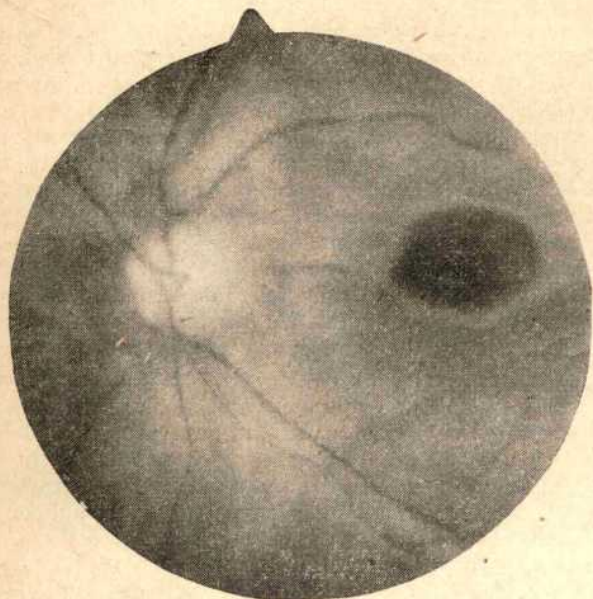


FIG. 5.—Fundal photograph on Day 93. There is continuation of the processes noted on Day 27.

COMMENT

There is a wide variation in tolerance to quinine, but symptoms are likely in anyone taking a single dose larger than 4 g. (60 gr.) (Polson and Tattersall, 1959). Most cases of quinine amaurosis in the United Kingdom follow its use as an abortifacient (Scott, 1953). There is no control over the sale of the drug.

There is a tendency for quinine amaurosis to recover (Duke-Elder, 1954), the likelihood being inversely proportional to the duration of blindness, and recovery may take months. Permanent blindness with optic nerve atrophy has been reported, however (Braveman *et al.*, 1948; Sir B. W. Rycroft, personal communication). The pathogenesis of blindness in quinine poisoning is a matter of dispute. Ballantyne (1917) thought quinine had a direct toxic effect on the retinal cells, particularly the rods, and that vasoconstriction was a secondary effect. Damage to the rods seemed to be confirmed by the deterioration of vision at dusk noticed in the present case. Ballantyne stated that visual loss occurs while the retinal vessels are normal in appearance and that vasoconstriction is a feature of the recovery phase. This is supported in our case, where arterial narrowing was not apparent until Day 9, six days after the onset of blindness. Many authors, however, point to the extreme constriction of the retinal vessels and believe this to be the cause of blindness by producing retinal damage. Some observers have

noticed the similarity to changes seen in occlusion of the central retinal artery (Turtz, 1957). Braveman *et al.* (1948), reporting a case in which blindness was permanent (and in which stellate ganglion block was not performed), noted persistent vasoconstriction.

Whatever the pathogenesis of amaurosis in quinine poisoning the only effective form of treatment appears to be that aimed at producing retinal vasodilatation. This is supported by experimental work in dogs. Giannini (1934) found that dogs could be protected from a blinding dose of quinine by the simultaneous administration of acetylcholine, while Vermes (1905) prevented blindness on one side only by previously sectioning the cervical sympathetic on that side.

Stellate ganglion block has been shown to produce dilatation of the retinal vessels. Wagener (1931) reported that retinal dilatation and miosis occurred with equal frequency after stellate ganglion block. Coston (1951) has shown its effectiveness in dilating the retinal vessels in his cases of embolism of the central retinal artery. Redslob *et al.* (1947) have also demonstrated its value clinically. They noted the dramatic improvement in both auditory and visual symptoms which followed bilateral stellate ganglion block in a patient who had aborted after the administration of 3 g. (45 gr.) of a quinine salt.

In a condition so dramatic, distressing, and with such crippling sequelae as quinine amaurosis the temptation to use polypharmacy is strong, and proved so in our case. This is ineffective to a greater or lesser extent. Stellate ganglion block, however, has proved to be universally effective, the degree of visual improvement being inversely proportional to the duration of blindness.

A plea is therefore made for it to be considered the first line of treatment for quinine amaurosis, and for it to be performed as soon as the diagnosis is made.

We wish to thank Dr. H. S. Brodribb and Dr. A. R. H. Worssam for their help and advice.

P. P. BRICKNELL,* M.B., B.S., D.A.,
Anaesthetic Registrar.

H. G. MIDDLETON, F.F.A.R.C.S.,
Consultant Anaesthetist.

A. HOLLINGSWORTH, M.B., B.S., D.O.M.S.,
Consultant Ophthalmologist.

E. M. L. EVANS, F.R.C.S.,
Consultant Ophthalmologist.

Hastings Group of Hospitals.

* Present address, Queen Victoria Hospital, East Grinstead, Sussex.

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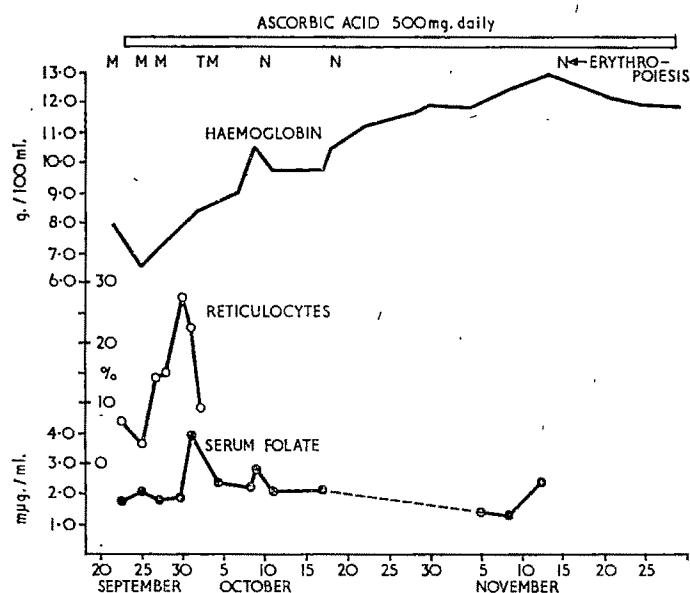
Scorbutic Megaloblastic Anaemia Responding to Ascorbic Acid Alone

Brit. med. J., 1967, **4**, 402

In recent years there has been discussion on whether the megaloblastic anaemia occasionally found in scurvy is due to deficiency of ascorbic acid or of folic acid. The diet taken by a scorbutic patient is usually also inadequate in folic acid. In many cases the apparent response of the megaloblastic anaemia to ascorbic acid may have really been due to the introduction of folic acid in the ward diet (Zalusky and Herbert, 1961). We here report the response of a scorbutic megaloblastic anaemia to ascorbic acid alone, the patient receiving a ward diet deficient in folic acid.

CASE REPORT

A 70-year-old man was urgently admitted to hospital in September 1963 complaining of painful swollen legs of three weeks' duration, with more recent spontaneous bruising. For four months before admission his general condition had deteriorated and he had lost weight. During this time his diet consisted of tea and toast with an occasional meat stew, and excluded fruit and vegetables. On examina-



tion the significant findings were pronounced anaemia, extensive bruising of both legs with perifollicular haemorrhages, cork-screw hairs, and hyperkeratosis. Both calves were very tender.

Investigations.—Haemoglobin 8.0 g./100 ml. M.C.H.C. 36%, M.C.V. 117 cu. μ . Reticulocytes 2%. Marrow: erythropoiesis was frankly megaloblastic and the iron stores were increased. Serum iron 125 μ g./100 ml.; serum vitamin B₁₂ 320 μ g./ml.; serum folate 1.7 μ g./ml. Ascorbic acid 500 mg. by mouth daily resulted in very little ascorbic acid excretion until the eleventh day.

The patient was maintained for the period of study on a folate-deficient diet composed of tea, bread, jam, egg, fish, chicken, minced meat, and potato. He was given 500 mg. of ascorbic acid daily by mouth. The haematological response is shown in the Chart. A good reticulocyte response was obtained. A series of marrow punctures showed a slow reversion of erythropoiesis to normal by the seventeenth day. The haemoglobin level showed a steady

rise, reaching 12.3 g./100 ml. in seven weeks. Frequent serum folate estimations were carried out, with repeatedly subnormal results except for one low normal figure. There was initially a dramatic improvement on ascorbic therapy, and then a gradual return to his normal state. Later a normal diet and folic acid 15 mg. daily were given.

DISCUSSION

The patient showed a complete response of megaloblastic erythropoiesis in scurvy to ascorbic acid alone.

Zalusky and Herbert (1961) treated a scorbutic patient on a folate-deficient diet with ascorbic acid and the megaloblastic erythropoiesis became more gross. Additional treatment with 50 μ g. of folic acid daily intramuscularly caused a reticulocyte response and rapid conversion of erythropoiesis. From this they adduced that the megaloblastosis found in scurvy is due to concomitant folic acid deficiency. In the literature we have found several reports of patients with megaloblastic anaemia and scurvy treated in a similar manner to ours, the diet during treatment with ascorbic acid being either the same as before admission to hospital (Bronte-Stewart, 1953; Goldberg, 1963), or deficient in animal protein and vitamin C (Brown, 1955; Neilson, 1960), or specifically folate deficient (Cox, Meynell, Northam, and Cooke, 1967). We therefore believe that dietary folic acid was not the cause of the response in these patients.

The experimental work of May and his colleagues showed that the megaloblastic erythropoiesis of monkeys fed on a diet deficient in vitamin C and folic acid reverted to normal when either vitamin was given (Sundberg, Schaar, and May, 1952), and that the explanation of this lay in the increased requirement for folic acid of the scorbutic animal (May, Hamilton, and Stewart, 1953). Haemorrhage and haemolysis, both features of scurvy, may lead to folate depletion in man (Rachmilewitz, 1965). The slow reversion of erythropoiesis to normal in our case and in that of Hyams and Ross (1963) favours the indirect nature of the effect of ascorbic acid on folate metabolism. The difference between the cases which have responded to ascorbic acid alone and the case of Zalusky and Herbert may be in the degree of tissue folate deficiency. A more fundamental role for ascorbic acid in folate metabolism has also been postulated (Vilter, 1964; Cox *et al.*, 1967), but this is still speculative.

We are grateful to Dr. A. Voss for his assistance with this case.

P. ASQUITH, M.B., CH.B., M.R.C.P.
M. H. OELBAUM, M.D., B.S.C., M.R.C.P.
D. W. DAWSON, M.R.C.P.ED., M.C.PATH.

Crumpsall Hospital, Manchester 8.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Postgastrectomy Problems—I

J. ALEXANDER WILLIAMS,* CH.M., F.R.C.S.

Partial gastrectomy has an excellent record in the treatment of peptic ulcer; in the well-chosen case its successes far outweigh its disadvantages. Nevertheless between 5% and 15% of patients continue to complain of serious symptoms after operation. As the number of patients subjected to partial gastrectomy in England and Wales in 1961 was approximately 26,000, if 10% of these develop some form of "postgastrectomy syndrome" then this will not be a rare problem. The commonest symptoms of patients who complain after gastrectomy are abdominal pain, vomiting, loss of weight, loss of energy, attacks of faintness, and diarrhoea. These symptoms usually do not occur singly but combine in an infinite variety of complexes that have become known as the "postgastrectomy syndromes." There is a good case for discarding the present concept of these as classical syndromes.

Many syndromes have been described, including those prefixed by the term dumping, afferent loop, and even efferent loop, long loop, and small stomach. To list these syndromes and describe their classical clinical pictures may help to place some of the known facts in an orderly fashion, but it is misleading in that it implies knowledge of the pathogenesis of the patient's symptoms. To categorize a patient as having the "afferent loop syndrome" implies that we know the cause of his symptoms and—often incorrectly—blame the afferent loop for their cause. Even the most closely studied and best understood postgastrectomy disease, the "dumping syndrome," has in its name an implied aetiology which explains only a small part of the syndrome. A further confusion is that the term dumping syndrome implies a different disease in different parts of the world. To some doctors the term is restricted to the feeling of faintness, nervousness, and flushing provoked by hypertonic foods, while others use it to encompass symptoms of vomiting, pain, and diarrhoea, or almost any symptom that occurs after gastric operations. Dumping may be a useful term to retain but only in the former limited sense.

This article will therefore be restricted to an evaluation and investigation of the symptoms of which patients complain, and readers who require descriptions of the variously defined syndromes are referred to the bibliography.

There are two groups of complications which usually present in different ways. Patients with abdominal complications such as pain, vomiting, or diarrhoea usually complain of these symptoms and demand attention from their doctor, while many of those with loss of weight, lack of energy, and the less dramatic symptoms of nutritional deficiency do not readily report for medical attention. However, the frequency of the nutritional complications is sufficiently high to justify a planned, even though infrequent, follow-up programme. The nutritional complications will not be considered in detail in this article.

Abdominal Pain or Discomfort

The patient who complains of continued or recurrent indigestion after an operation designed for the cure of this symptom needs careful investigation.

Once it is established that the pain or discomfort is associated with digestion and is not due to cardiac ischaemia or renal disease, it is then necessary to differentiate between recurrent peptic ulceration, oesophagitis, and biliary or pancreatic disease.

A carefully taken history and physical examination are essential, though these rarely establish the diagnosis with any certainty. Special investigations are therefore essential, and a programme should be designed to permit a thorough evaluation with the minimal discomfort to the patient. A full investigation is important, for it is never safe to assume that the presence of, say, oesophageal reflux or gall stones necessarily means that this is the cause of the patient's symptoms.

Haematological and Biochemical Screening

At the initial consultation a venous blood sample should be examined for haemoglobin and absolute indices. In addition, the level of serum vitamin B₁₂ should be estimated, as B₁₂ deficiency is almost invariably incompatible with recurrent ulceration. Estimations of serum bilirubin, alkaline phosphatase, and amylase are of value as indices of biliary or pancreatic disease. A high serum calcium level will suggest disease of the parathyroids and possibly of the pancreas. If laboratory facilities for plasma pepsinogen estimations are available this is a valuable screening test for recurrent ulceration.

The stools may be tested for occult blood, though I find this test of relatively little value even when repeated on successive days. A positive test can occur in so many conditions—stomal ulceration, erosions, oesophagitis, or carcinoma of the gastric remnant.

Radiography

The next least disturbing investigations are radiological; each patient should be studied with a plain abdominal film, a cholecystogram, and a barium meal. The erect and lateral abdominal films may show biliary or pancreatic calcification or distension of the gastric remnant or small bowel with air or fluid.

A cholecystogram is advisable in all patients. I have seen patients who have had vagotomy and even revision gastrectomy for symptoms that eventually were cured only by cholecystectomy. Gall bladder disease had not been suspected because the gall bladder had been judged normal at the original gastrectomy. It has been suggested that gastrectomy pre-

* Consultant Surgeon, United Birmingham Hospitals, External Scientific Staff, Medical Research Council.

disposes to biliary disease. Though this hypothesis lacks proof, the association is sufficiently common always to be considered in differential diagnosis and complete evaluation.

Barium contrast radiology is the most useful single investigation in the detection of stomal ulceration. Despite the popular belief that it is difficult to establish a diagnosis on barium meal examination, I have found that in all of ten cases of proved recurrent peptic ulceration there was a large crater demonstrated radiologically.

Some experts have advocated gastroscopy and gastro-photography as more reliable investigations than radiology in the diagnosis of these lesions, though endoscopy is less well tolerated by the patient than radiology. It is true that at gastroscopy it is often possible clearly to see the stomal ring and the jejunum beyond, and to see surface "erosions" at the stoma that are not detected on x-ray. However, it is also possible, even on an apparently satisfactory gastroscopy, to fail to see a large recurrent ulcer, while the examination is often made difficult by the reflux of bile and duodenal fluid. This is an examination for the few experienced experts. Too great an importance should not be given to the presence of stomal erosions. In my experience it is not justifiable to class these as recurrent ulceration and treat accordingly. It is only those cases with unequivocal stomal or jejunal ulcer craters that respond satisfactorily to surgical treatment. It is a commoner error to diagnose recurrent ulcer where none exists than to fail to diagnose it on a good x-ray examination.

In addition to the search for recurrent peptic ulceration on barium meal, it is necessary to look for evidence of hiatus hernia and oesophageal obstruction or reflux. The presence of oesophageal reflux or hernia does nothing more than suggest that the patient might have oesophagitis. The suggestion needs confirmation by the next series of investigations.

Secretion and Provocation Tests

Acid Secretion Tests.—The radiological sign of an ulcer is a constant barium-filled niche or pocket. The finding of such a niche, however "classical" its appearance, can be labelled as a peptic ulcer only if the patient's gastric secretion will permit peptic digestion. Stomal ulceration is often erroneously diagnosed in postgastrectomy patients who are hypochlorhydric or even achlorhydric. To substantiate the diagnosis of stomal ulcer, therefore, it is necessary for the secretion to be able to reduce the gastric pH to below 3.5. This can be tested either by measuring intragastric pH or by aspiration under conditions of maximal stimulation with histamine or gastrin or their analogues. In these tests it is essential to place the pH probe or aspirating tube accurately under fluoroscopic control. In practice some tests are unsatisfactory and a second test is always worthwhile if the diagnosis is in doubt.

Acid Provocation Tests.—It has been claimed that the presence of a stomal ulcer can be confirmed by lowering the pH of the gastric remnant by N/10 HCl infusion via a nasogastric tube and provoking the symptoms of which the patient complains. In my experience this test is unreliable and is more likely to produce the symptoms of oesophagitis than of stomal ulcer (Fig. 1).

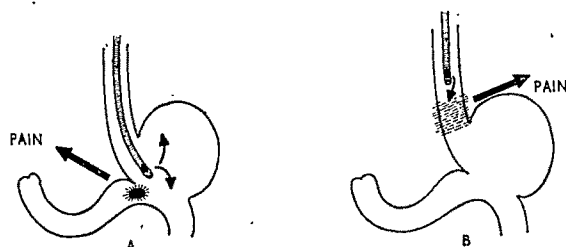


FIG. 1.—Acid provocation test using N/10 HCl. For stomal ulcers (A) the test is not reliable; but it is valuable for oesophagitis (B).

The test is, however, of value in confirming that the patient's symptoms may be due to oesophagitis, which may be present even when it is not possible to demonstrate oesophageal reflux on one barium examination.

The oesophagitis provocation test is performed by slowly perfusing N/10 HCl into the lower oesophagus through a nasogastric tube. If this perfusion produces the symptoms of which the patient is complaining, then it is likely that these are due to oesophagitis. The test is also positive in patients with a bile oesophagitis; so the cause of the inflammation can be determined only by means of intra-oesophageal aspiration or pH monitoring. It is always advisable to confirm the final diagnosis of oesophagitis by endoscopy and biopsy. As these are the most unpleasant and hazardous of the investigations of oesophagitis they should be reserved for final confirmation.

Management of Recurrent Dyspepsia

Once having reliably evaluated the cause of the patient's dyspepsia, the problem of treatment remains. Stomal ulceration¹ and pancreatitis² require detailed consideration beyond the scope of this article. The treatment of gall bladder disease presents few problems but that of oesophagitis is difficult. Non-acid oesophagitis may be alleviated by a conversion gastrectomy with an interposed jejunal loop, while oesophagitis with a hiatus hernia may warrant surgical repair of the hernia. The results of surgery are, however, sufficiently unreliable to make it worthwhile first attempting symptomatic control by simple measures of posture, local anaesthetics, or polysiloxane compounds.

Vomiting

Patients complaining of vomiting after partial gastrectomy are usually difficult to evaluate and to treat. A few will have some form of organic obstruction and in them diagnosis and treatment are usually straightforward.

The symptoms that suggest an organic obstruction are unremitting vomiting with loss of weight and dehydration occurring in a patient who had previously been well since his gastrectomy. Upper intestinal dilatation may be detected on physical examination.

The x-ray signs are, once again, the most informative. On the erect and supine plain films dilatation and fluid levels may be seen in the upper gastrointestinal tract. Contrast studies with barium usually confirm the site of the organic obstruction and may indicate its cause. Recurrent ulceration, external compression of the bowel, or carcinoma of the gastric stump may be seen. Gastric carcinoma should always be suspected, as there is evidence to suggest that partial gastrectomy increases the risk of its development in patients with peptic ulcer. The radiological picture is often confusing, and suspicion of carcinoma should always lead to confirmatory tests by exfoliative cytology or endoscopy. Ulcerogenic endocrine tumours or "retained gastric antrum" should also be suspected, particularly if gastric acid secretion is high.

The treatment of an organic obstruction is almost invariably surgical. Extrinsic obstruction from bands of adhesions respond well to reoperation only when there is unequivocal evidence of proximal dilatation. The patient with vomiting and no definite sign of obstruction who is subjected to reoperation and has only bands of adhesions divided is rarely cured for long of his symptoms. It is likely that his vomiting is not due to the adhesions but rather to one or more of the many factors discussed below.

No Organic Obstruction

When, as in the majority of patients complaining of vomiting after gastrectomy, there is no x-ray evidence of obstruction,

evaluation and treatment are much more difficult. The so-called "afferent loop syndrome" is classically described as post-cibal discomfort or pain, relieved by vomiting bilious fluid, and associated with weight loss and malabsorption. The suggested aetiology is an intermittent obstruction of the afferent loop of a Billroth II type gastrectomy. X-ray studies of patients with copious bile vomiting show that there is no afferent loop obstruction and that symptoms occur when the stomach is distended by the juice ejected rapidly from the afferent loop. In 19 patients with these symptoms abolition of the afferent loop by conversion to a Billroth I gastroduodenostomy has not always cured the symptoms. True afferent loop obstruction does occur but is rare. It is uncommon to find a surgically remediable cause for the symptoms of nausea and vomiting after gastrectomy. In those patients with no radiologically demonstrable obstruction it is important to study the emesis threshold, which varies widely.

Three factors need to be considered: emotion, cardio-oesophageal competence, and gastric sensitivity.

The emotional factors are the most difficult to assess, but they are probably the most important. Some patients give a history of easy vomiting since childhood and were often subject to emotional or travel sickness. Vomiting was often a predominant symptom before gastrectomy, even in the absence of any ulcer stenosis. Other patients experience vomiting later in life as a manifestation of endogenous depression.

Cardio-oesophageal incompetence may be one reason why some patients with nausea vomit easily. Incompetence may have been present before operation; however, there is some evidence that partial gastrectomy interferes with normal competence, possibly by opening out the cardio-oesophageal angle. The incompetence may be assessed by barium examination, but because it can be an intermittent phenomenon it may not easily be detected.

Some patients have a stomach or stomach remnant that is, in some way, more than normally sensitive to stimuli. The stimulus may be distension, but in some cases it appears to be by direct mucosal stimulation. Patients with bilious vomiting after gastrectomy appear to be sensitive to the presence of duodenal juice in the stomach. If their symptoms are provoked by a meal, it is often possible to aspirate bile-stained fluid from their stomach and so relieve their symptoms. The symptoms are brought on again by reintroducing the fluid back into the stomach. This fluid will provoke nausea in another patient with the same symptoms, whereas a post-gastrectomy patient without symptoms of bile vomiting appears to be unaffected if the fluid is introduced into his stomach. It seems likely that the components of this fluid responsible for producing symptoms are bile salts.

Treatment of Non-obstructive Vomiting

A complete appraisal of the patient's nutritional state must be made, with particular reference to any deficiencies of iron, vitamin B₁₂, and folic acid. Correction of deficiencies and improvement in the patient's health and feeling of well-being are sometimes all that is required to control the nausea and

vomiting. When indicated, treatment for depressive neurosis with anti-depressant drugs should be the next line of treatment. In the emotional "easy vomiter" the first line of treatment should be the anti-emetic drugs of the dimenhydrinate or prochlorperazine variety.

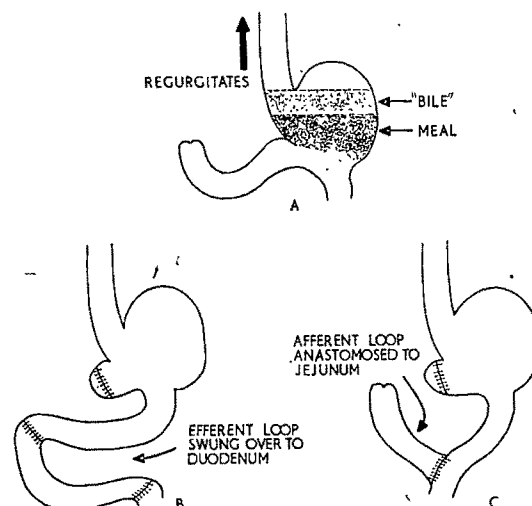


FIG. 2.—Vomiting caused by excess regurgitation of bile into the gastric remnant after meals (A). Treatment is by diversion of the bile away from the stomach.

Where this initial treatment is not indicated or fails cardio-oesophageal competence should be assessed by barium meal examination. Regurgitation of bile into the stomach is assessed by tube aspiration and may be confirmed by barium-potato-meal examination. Testing the provocation effect of intragastric bile or taurocholate solution may also be helpful. A small number of patients will then be found in whom gross regurgitation of bile into the gastric remnant appears to be the main cause of their symptoms. These can be effectively treated surgically by operations designed to prevent bile regurgitation, such as jejunal loop interposition or roux-en-Y conversion (Fig. 2).

(This article will be concluded next week, together with a list of references and a bibliography.)

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Mycosis Fungoides

Q.—What treatment is there for mycosis fungoides?

A.—Mycosis fungoides is a malignant reticulosis which involves predominantly the reticulo-endothelial system of the skin at all stages of its prolonged course. It is a distinct entity, histologically and clinically, like Hodgkin's disease, and like it may occasionally terminate in other patterns of reticulo-endothelial disorder. Unfortunately the term is still sometimes misapplied to cases which are more appropriately classified with other reticuloses, merely because they show unusual features. Obviously no advice on treatment can be valid unless the diagnosis has been reliably established. A useful and well illustrated account of mycosis fungoides appears in *Cutaneous Manifestations of the Malignant Lymphomas*.¹

In most cases there is a distinctive "pre-reticulosis" stage which characteristically lasts many years. During this stage only symptomatic measures are available. There is no evidence whatever that vigorous treatment modifies the subsequent course, and it may do harm.²⁻⁴

During the malignant stage radiotherapy is the treatment of choice. The dose given to each lesion should be the smallest which is effective, and, since the disease is highly radiosensitive the dose can usually be very small indeed. Patients' lives are sometimes shortened by the mistaken application of unnecessarily high doses in a disease which will almost inevitably recur at intervals at the same or other sites. Such recurrences are not prevented by high dosage. Conventional radiotherapy is usually employed, but when it is available beta-ray therapy is preferable, and is in my opinion the treatment of choice.

When the disease is widespread the beta-ray therapy is still often appropriate. It is much better tolerated by the patient than the antimitotic agents which must be employed if beta ray is not available.

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- 1 Bluefarb, S. M., *Cutaneous Manifestations of the Malignant Lymphomas*, 1959, Oxford.
- 2 Abele, D. C., and Dobson, R. L., *Arch. Derm.*, 1960, 82, 725.
- 3 Blaylock, W. K., Oppenheim, J., and Malmgren, R. A., *J. invest. Derm.*, 1966, 46, 28.
- 4 Cyr, D. P., Geokas, M. C., and Worsley, G. H., *Arch. Derm.*, 1966, 94, 558.
- 5 Farber, E. M., Cox, A. J., Steinberg, J., and McIntock, R. P., *Cancer (Philad.)*, 1966, 19, 237.

Brass as Irritant

Q.—Is an allergy to brass commonly met with, and could it be the origin of an apparently universal superstition that a brass finger-ring will poison the wearer?

A.—Brass is an alloy of copper and zinc. Allergy to it in the true immunological sense is almost unknown. Men working with brass develop brass "ague" and skin rashes.¹ These are due to irritant effects and not to allergy.

Much brass is impure, and the impurities are thought to be responsible for some of the irritant effects. The superstition that a brass finger-ring will poison its wearer has no foundation in fact.

REFERENCE

- 1 Schwartz, L., Tulipan, L., and Birmingham, D. J., *Occupational Diseases of the Skin*, 3rd ed., 1957, London.

Hepato-lenticular Degeneration

Q.—What are the chances of parents who have lost a child with hepato-lenticular degeneration having another child with the disease?

A.—Hepato-lenticular degeneration (Kinnier Wilson's disease) is an autosomal recessive condition.¹ The recurrence risk is one in four.

REFERENCE

- 1 Bearn, A. G., *Ann. hum. Genet.*, 1960, 24, 33.

Epithelioma Adenoida Cysticum

Q.—The maternal grandfather of a patient with epithelioma adenoida cysticum had the condition. The patient's mother had it, and her sister had two daughters with the condition and three sons without it. The patient is one of two sons and his brother is healthy. What is the risk of the patient's children having the disease?

A.—Epithelioma adenoida cysticum is probably an autosomal dominant condition. Some families, including this one, are compatible with X-linked intermediate inheritance, but in others this is excluded by male-to-male transmission of the condition. In either case there is a substantial risk to offspring. If the condition is autosomal the risk to offspring is one in two, regardless of sex, and if it is X-linked there is no risk to sons but all daughters will be heterozygotes (though not necessarily clinically affected).¹⁻³

REFERENCES

- 1 Goldman, H. J., *J. Amer. med. Ass.*, 1940, 115, 2253.
- 2 Fliegelman, M. T., and Kruse, W. T., *J. invest. Derm.*, 1948, 11, 189.
- 3 Gartler, S. M., Ziprkowski, L., Krakowski, A., Ezra, R., Szeinberg, A., and Adam, A., *Amer. J. hum. Genet.*, 1966, 18, 282.

Cervical Smear in Early Pregnancy

Q.—Is taking a smear for cervical cytology contraindicated in early pregnancy?

A.—There need be no fear that taking a cervical smear in early pregnancy might provoke a miscarriage. In the early days of cervical cytology there was some doubt whether in pregnancy benign changes could be distinguished from malignant ones. Most authorities now consider that cervical smears can be interpreted in exactly the same way during pregnancy as in the non-pregnant woman.¹

The question, however, of whether, having found repeatedly positive smears in early

pregnancy, it is desirable to pursue the diagnosis to the extent of performing cone biopsy without delay, is more difficult to answer. Some of the arguments have recently been summarized.^{1,2} Because of the complications that are associated with up to one-third of the cone biopsies carried out during pregnancy, it has been suggested that taking cervical smears is best delayed until the puerperium, when a positive cervical smear can be acted on by conization without fear of the consequences.

In young women of low parity this argument is probably justified. In older women, however, and particularly in those of high parity or in those who have had irregular or post-coital bleeding, there is every reason for taking a cervical smear and, if necessary, for cone biopsy during pregnancy.

REFERENCES

- 1 Rogers, R. S., and Williams, J. H., *Amer. J. Obstet. Gynec.*, 1967, 98, 488.
- 2 Stallworthy, J., and Bourne, G., *Recent Advances in Obstetrics and Gynaecology*, 1966, 11th ed. London.

Brucella in Milk

Q.—Is it hazardous to drink raw milk infected with brucellosis but diluted by bulking so that culture is negative, though positive ring and guinea-pig tests are positive?

A.—Yes, it is hazardous. If a guinea-pig shows evidence of infection with brucella after inoculation it must mean that the milk sample contains live brucella organisms, and is therefore capable of causing human infection.

The bulking of milk of a herd containing a few animals excreting brucella dilutes out the antibodies in the milk, and this may be to the extent of rendering the milk ring test (M.R.T.) negative while both cultural and biological tests remain positive. Conversely a persistently positive M.R.T. can occur when the cultural and biological tests are constantly negative. This is due either to intermittent excretion of the organism by the udder or to adult vaccination with Strain 19. This can be determined by the herd inoculation history and by various serological tests on the individual animal.

Endotracheal Tubes

Q.—For how long can oral endotracheal tubes be left in position with safety in (a) adults and (b) babies, and are plastic tubes less irritant than rubber ones?

A.—Unfortunately it is impossible to be quite sure how long an endotracheal tube can be left in place without the risk of damage to the larynx and trachea. Experience shows that in both adults and babies tubes can be safely left for a period of up to 48 hours. Beyond that the risk of subglottic stenosis, the most important complication, becomes more than a remote possibility.¹ Plastic tubes seem to be less irritant than rubber ones, though plastic ones are also capable of causing damage.

REFERENCE

- 1 *Brit. med. J.*, 1967, 1, 321.

Book Reviews

Immunization: its Benefits and Dangers

The Hazards of Immunization. By Sir Graham S. Wilson, M.D., LL.D., F.R.C.P., D.P.H. (Pp. 324+x. 45s.) London: Athlone. 1967.

The subject of the hazards attendant upon immunization procedures is one that few have hitherto had the courage to tackle. Fear of providing fuel for the sometimes justifiable arguments of the anti-vaccinationists may have constituted the main and very obvious objection, but the formidable nature of the task, entailing the collection and perusal of countless records, must have also deterred many. That this nettle has at last been grasped and by so eminent an authority as Sir Graham Wilson, who is equipped by a lifetime of almost unique experience in this field to give a broad and impartial presentation of the subject, is something that will be universally welcomed. Although he had long had in mind the need for a book of this nature, it was a remark made by a university lecturer in bacteriology to the effect that the Lübeck disaster of 1930 was the first recorded instance of disaster associated with a vaccine that finally impelled the author to make a compilation of all recorded accidents occurring after immunization, a long series of which could be found in the 40 years before 1930. The result of his labours was incorporated in a series of Heath Clark lectures given at the London School of Hygiene and Tropical Medicine in 1966.

The subject matter is conveniently divided into six main sections—namely, (1) normal toxicity, (2) faulty production, (3) faulty administration, (4) abnormal sensitivity of the patient, (5) allergic phenomena, and (6) indirect effects such as damage to the foetus or provocation of disease. Under faulty production and faulty administration very full and detailed accounts are given of the various mishaps, some unavoidable, others the result of carelessness or stupidity, which have shaken the confidence of both lay and medical men from time to time but which nevertheless provided the experience from which modern techniques have been evolved. Examples of “inherent toxicity” have nearly all followed the use of toxin-antitoxin mixtures (T.A.M.) against diphtheria which became unstable on freezing, liberating toxin. Under “inherent infectivity” the author examines the failure to inactivate the early Salk vaccines (owing to delay in recognition of the limitations of formaldehyde as a disinfectant in the presence of protein) which finally culminated in the Cutter incident. There may not be general agreement with Wilson in his view that the case against both the Salk and Sabin vaccines as a cause of poliomyelitis remains unproved, but none could doubt that the presence of Simian viruses, such as SV 40, which may be found in both Salk and Sabin vaccines, is undesirable, though there is as yet no evidence that they are harmful to human beings. Extensive accounts are given of the many incidents in which vaccines or antisera have become contaminated during production; these largely resulted from the

introduction of staphylococci, but instances of contamination of plague vaccine, diphtheria antitoxin, and smallpox vaccine with tetanus bacilli are also given. Serum hepatitis is a reminder of the ease with which virus agents may contaminate materials and apparatus, with unhappy results. Yet the evolution of modern techniques, based on lessons learned from such experiences, the use of disposable syringes and needles, and constant vigilance on the part of those who administer the agents should go far to eliminate the possibility of such events recurring in the future. Indeed, a chapter dealing with contamination originating in the operator reminds us of the need to impress upon undergraduate and graduate alike the dangers that may arise for patients treated by doctors and nurses who are themselves suffering from infections, particularly sore throats and boils.

A large section of the book is devoted to accounts of the various types of allergic manifestation that may result from immunization; these include the once all-too-common serum sickness as well as serum neuritis and post-vaccinal neuritis. An account of the history of encephalomyelitis following smallpox vaccination is of outstanding value. The distinction is clearly made between cases of encephalopathy found in children under 2 years of age and those of encephalomyelitis of the demyelinating type which occur predominantly over this age, and the three main views on pathogenesis are critically examined. Methods of prophylaxis based on the use of a concomitant dose of dried gammaglobulin or preliminary vaccination with a killed vaccine, the efficacy of which is not yet proved, are rightly dismissed in favour of the simpler and more straightforward measure of restricting vaccination to the first two years of life. The occurrence of encephalomyelitis following the use of other vaccines is also discussed. Of current interest is that which is associated with pertussis immunization. Although little is known about the histopathology, it is clear that this is a special form of encephalitis, more of a toxic than of an allergic nature; the clinical manifestations are indistinguishable from the encephalitis which may follow a natural attack of the disease, and it is therefore logical to assume that both are the result of the action of the endotoxin of the bacillus. The high incidence of neurological complications following the use of the vaccine in Sweden convinced Ström that its use was not justified. Indeed, these tragic sequelae of whooping-cough immunization compel a critical review of the position, and the author considers that in view of the low mortality and lack of any positive evidence that the vaccine is successful there is a good case for discontinuance.

A very full account of anaphylactic reactions following the use of both sera and vaccines is given. Under conditions of mass immunization these are inevitable, but careful

inquiry as to a history of allergy, and a preliminary small subcutaneous test dose, may go far to prevent such reactions in individual cases.

While there can be no doubt that much more benefit than harm has accrued from immunization procedures they can never be regarded as wholly free from danger, and Wilson insists that they should never be used as a means of avoiding the “tedious, troublesome, and sometimes expensive process of improving personal and environmental hygiene.” He strongly condemns mass immunization with its inevitable masking of much latent infection, and, as was seen in the mass immunization that attended the smallpox scare of 1962, much in the way of allergic reactions or more sinister complications such as eczema vaccinatum or progressive vaccinia. A very thorough programme of immunization during childhood is essential if mass immunization is to be avoided, and in this respect Wilson considers that we have much to learn from the Soviet Union, where children attend for general examination, immunization, and repeat immunization once a year up to the age of 7 years.

This is a work of outstanding merit. Its scholarly nature, the masterly exposition of a subject on which there is widespread ignorance, the compilation of records and facts of intense historical interest, and the very fair and balanced assessment of present knowledge render it a landmark in medical literature.

A. MELVIN RAMSAY.

Testicular Function

Endocrinology of the Testis. Ciba Foundation Colloquia on Endocrinology. Vol. 16. Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.J.Biol., and Maeve O'Connor, B.A. (Pp. 331+xiii; illustrated. 60s.) London: J. & A. Churchill. 1967.

When one considers the embarrassing volume of new work on other endocrine glands, it is surprising how little is written about the testis, though some notable advances have been made in recent years. Of these, few have found clinical application at present, and this book, excellent though it is and stuffed full of basic learning, apparently takes the clinician no nearer to the solution of his own problems than he was 30 years ago.

It is important to stress the word “apparently,” for a careful perusal will disclose an occasional shaft of light, albeit pencil-sized, that may one day expand into a beam capable of illuminating the problems of the physician. There is hope in the work of B. Lunenfeld on the effects of human menopausal gonadotrophin in azoospermia, and in the discussion after Dr. L. M. Fishman’s paper of the role of the testis in oestrogen production. There appears to be a presumption that the oestradiol comes from the Leydig cells, but as R. G. Harrison pointed out it might come from the Sertoli cells, about which surprisingly little seems to be known. The work

of N. Törnblom, who thought that it came from the germinal epithelium, seems to have been forgotten. The discussion on the effects of cirrhosis on the plasma testosterone level certainly reached a clinical level.

Nevertheless, this is a book for the physiologist, for whom it is a necessary reading, rather than for the clinician.

RAYMOND GREENE.

The Case for "Homo Sportivus"

Energy, Work and Leisure. By J. V. G. A. Durnin, M.B., D.Sc., and R. Passmore, M.D. (Pp. 166+ix; illustrated. 25s.) London: Heinemann. 1967.

The contents of this book are indicated in the title, and are certainly of importance to everyone practising or associated with medicine. The authors, who are widely known for their extensive work on energy requirements, published a paper in *Physiological Reviews* in 1955 on "Human Energy Expenditure."¹ This paper is constantly quoted, and may reasonably be described as classic, using the Oxford English Dictionary definition of the term as "of the first class; of allowed excellence."

The book the authors have now prepared is a logical development of their famous paper and will further extend their reputation. I have read it with pleasure and profit, because the book is clearly written and the many tables are so well presented, and because I have learnt much about a subject which I considered to some extent my own. This does not mean I agree with everything; indeed such agreement could imply criticism, since there are many controversial aspects of the general problems of energy balance in man. The authors have some hard things to say about basal metabolic rate, and question the validity of the usual standard tables. They prefer to use the term "resting" metabolism, and have prepared a table of standard values based on body weight and an estimate of body fat. The argument is presented vigorously and attractively, and many will agree that the concept of "basal" metabolic rate is due for criticism.

The most important part of the book is the collection and presentation of energy expenditure figures. These are based on the thousands of measurements made by the authors, as well as on material published by others. Tables are not usually exciting in themselves, but the authors have succeeded in making theirs interesting to the general reader as well as invaluable to the specialist.

I warmly recommend this book, and I hope it will be widely read. The housewife can learn the calorie cost of shopping and cooking; the industrial medical officer will be concerned with the energy expenditure of various occupations; and all of us can read with concern the authors' comments on *Homo sedentarius*. We are evidently lazy creatures; Dr. Durnin and Dr. Passmore wish to convert us for our own good to *Homo sportivus*.

O. G. EDHOLM.

REFERENCE

- ¹ Passmore, R., and Durnin, J. V. G. A., *Physiol. Rev.*, 1955, 35, 801.

Renal Pathology

The Kidney. Edited by F. K. Mostofi, M.D., and David E. Smith, M.D. (Pp. 592+xiii; illustrated. £7 18s.) Edinburgh and London: E. & S. Livingstone. 1967.

This book is the sixth of a series of monographs published by the International Academy of Pathology, and is a notable advance in detailed description of renal pathology. It is written by 33 distinguished authors, 23 of whom are American workers. Dr. E. M. Darmady, who wrote an important and lucid chapter on the renal changes in some metabolic diseases, is the only contributor from this country, but several of the other authors were trained in Britain.

The book is divided into three sections. The first deals with the general pathology of renal disease, the second with immunological injury to the normal and the transplanted kidney, and the third with variations in renal pathology in relation to geography and climate.

All of the 28 chapters are clearly written and excellently illustrated. The book is not suitable, nor is it intended, for the beginner in renal disease and pathology. It will, however, be invaluable to any pathologist interested in modern advances in diseases of the kidney, and to the clinician using the technique of percutaneous renal biopsy. The authors have not felt restricted to keep to established facts, but have often indulged in valuable and well-informed speculations on the advancing fronts of research on renal pathology.

The single fault of the book is well documented by Dr. F. K. Motofi in the preface. This is the lack of uniformity of terminology to illustrate the extent of both renal and glomerular involvement in disease. One important message would seem to be the necessity for an international committee to standardize nomenclature in this important branch of pathology.

M. D. MILNE.

Dream Analysis

Studies in Analytical Psychology. By Gerhard Adler, Ph.D. (Pp. 250; illustrated. 25s.) London: Hodder and Stoughton. 1966.

With the exception of a new preface and a foreword by Jung, from the German version of 1952, this edition for "technical considerations" is unchanged. For the author, this is regrettable. Given the opportunity he would have laid more emphasis on the analysis of the transference and altered details of procedure such as the number of weekly interviews. Nevertheless, the greater part of the earlier work is still valid and the author is convinced that dream-analysis holds its place as the main clinical tool for those who practise analytical psychology.

Jung was the first clinician to encourage his patients to give visible form, through painting and drawing, to the imagery of their dreams. To his surprise he found that those in the second half of life welcomed this form of expression. Not infrequently the urge to paint pictures or to make models arises spontaneously. For generations patients on their own initiative have produced pictures which were dismissed as meaningless scribbling.

Jung, however, proved the therapeutic value of such daubs.

Adler amplifies Jung's work, and his commentary upon the series of nineteen pictures, here produced, is a notable contribution to present-day investigation of the unconscious. Through the detailed analysis of a dream he demonstrates the significance of Jung's hypothesis of the collective unconscious and how the technique of *active imagination* may be used to bridge the gap between the ego and the non-ego.

Psychiatrists, even those without experience of psychological analysis, will find the well-presented case histories full of therapeutic hints. One thing becomes evident—the need to examine ego psychology in conjunction with the psychology of the personal and the collective unconscious.

This lucid study of the theory and practice of analytical psychology can be recommended to every psychotherapist whatever his affiliation to this or that "school."

E. A. BENNET.

Bronchoscopic Appearances

Atlas d'Endoscopie Bronchologique. Aspects Normaux et Pathologiques. By Jean Ioannou. (Pp. 64+vi; illustrated. 60 F.) Paris: Masson. 1967.

This excellent atlas of bronchoscopic appearances will be of value to all interested in chest disease or in endoscopy. Printed on high-quality paper, the text, in French, is short and describes the anatomy and the illustrations. Ninety reproductions of colour photographs, each 2 in. (5 cm.) square, accurately illustrate inflammations, neoplasms, and sequelae of operations. Similar black-and-white reproductions demonstrate normal anatomy and its variants and some less common diseases.

The student of bronchoscopy will find these pictures a useful guide; but he should remember that the camera records all it sees, and does not always mirror the emphasis that the surgeon's eye places on salient features—an emphasis which the painter can record; nor under the difficult circumstances of endoscopy can the camera always demonstrate perspective. Neither surgical nor photographic techniques are described, nor are any details of apparatus used given. There are no illustrations of foreign bodies in the air passages.

The photographs of tuberculous endobronchitis are especially welcome. This condition is seldom seen since its dramatic response to streptomycin therapy was recognized, but it remains important and an occasional diagnostic trap. British readers will be glad to note reference to the bronchus of Nelson. This eponym, seldom used in current English literature, commemorates the young thoracic surgeon who died a generation ago of an overwhelming infection due to a finger-prick received during an operation.

Dr. Ioannou records that of 40 patients he examined after tracheostomy, two-thirds showed important endoscopic lesions when apparently healed, confirming the now widely held opinion that the after-effects of this easily undertaken procedure may be serious.

An endoscopic photograph or a series can profitably form part of a patient's case record dossier. Those who are considering such a practice should turn to this atlas in the hope of emulating the high standard it sets.

M. MEREDITH BROWN.

"A Tentful of Scientists"

Reflections on Research and the Future of Medicine. A Symposium and Other Addresses. Edited by Charles E. Lyght, M.D. (Pp. 209+vii; illustrated. 81s.) London: McGraw-Hill, 1967.

This book is the record of a two-day colloquium on the occasion of the dedication of new research buildings at the Merck Sharp and Dohme research laboratories at Rahway, New Jersey, in May 1966. The speakers on the first day were Sir Macfarlane Burnet on autoimmune disease, E. L. Tatum on molecular biology and nucleic acids, F. O. Schmitt on molecular dynamics and brain function, and Sir George Pickering on degenerative diseases. On the second day W. H. Gadsden on research and public responsibility, M. Tishler on the challenge of pharmaceutical research, E. B. Chain on the quest for new biodynamic substances, H. W. Gadsden on the role of research at Merck, and Sir Henry Dale looked back to similar occasions at Merck in 1933 and 1953.

Americans have a particular affection for ceremonies of commencement, graduation, dedication, and rededication, which are of the nature of corporate acts of homage to education, science, or research as the case may be. The ceremonies are inspiring to the participants, but accounts of them, like other *Festschriften*, do not make particularly good reading.

Björck some years ago demonstrated by actual experiment how difficult it is even for young men to predict the future of medicine, and the speakers at Rahway were all senior. One of the photographs with which the book is illustrated is entitled "A Tentful of Scientists at the Rahway Dedication Ceremonies," and that is perhaps a good description of the book as a whole.

L. J. WITTS.

Disabled Children — Speech and Vision

Assessment of Cerebral Palsy. Vol. 2. By K. S. Holt, M.D., M.R.C.P., D.C.H., and J. K. Reynell, B.Sc., Ph.D. (Pp. 187+viii; illustrated. 40s.) London: Lloyd-Luke, 1967.

This Volume 2 is an excellent and authoritative yet easily read guide to the assessment of vision, hearing, language function, and intelligence in disabled children. As such it provides a useful reference volume to all the lay and professional workers involved in this important field.

It must be emphasized that apparently normal children may require assessment in their early years lest they should be victims of some slight perceptual or other disability which interferes with psychological development. For this reason teachers, social workers, and also parents should look through this book.

W. RITCHIE RUSSELL.

Doctor in India

Doctor Sahib. By Stephen Kerry. (Pp. 204. 30s.) London: Cassell, 1967.

In the late nineteen thirties, with the Government of India Act on the stocks and with independence apparently just round the corner, the Secretary of State for India announced the creation of new clinical civil posts in India reserved for European members of the Indian Medical Service, and started a recruiting drive for high quality officers with a promise of only brief military service in pleasant stations of the applicant's own choosing. This extraordinary appeal was most successful; a number of highly qualified "registrar types" from Great Britain, Canada, and Australia responded, and the I.M.S. had an intake of as high a quality as it ever had in its heyday.

Those of us who, as senior teachers, had for many years been training Indian doctors to take over the highest posts were somewhat disconcerted, and Indian political leaders and the entire Indian medical profession responded with anger and indignation at this apparent *volte face*. This move, in fact, hardened the

determination of leading Indian statesmen to abolish an all-India medical service when independence was achieved. They did so—a fact which some of them regret today.

One of this group has published his autobiography under the pseudonym of Stephen Kerry, and the account of his short prewar service in a popular hill station at a Gurkha battalion headquarters, and later as a civil surgeon in Bihar, makes compelling reading. The book has been deservedly acclaimed in the British press as eminently readable, fascinating, and absorbing, and is so well written and slanted to interest and to titillate the non-medical reader that one suspects the collaboration of a skilled professional writer.

The accounts of the investigation and control of an outbreak of cholera in a remote village in the Himalayas is very well done indeed, and the scene of famine and epidemic on the plains of Bihar are only too topical today. One of the better aspects of our work in India was the control of jails by medical men. As a young man devoted to a surgical career Kerry detested his jail duties, and the gallows is used inevitably with great effect in this para-autobiography.

One need not accept every incident as factual, but the general picture painted represents its period accurately; the busy absorbing life of a civil surgeon and district medical officer in India is skilfully depicted. *Doctor Sahib* is a moving but unsensational story of the life of a young introspective idealist in full sympathy with Indian aspirations. It is certainly the best of the "doctor" books published since the war.

GEORGE R. MCROBERT.

In his latest novel, *The Facemaker*, Richard Gordon recounts the fortunes of a plastic surgeon up to the outbreak of the first world war. Though at once self-assertive and priggish, the hero, Graham Trevoise, often engages the reader's sympathy owing to the prejudice that he meets from professional colleagues and social acquaintances. Forsaking the comic vein from which he dredged *Doctor in the House* and many irreverent successors, the author presents his characters now in a serious if no less recognizable setting. *The Facemaker* is announced as the first of a trilogy, and is published by Heinemann (pp. 244: 25s. net).

Books Received

Review is not precluded by notice here of books recently received.

Bedsore. By B. N. Bailey, M.B., B.S., F.R.C.S. (Pp. 130+vii; illustrated. 50s.) London: Edward Arnold, 1967.

The Physiological Clock. 2nd edition. By Professor Erwin Bünning. (Pp. 167; illustrated. 24s.) London: Longmans, Green, 1967.

Marriage Difficulties. By Dr. Paul Tournier. Translated by John S. Gilmour. (Pp. 63. 6s.) London: SCM Press, 1967.

Decompression of Compressed Air Workers in Civil Engineering. Proceedings of an International Working Party, London, 1965. Edited by R. I. McCallum, M.D.(Lond.). (Pp. 329+xxi; illustrated. 42s.) Newcastle: Oriel, 1967.

Integration in Internal Medicine. Proceedings of 9th International Congress of Internal Medicine, Amsterdam, 1966. Edited by A. J. Dunning. (Pp. 559+xv; illustrated. £9 7s. 3d.) Amsterdam: Excerpta Medica Foundation, 1967.

The Diabetic ABC. 14th edition. A Practical Book for Patients and Nurses. By R. D. Lawrence, M.A., M.D., F.R.C.P.(Lond.), Hon.LL.D. (Toronto). (Pp. 91+x. 7s.) London: H. K. Lewis, 1967.

Time of One's Own. Leisure and Young People. By Pearl Jephcott. (Pp. 165+xii; illustrated. 30s. Paper 18s.) Edinburgh: Oliver & Boyd, 1967.

Ultrasonics in Ophthalmology. 20th International Congress of Ophthalmology, Munich, 1966. Edited by A. Oksala and H. Gernet. (Pp. 240; illustrated. £5 19s.) Basel and New York: S. Karger, London: Academic Press, 1967.

The Doctor Shortage. An Economic Diagnosis. By Rashi Fein. (Pp. 199+xi. \$2.50. Washington: Brookings Institution, 1967.

Neurologie. Für Ärzte und Studenten. By Marco Mumenthaler. (Pp. 383+xii; illustrated. DM. 9.80.) Stuttgart: Georg Thieme, 1967.

The Pharmaceutical Industry. A Personal Study. By Wyndham Davies, M.B., Ch.B., D.P.H., D.I.H. (Pp. 240+viii. 63s.) Oxford: Pergamon, 1967.

The Hospital Chaplain. By the Birmingham Regional Hospital Board. (Pp. 33.) Available from B.R.H.B., Arthur Thomson House, 146 Hagley Rd., Birmingham 16, 1967.

Glaucoma. Tutzing Symposium. 20th International Congress of Ophthalmology, Munich, 1966. Edited by W. Leydhecker. (Pp. 265; illustrated. £6 17s. 6d.) Basel and New York: S. Karger, London: Academic Press, 1967.

Middle Articles

MEDICAL HISTORY

Tercentenary of Blood Transfusion

Sir GEOFFREY KEYNES, M.D., F.R.C.S.

Brit. med. J., 1967, 4, 410-411

In July 1667 Jean Denis, Professor of Philosophy and Mathematics at Montpellier and Physician to Louis XIV, sent a letter to the editor of the *Philosophical Transactions* of the Royal Society of London. This was a translation of "Copie d'une lettre touchant une nouvelle Manière de guérir plusieurs Maladies par la Transfusion du Sang," addressed

power. He then proceeded to state that, though transfusion of blood may have been conceived in other parts, "it is notorious that it had its birth first of all in England," through the hands of Dr. Lower and Dr. Edmund King, who had published accounts of it in November and December 1666. Denis's letter had, it seems, "come abroad" in July 1667, but it was omitted from most copies of the *Transactions*. In this manner a battle of priorities began, and it might be doubted whether the three hundredth anniversary of the practice of blood transfusion should be noticed in 1966 or 1967. From the fact that the present article is published in 1967 it may be guessed that the second date is to be preferred. It is not due to an oversight.

Denis himself in his first sentence emphasized that the conception of transfusion happened "about ten years ago in the illustrious Society of *Virtuosi* which assembles at your house," and that the Society had received Denis and a friend as visitors to see the experiments. As is well known, the investigations were initiated by Dr. (later Sir Christopher) Wren, who suggested injecting various liquors, such as milk or beer, into the circulation of animals. Subsequent experiments were carried out chiefly by Dr. Richard Lower, accounts of these being published in a series of papers in the *Philosophical Transactions*. Lower was a careful investigator and limited his experiments mainly to transfusing blood directly from an artery of one dog to the jugular vein of another. In this way he showed that a dog could be exsanguinated to the point of death and then be completely recovered by transfusion. He rightly concluded that the "most probable use of this Experiment" would be for replacing blood lost or for rectifying corrupt blood.

Once Denis's letter became known the London experimenters were not slow to complain, in the *Transactions* for 21 October 1667, that he was claiming a priority due to them. This seems ungenerous, since Denis had deliberately assigned to them the first conception of transfusion. He was, however, announcing an advance in technique by stating his idea of transfusing blood from one species of animal to another species—calf to dog—and finally, in logical sequence, from an animal to man. He then told how he actually carried this out as a therapeutic operation. On 15 July 1667 he had noticed a youth of 15 or 16 who had suffered 20 bleedings for "a contumacious and virulent fever, in order to assuage the excessive heat. Before this disease, he was not observed to be of a lumpish dull spirit, his memory was happy enough, and he seemed chearful and nimble enough in body; but since the violence of this fever, his wit seemed wholly sunk, his memory perfectly lost, and his body so heavy and drowsie that he was not fit for any thing. I beheld him fall asleep as he sate at dinner, as he was eating his Breakfast, and in all occurrences where men seem most unlikely to sleep. If he went to bed at nine of the clock in the Evening, he

(489) *Num. 17.*
A LETTER

Concerning a new way of curing sundry diseases by Transfusion of Blood, Written to Monsieur de MONTMOR, Counsellor to the French King, and Master of Requests.

By J. DENIS Professor of Philosophy, and the Mathematicks.

Munday July 22. 1667.

SIR,



THE project of causing the Blood of a healthy animal to passe into the veins of one diseased, having been conceived about ten years ago, in the illustrious Society of *Virtuosi* which assembles at your house, and your goodness having received M. Emmery, & my self, very favorably at such times as we have presum'd to entertain you either with discourse concerning it, or the sight of some not inconsiderable effects of it: You will not think it strange that I now take the liberty of troubling you with this Letter, and design to inform you fully of what purposes and successes we have made in this Operation; wherein you are justly intitled to a greater share than in any other, considering that it was first spoken of in your *Academy*, & that the Publick is beholding to you for this as well as for many other discoveries, for the benefits & advantages it shall reap from the same. But that I may give you the reasons of our procedure & con-

Ccc

vince

on 25 June 1667 to Monsieur de Montmor, Counsellor to the King. The letter was set up in type to be issued as No. 27 of the *Transactions* dated "Munday July 22. 1667," but it was suppressed before general publication. The issue numbered 27 actually published was dated "Munday, Septem. 1667" for the months of July, August, and September. The number begins with "An Advertisement concerning the Invention of the Transfusion of Blood," in which the editor, Henry Oldenburg, explained that he was "returning to his former exercises which by an extraordinary accident he was necessitated to interrupt for some months past." The "extraordinary accident" was in fact his confinement in the Tower of London on suspicion of spying for a foreign

needed to be awakened several times before he could be got to rise by nine the next morning, and he passed the rest of the day in an incredible stupidity."

Denis attributed this state of affairs to loss of blood rather than to the fever. He accordingly bled the boy of 3 ounces (86 g.) and transfused about 9 ounces (255 g.) into his arm from the carotid of a lamb. The boy felt a burning along his arm, but had no other symptoms and quickly recovered from his drowsiness, becoming as nimble as before and putting on weight. Encouraged by this result, Denis tried another transfusion on a man of 45 "having no considerable indisposition"—in fact the experiment had little justification. The man was bled 10 ounces (283 g.) and was given 20 (567 g.) in exchange from a lamb. He had the same pain along his arm as the first patient, but felt stronger than before and cheerfully slaughtered and flayed the donor lamb, being a butcher by profession. Later Denis performed further transfusions, and one patient, suffering from "an inveterate phrenzy," showed every sign of having received a considerable amount of incompatible blood, exhibiting pain in the arm, a rapid and irregular pulse, sweating, pain in the back, vomiting, diarrhoea, and finally passing urine almost black with haemoglobin.

The best the London *virtuosi* could do was to publish in the *Transactions* for 21 October 1667 part of a letter from Dr. Edmund King describing his *preparations* for transfusing a man from an animal, though the experiment had not actually been done. It was not until 23 November of that year that Arthur Coga, an indigent Bachelor of Divinity of Cambridge, was transfused with lamb's blood by Drs. Lower and King at Arundel House. He suffered no inconvenience and asked for a second transfusion, no doubt in return for a

suitable reward. Samuel Pepys witnessed both the early experiments and the first one done on a man, making many pleasant quips about it in his diary.

It is clear that, though London had priority for the initiation of the preliminary transfusion experiments, Paris could justly claim it for the therapeutic operation on a human being. Even when London first transfused a man, it was purely experimental, not therapeutic. So let us hand the laurel to Paris in this, the tercentenary, year—though we must also record that the value of this priority was soon to be sadly discounted. Denis published five more pamphlets in 1667 and 1668, but in the latter year one of his patients died after three transfusions, and proceedings against the doctor were instituted by the widow. When brought to trial Denis was exonerated, the patient's death having been proved to be due to arsenic administered by his wife. Nevertheless a law was introduced forbidding the performance of any transfusion without the permission of the Faculty of Medicine of Paris. The Faculty was in any case strongly opposed to the whole idea and the practice of transfusion from animals was quite rightly abandoned. In London, too, no account of the second transfusion given to Coga was ever published, since the affair was bringing ridicule and discredit on the Royal Society. Indeed, little further was heard of blood transfusion for more than a hundred years. A tercentenary likely to elicit more enthusiasm will not be due until the year 2118. It was on 22 December 1818 that James Blundell, obstetrician to Guy's and St. Thomas's Hospitals, described in a paper delivered to the Medico-Chirurgical Society the first blood transfusion from *man-to-man*, performed with the help of a surgeon, Henry Cline. That was the true beginning of modern therapeutic transfusion.

CONTEMPORARY THEMES

Some Weaknesses in Hospital Service Organization

GEORGE DISCOMBE,* M.D., B.S.C., F.C.PATH., F.R.I.C.

Brit. med. J., 1967, 4, 411-413

It is now clear that no appeals or protests are likely to produce a big increase in the money allotted to the National Health Service. This is a political decision taken because taxation is already heavy, and all Government spending must be kept within the bounds of practicable taxation. Cries to "Take the N.H.S. out of politics" are futile; though everybody wishes to provide excellent medical care, the cost—over £1,500m., or over £30 for every man, woman, and child in the country—can be provided only by the Government out of taxation, which must always be a political matter.

Waiting-lists

The waiting-list for admission to hospital remains steadily at about half a million—about four weeks' admissions; but since in many hospitals half or more of admissions are emergencies the delay for elective admissions may be several months, so that a patient with a simple hernia or with varicose veins may wait for several months. A reduction in stay of only one day for each patient would increase the throughput of the N.H.S. hospitals by about 300,000 each year, and presumably reduce the waiting-list.

The reasons for waiting-lists, like their size, vary from region to region, from hospital to hospital, and from department to department. About 15% of hospital beds for acute cases are occupied by long-stay patients, many of whom are suitable for local authority geriatric homes, were there enough of them; but these again have to be provided for out of taxation. In my own hospital some specialist waiting-lists are inflated because many of those on them have been offered admission but have asked for a delay, thus wasting one or two bed-days. Those who refuse are usually women who cannot arrange for their young families to be looked after during their absence. Closer co-operation between hospital admission officers and local authority social services might reduce these difficulties. Some waiting patients need investigations which could be done while they were outpatients were a day ward available, or radiological or laboratory facilities improved, or, what may be equally important, if sufficient specialist time was available for cystoscopy, gastroscopy, and the like.

In some hospitals the limit to surgical admissions is the time available in operating-theatres. I have heard one surgeon complain that within a month two of his patients had died while he was waiting for an operating-theatre to become available. Registrars complain to me that patients are avoidably detained in hospital to await specialized radiological or

* Pathologist, Central Middlesex Hospital, London N.W.10.

biochemical investigation. During the past few years I have visited several laboratories to study their needs, and repeatedly found that within the space available at present each needed to spend £4,000 to £6,000 to make the laboratory reasonably effective—quite apart from needing more building because they were grossly overcrowded. In these hospitals, as in my own, inadequate laboratory services are a considerable check on patient throughput. In some hospitals this check can be removed by improvements in equipment, though others need more buildings or more staff. Since the demand for biochemical investigations doubles every five or six years, the laboratory will increasingly limit the throughput of a hospital.

Limits to Throughput

Thus the factors which limit throughput are often not a lack of beds but lack of operating-theatres and of radiological or laboratory facilities. We do not know for how many hospitals this is true; but in such hospitals it is much cheaper to improve these facilities than to provide more beds, which in such cases would not affect throughput and yet would demand more nurses, thus uselessly increasing the cost of treatment.

Most hospitals would benefit from an analysis of the factors which limit throughput; in many cases the different clinical units would be affected differently by single specific changes—thus the gastroenterologists may need more laboratory and radiological investigation and the surgeons more theatre time or radiological services. Some sort of analysis of social effectiveness is also needed so as to evaluate the importance to families and to the body politic of clinical advances; for example, an intensive coronary care unit may cut the early death rate by 20% but produce semi-invalids of limited or zero ability to work. Such analyses and comparisons are notoriously difficult, but might indicate directions in which expenditure would be most effective.

Operating-theatres, laboratory facilities, radiological departments, day wards are not cheap to provide, because they usually require new buildings; but within each building there are individual items of equipment that are much less expensive—air-conditioning or operating-tables for the theatre, auto-analysers or data-processing equipment for the laboratory, image-intensifiers or developing units for the radiological department. Such individual items cost £500 to £5,000—0.025 to 0.25% of the annual expenditure of a hospital but 10 to 100% of the money available for all innovations. An increase in revenue of 1% might produce enough to bring considerable improvements to the services available by making it possible to purchase modern equipment.

How can individual hospitals obtain such an increase without recourse to taxation? There are three possibilities—the encouragement of private beds within the hospital service, the encouragement of charitable gifts through the Leagues of Friends, and the imposition of direct charges. This last is very much a political problem, so that here I will confine myself to the former two.

Private Beds

A system where private practice continued separately from and independently of the N.H.S. would inevitably lead to a division of the profession into two groups. The founding fathers of the N.H.S. hoped to overcome this danger by establishing part-time hospital appointments for senior men ("consultants") and by paying salaries sufficient to provide an income comparable to those which could be obtained in private practice. We are now faced with a situation in which an increasing proportion of the middle class are paying insurance premiums in order to obtain the facilities of private attention, oblivious to the fact that outside the N.H.S. are few hospitals with the facilities required for all modern medical

services. Whereas in my hospital a surgeon can, if it be essential, organize an emergency blood transfusion within minutes, and at my outlying hospitals within an hour, the delay in most private hospitals and nursing-homes is far greater, so that in the few cases of unexpected emergency in private hospitals to which I have been called I have preferred to transfer the patient to an N.H.S. hospital—a course adopted by many others.

The facilities which can be obtained in private practice are few, but they are important to many middle-class patients. Among them are privacy, some choice in the time of admission or at least advance warning, and the assurance of the personal attention of the chosen consultant. The importance of privacy can be overstressed—indeed, it is most important for patients whose illness is not severe, such as the business executive recovering from an elective operation. Advance warning of the time of admission is very important to those with managerial responsibilities, whether in office, factory, or home (the housewife is a manager and frequently refuses admission when offered because of the difficulties of running her home). Assurance of personal attention is said to be the backbone of the system of personal doctoring, though I confess that in hospital today the individual consultant is becoming submerged in his team.

There seems to be a choice of two courses: to have two distinct services, clearly separate, one marked "private," the other marked "N.H.S.," or to have a choice within the N.H.S. between two categories of service—the one very much as it is today for most of the population, the other a "private" service providing greater privacy and facilities for such business or social activity as is possible, a reasonable choice in the time of admission, and the certainty of the attention of the consultant of choice and his team.

The cost of private beds anywhere is upwards of £7 daily, the average cost of any N.H.S. bed. At present many large hospitals have no private beds, others barely 1% of their total; many less well equipped small hospitals have 2 to 3%. These proportions could with advantage be reversed: if a 75% bed occupancy were secured for private beds numbering 2% of the total beds in a hospital, then the contribution of 1.5% to the hospital's expenditure would make a considerable difference to the facilities available, and if it resulted in improvements to the services which were limiting throughput it might well result in an increase in the patient-turnover of the hospital as a whole. This assumes, of course, that the receipts from private beds would remain with the hospital group and not be remitted to the Exchequer as is the present practice.

Treasury's Accounting System

The standard accounting system is no doubt admirable for administrative departments; but it is not so admirable for service departments like the N.H.S. in which changes are often needed at short notice. To insist that underspending in one section of accounts may not be set off against overspending in another seems absurd when a capital investment of £2,000 may produce a revenue saving of £800 a year. To insist that sums received by a hospital management committee shall be returned to the Treasury rather than be retained by the committee discourages those officers who are concerned with the collection of such dues, whereas if these receipts were available as extra money for the hospital management committee there would be a direct incentive for the officers to collect every possible penny. No hospital management committee is encouraged to save when any "underspending" is returned to the Treasury at the end of the financial year; but if saving from year to year were permitted (especially of the small sums allowed for "innovations") great care would be exercised in the choice of equipment, contrasting with the present hectic spending spree which starts in February when

the treasurers of regional hospital boards and hospital management committees discover that they may have a surplus.

League of Friends and Charity

From the inception of the N.H.S. it has been policy to prevent hospital administrators soliciting gifts to their hospitals. The reasons are many, but the most important was to break down the idea that the N.H.S. was a charity instead of a service provided by taxpayers for themselves and their dependants to use as a right; and I, for one, think that this break with mediaeval tradition was right and necessary. But now, after 20 years' work, the idea of the N.H.S. as a "charity" must be dead except among the most elderly and those who will never accept any change. Local patriotism is still active.

Most people are benevolent and find the chance of exercising benevolence pleasurable. Until the last war hospitals were the most important object of benevolence, and an organization such as that of the Freemasons supported equally education, the care of the aged, and hospital care. What the Freemasons realize, and what most of the population have not discovered, is that all these establishments need to be maintained. It is comparatively easy to persuade people to give money for bricks and mortar, which they can see and take pride in; it is much more difficult to persuade them to pay for porters, domestic orderlies, postage, and mechanical aids to cleaning. Their consciousness of having exercised benevolence seems to make them expect others to exercise benevolence by giving their services free; yet administrators know that the annual maintenance of a unit such as a pathology laboratory may equal or exceed the initial capital expenditure on building and services.

The conclusion is therefore that if we are to encourage people to give to their local hospital the gifts should be used to buy equipment which demands the minimum of revenue expenditure. Building and general planning must remain the prerogative of the regional hospital board and hospital management committee; but much of a department's equipment, and certainly replacements for old and obsolete equipment, could be given by the public. Yet these are the very things of

which the public can have little or no knowledge unless it receives specific instruction.

Such specific instruction should not be the prerogative of individual consultants trying to build up a department, because when this happens other parts of the hospital—for example, radiology and clinical laboratories—may be overloaded. Further, it should be organized on a group basis, rather than for individual hospitals, partly to minimize jealousy between hospitals and partly to make sure that large gifts are not devoted to hospitals unable to use them effectively and efficiently. It seems reasonable for hospital needs to be analysed by the group medical advisory committee, and the order of precedence and sums required communicated to the lay organization through the hospital management committee mechanism, preferably by the group secretary or his deputy, who will be able to advise the group medical advisory committee about possible future changes in organization.

Conclusion

From the point of view of national finance these suggestions seem harmless. They require no increase in taxation. They would divert income, after taxation, away from personal expenditure into a field which is notably short of money, and much of this income would be spent on the purchase of scientific equipment, most of which home industry is able to supply. It is generally considered that a flourishing and stable home market is a necessary condition for satisfactory exports, so that the changes I have suggested might even improve the balance of payments.

There is a strong and universal emotion that wealth should not control access to medical facilities—a feeling which to a large extent I share; but if wealthy people wish to pay so that more attention is given to their convenience and comfort than can be provided by the N.H.S. for the general run of the population, then surely it is better for this desire to be satisfied within the N.H.S. than outside it. This would be valuable if the money thus received were retained in the hospital group and devoted to improving local facilities. I am satisfied that in some hospitals this would actually increase the number of patients treated in "non-private" beds rather than reduce them.

CONFERENCES AND MEETINGS

Clinical Electroencephalography in Childhood

[FROM A SPECIAL CORRESPONDENT]

A symposium on electroencephalography in childhood was held in Gothenburg in Sweden in August. There was a wide range of topics, from studies on young animals to clinical investigations on children, and, in addition, advanced apparatus was discussed.

Dr. N. MONOD and Dr. P. DUCAS (Paris) discussed the prognostic value of the electroencephalogram (E.E.G.) in the first two years of life of a child. A grossly abnormal E.E.G. in full-term or premature newborn babies was related to an unfavourable clinical evolution in 95% of the cases. An exception to this trend was represented by mongolism and kernicterus, where in spite of the severe clinical sequelae the E.E.G. abnormalities in the neonatal period were minimal. Dr. C. DREYFUS-BRISAC and A. MINKOVSKY (Paris) had studied the E.E.G. of 96 "small for dates" newborn babies. The assessment of

gestational age could be correctly made (within two weeks) in 73 babies who were in reasonable general conditions (out of a total of 96 babies). Dr. Dreyfus-Brisac had been able to recognize differences in the E.E.G. features between true prematures (born before 37 weeks) and "small for dates" newborn babies in 90% of the cases.

The host of the conference, Professor INGEMAR PETERSEN (Gothenburg), reported with his co-workers Dr. EEG-OLOFSSON and Dr. SELLDEN on the occurrence of paroxysmal activity in the E.E.G. of normal children. They had found that out of 1,000 normal children some form of paroxysmal activity in the E.E.G. occurred in 99. When this figure was broken down, however, 38 children showed only abnormal responses to photic stimulation, while a further group of 36 children showed only paroxysmal discharges

during sleep. These workers had found that the amount of paroxysmal phenomena in the E.E.G. was significantly greater in girls than in boys. The prognostic importance and the correct evaluation of these abnormal E.E.G. features in apparently normal children could not be fully appreciated without a very long-term follow-up.

Localization Technique

Some of the papers dealt with applications of special techniques to particular problems. Among these Dr. BECHTEREVA (Leningrad) reviewed special techniques for the localization of lesions, and Dr. W. A. COBB (London) was able to record peculiar phenomena from the depth of the brain in one patient with subacute sclerosing leukoencephalitis.

Among the clinically orientated papers Dr. G. PAMPIGLIONE and M. LEHOVSKY (London) presented a follow-up study on a group of 24 children with histologically proved neuronal lipidosis (eight with Tay-Sachs disease and 16 with so-called amaurotic family idiocy). In the group of children in whom the symptoms began between the age of 2 and 4½ years there was a peculiar combination of E.E.G. features even at an early

stage of the disease, which was not seen in patients with other diseases in this age group. The peculiar neurophysiological findings (both E.E.G. and polyelectromyographic studies) were demonstrated in children of similar age groups but at different stages in the course of individual illness. It was clear that the current classification of the neuronal lipidoses was inadequate.

Dr. A. G. Z. ZEMSKAYA (Leningrad)

presented her results of surgical treatment in over 100 children with epilepsy. Direct recording from the exposed brain and direct stimulation of the cortex had helped her a great deal in the surgical treatment of children with focal epilepsy. In particular direct recording had been found valuable not only as a localizing tool during cortical excisions but also as a basis for stage-by-stage removal of the epileptogenic focus.

Disabilities in Middle-age

[FROM A SPECIAL CORRESPONDENT]

The fourth biennial Chelmsford symposium, organized jointly by the Mid-Essex Division of the B.M.A. and the Chelmsford Medical Society, was held at Broomfield Hospital on 28 and 29 October, and dealt with "Disabilities in Middle-Age."

In a review of "The Factors Influencing Disease in the Middle-Aged" Sir JOHN RICHARDSON (London) drew attention to the rising figures of absence from work through sickness in Britain. Since the war the rate had doubled and for some occupations at least this was particularly true of the younger age groups. This, he suggested, might reflect a new attitude to going sick, which was now socially and economically more acceptable. If, when these younger employees became middle-aged themselves, they carried this pattern with them, the rise in sickness rates would accelerate. Comparative international statistics showed an inverse ratio between sickness rates and unemployment rates, even though death rates differed little from country to country. There was also much evidence that with responsibility and rank sickness rates fell.

The partially successful, who had reached their peak of attainment, but who could not accept that future advancement was unlikely, might retreat into illness in middle-age if the opportunity offered. There were others who had gone too far for their capacities and who became anxious or depressed because of the stress involved in keeping up the pace. The ruthlessly successful often hid self-doubt and might unconsciously exaggerate their physical handicaps to escape the pressure, or might develop psychiatric difficulties. The too successful risked ignoring the early symptoms of organic diseases, especially those arising from stress. Concluding, Sir John quoted evidence that in later middle life a man off work for many months might never return to work at all. Not only was it important to appreciate the seriousness of disease in this age group, but it must be remembered that this was often due as much to modes of life and social pressures as to primary organic pathology.

Carpal Tunnel Syndrome

Dr. F. LEES (Chelmsford) showed that little could be added even now to the descriptions given by many physicians in the nineteenth century of what McArdle in 1949 had named the carpal tunnel syndrome. He stressed that abnormal neurological signs were often absent in those patients with most disturbing symptoms and believed that the diagnosis should be made on the history alone, supported sometimes by therapeutic

trial with diuretics, corticosteroids, or splints, and very occasionally by nerve-conduction tests. The simplicity of the operative treatment of the syndrome was demonstrated by Mr. BRUCE PENDER (Chelmsford).

Mr. B. W. BROADHURST (Southend) felt that very few of the middle-aged patients who presented with lumbar spine and root pains were suffering from true prolapse of an intervertebral disc. For those who were he considered that surgical excision of the disc was the only satisfactory form of treatment. The majority of middle-aged patients with this syndrome were suffering from multiple disc degeneration with narrowing and deformity of the disc spaces on x-ray examination. This group of patients could be helped by the usual conservative methods, such as manipulation, surgical supports, physiotherapy, and bed boards. Nevertheless, in probably two-thirds of patients with low back pain psychogenic factors were important in causation, and correction of social and economic difficulties could be curative.

In a survey of osteoarthritis Dr. J. T. SCOTT (London) pointed out that a field study had shown that this condition accounted for one-quarter of the rheumatic complaints affecting an urban population. The chemical basis for the primary degenerative changes in the joint cartilage was not understood. There was often a discrepancy between the severity of the pain and the extent of the pathological changes, and the importance of assessing the influence of emotional factors on an individual patient's symptoms was agreed by speakers during the subsequent discussion. The appearance of symptoms, or a rapid deterioration in the symptoms, of osteoarthritis might indicate the development of a depressive state.

Rheumatoid Disease

Professor E. G. L. BYWATERS (London) said that the discovery of the cause of any form of chronic inflammatory polyarthritis would provide the aetiological explanation of them all. Dealing in details with "rheumatoid disease," which he regarded as a multifocal systemic disorder, he indicated one clue to aetiology in the predilection of the disease for tissues affected by, and specialized for, movement. One illustration of this was the relative freedom from nodule formation of single limbs immobile because of severe joint disease or coincident hemiplegia. It appeared probable that rheumatoid disease was an autoimmune disorder; movement, particularly of inflamed tissue, produced an antigen, and the subsequent tissue reaction

induced further joint damage. Rheumatoid lesions in synovial and other soft tissues were reversible, but those affecting bones were not. The proportion of the population whose serum contained rheumatoid factor increased with age, but most did not have rheumatoid arthritis. The most severe types of the disease occurred independently of the presence or absence of a positive rheumatoid factor test.

Analysing some of the evidence for the presence of a strong genetic factor in the aetiology of rheumatoid disease, Dr. W. WATSON BUCHANAN (Glasgow) concluded that the genetic influence was small. Until some biochemical-marker of this genetic influence was identified epidemiological research of this type was unlikely to be of much value.

The cardiac lesions of rheumatoid disease were described by Professor T. B. COUNIHAN (Dublin). Histologically, the pericardium was involved more than twice as often as the endocardium or myocardium, while there was often disease of the proximal aorta. Clinically, evidence of such cardiac involvement was uncommon, and even then could in some cases be due to concurrent rheumatic fever. The commonest valvular lesion was aortic incompetence, but signs of severe haemodynamic disturbance were infrequent. Congestive failure was very rare, perhaps because the pathological changes were rarely severe until late in the disease, when mobility was very limited.

Dr. R. M. MASON (London) reported a double blind controlled trial of prayer in the treatment of rheumatoid arthritis. Analysis by the sequential method showed no significant difference between the treated and the control groups. In his experience, of every 20 cases of rheumatoid disease seen in hospital practice roughly five had a complete cure, five were cured with only minimal residual damage, eight required continued treatment, and one or two were very severely disabled. He found it very difficult to predict into which group any patient would fall. The principles of treatment were to modify the patient's disease, to modify the environment, and to obtain by explanation the co-operation of the patient and his relatives in these attempts. He believed that most of the common drugs for rheumatoid arthritis were, in the doses usually employed, analgesic rather than anti-inflammatory. He regarded aspirin as the simplest and safest. A preliminary pilot study of azathioprine (Imuran) in nine patients with rheumatoid disease of potentially disastrous severity had enabled the dosage of corticosteroids to be reduced in four and had led to the disappearance of arteritic lesions in three of four cases. Although severe toxic

effects had occurred in half the cases the results were sufficiently encouraging to justify a double blind trial of immunosuppressive therapy, which had now started. Dr. Mason was asked at what stage in the disease should corticosteroid therapy be introduced. He suggested it was often possible to identify a situation when the inflammation had settled to a degree which could be controlled by relatively small doses of corticosteroid and when structural damage was not yet extensive.

Sexual Problems

Patients had to be persuaded that the menopause was a change in life and not the end of life, said Mr. D. B. BROWN (Chelmsford). Explanation of how to adjust to the few physiological and the many psychological problems of this age was usually all that was required. If simple advice, aspirin, and sedatives failed to relieve the distress of the menopausal flushes, oestrogens should be given for several months, rather than for a few weeks. Advice should also be given on the use of vaginal lubricants during coitus, and on contraception. Up to the age of 45, Mr. Brown favoured the use of the contraceptive pill, but an intrauterine device was very suit-

able for those older than this, in whom its lesser efficiency was counterbalanced by less frequent ovulation.

Mr. R. H. BOYD (Chelmsford) said that impotence in middle-age required more careful assessment than in younger men, in whom it was almost always psychogenic. Interruption of established rhythms of sexual activity was a frequent cause of sexual difficulty. Physical causes included frontal and pituitary tumours, pernicious anaemia, local ischaemia, and, above all, diabetes. So far as psychological factors were concerned, reasons included wives with faded attractions and increased libidos, and the tendency of accountants and business men to go to bed with the wrong sort of figures. He believed a wise attitude to the inevitable effects of age was shown by a countryman of his acquaintance who after marrying a much younger woman as his second wife, said: "It may take longer, sir, but I don't grudge it time."

The final lecture of the meeting was given by Professor Sir EDWARD WAYNE (Gloucestershire), who spoke on retirement. This was an important subject when it was remembered that the expectation of life for a man aged 65 was now 13 years and for a woman aged 60 was 21 years, and that one in seven of the population were above the

usual ages of retirement. This was a problem particularly for the present generation of middle-aged people, who had been brought up with the view that work was a social responsibility and, having had experience of the Depression, might fear that retirement differed little from unemployment. The problem, which was really one of disengaging without undue psychological or financial deprivation, varied in pattern with the social class. For the worker one of the greatest stresses might be the loss of companionship with associates at his job, which now so often involved close team-work. Sometimes retirement was a relief to the man, but was a great strain to his wife, who now had her husband at home all day.

For the professional man, Sir Edward felt that it was wise to beware of retiring to the district with happy memories of sunny holidays, to live near—but not with—close relatives or friends, to remember that the chance of illness of one or other spouse was high (therefore avoid a large house with a large garden, far from the shops), and to be prepared to face the death of a partner. If financially possible, there was much to be said for retirement two or three years earlier than was officially enforced, to allow more time for the achievement of one's plans.

NEW APPLIANCES

New Bone Needle

Mr. B. HELAL, consulting orthopaedic surgeon, Chase Farm Hospital, Enfield, writes: A bone needle was designed to facilitate research into the intraosseous venous circulation. One of these needles is still in use after five years. It has been introduced into bone more than a hundred times.

The needle consists of a 6-in. (15-cm.)

cannula, 5/32 in. (4 mm.) in diameter, into which can be locked a trocar which has a large handle at its proximal end (Fig. 1). These together form at the point of the needle a self-tapping screw, 1 in. (2.5 cm.) in length. The needle is inserted by making a 3/4-in. (6-mm.) stab wound through the skin. It can then be introduced through the cortex of any bone (Fig. 2). Once the screw has

bitten into the bone no force is required to advance the needle.

It can be used to withdraw blood or marrow from the medullary bone or to introduce radio-opaque dye to outline bone sinusoids or the deep veins of the limb. The screw end of the needle helps to prevent any leak back of dye. At any time the trocar can be withdrawn and the needle advanced to pick up a core of bone for biopsy. When connected to a manometer it has been used to take direct measurements of marrow pressures.

In summary, its advantages are its strength, which is a guard against accidental breakage in the bone, and the large bore of the cannula through which bone contents can be aspirated with ease and radio-opaque dye introduced without difficulty, the screw end helping to prevent leak back of the dye. Its large handle allows it to be manually introduced with great ease, and once the screw has taken hold no force is required to advance the needle, so that accidental overpenetration is avoided. It appears to be popular with my general surgical colleagues for transosseous venography.

This needle is being made by the London Splint Company.

I am indebted to Mr. H. R. Vincent, instrument curator at Chase Farm Hospital, Enfield, for making the prototype for me.

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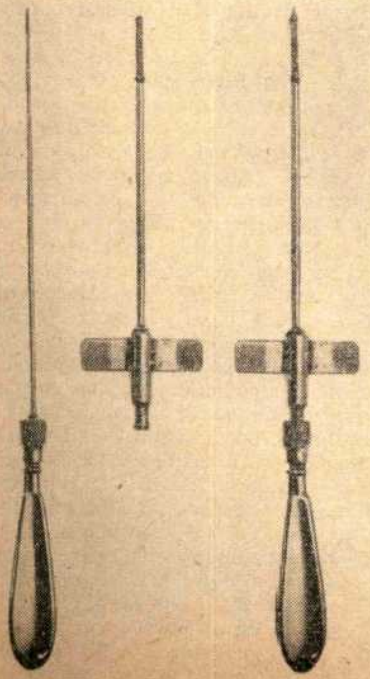


FIG. 1



FIG. 2

Correspondence

Letters to the Editor should not exceed 500 words.

Deaths from Tuberculosis

SIR,—Despite current optimism, many patients in Britain suffering from tuberculosis die unnecessarily and avoidably. During the past few years cultures from patients with organisms resistant to one or more of the standard antituberculosis drugs (streptomycin, P.A.S., and isoniazid) have been sent to a central register for these cases. By 31 December 1965, out of 1,257 patients with cultures resistant to all three drugs, 33% had died and 23% had obtained negative sputum.¹ Among the 1,170 patients whose cultures were resistant to only two of the standard drugs the results were scarcely better.¹ These figures are appalling and the public health danger obvious.

Using the "reserve" or second-line drugs available, several studies have shown that the sputum can be rendered negative in 80–95% of patients whose cultures were resistant to the three standard drugs^{2–5}; during observation for periods up to five years afterwards few patients have relapsed. These results have been obtained in centres where physicians have taken particular interest in such problems. The patients themselves are often unenthusiastic, uncooperative, persistent self-dischargers, drunks, or psychopaths; the drugs are frequently unpleasant and need careful control for toxicity; and the possible combinations of drugs need precise and

critical appraisal, with the help of expert bacteriological studies. Much experience, time, patience, and persistence are required.

Treatment will often fail when undertaken in centres with comparatively little experience of these problems. This was shown during a co-operative study in a number of centres in 1963, when 103 out of 117 patients given "reserve" drugs failed to complete 12 months of treatment.⁶ Three years later the results seem little better.

Surely, Sir, patients suffering from drug-resistant tuberculosis should be treated in special centres, as others have advocated.^{7,8} Otherwise the present disturbingly low cure and high death rates will continue.—I am, etc.,

Ware Park Hospital,
Ware, Herts.

A. PINES.

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"Big Spleen" Disease

SIR,—The article by Dr. P. J. S. Hamilton and others (30 September, p. 823) and the one by Dr. D. S. Pryor (same issue, p. 825) advocating splenectomy should not go unchallenged. In both papers it is suggested that in areas where malaria is endemic this infection may be responsible for some cases of massive splenomegaly. Our experience in Ibadan, Nigeria, is that the majority of patients in whom there is no evidence of other disease respond well to continuous suppressive therapy with proguanil 100 mg. daily. After a year's treatment their anaemia is corrected, the spleen is considerably reduced in size, and there is a great improvement in body weight and well-being. The relationship is obscure, as these patients have neither overt clinical malaria nor an increased parasitaemia; we think the mechanism is rather one of an abnormal immune response to repeated infection. Our results of continuous treatment for three to five years in 40 patients will shortly be published.

Dr. Hamilton and his colleagues discuss the dangers of splenectomy, but had little trouble in their seven cases. On the other hand, Dr. Pryor had one immediate and two late deaths in his group of 15 splenectomies

(an overall mortality of 20%). Others¹ have reported a similar high mortality, and our experience that death from cerebral malaria occurred in a person who before splenectomy had an apparent high resistance is supported by the finding of reduced resistance after splenectomy in chimpanzees.²

Our purpose here is to suggest that continuous malarial suppression therapy should be the treatment of choice in unexplained splenomegaly in malarious areas. Splenectomy should be considered only when at least one year's treatment has been ineffective.—We are, etc.,

E. J. WATSON-WILLIAMS.

Department of Clinical
Haematology,
The University and Royal Infirmary,
Manchester 13.

N. C. ALLAN.

Department of Haematology,
The Western General Hospital,
Edinburgh.

A. F. FLEMING.

King Edward Memorial Hospital,
Subiaco, Western Australia.

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North America Interview Board

SIR,—Dr. C. C. M. Watson (14 October, p. 114), referred to the campaign to coax emigrant doctors to return to Britain. May I relate my experience of the recruiting team that toured America?

On 11 October I received a circular letter from the British Post in Edmonton informing me that the team would be in Banff on 14 and 15 October, and in Calgary on 16 and 17 October. If I wished to interview them, would I please phone the Post for an appointment. This I did, to be told to phone the team direct. An evening phone call to Banff failed to find any of the team available. On 16 October I was in Calgary and went to the hotel where the team was in residence. A phone call from the foyer to a suite above was answered by a deputy—"What is your specialty?" On being told general practice, the interest ceased and no interview could be arranged before 5.30 p.m., and only then if I was definitely interested in returning to Britain.

Having been in general practice in Britain for 16 years I feel I gave the National Health Service a fair trial, hoping year by year that conditions would improve. I was keen to know if the conditions had changed for the better, and if so in what way. These questions remain unanswered, and the only conclusion I can draw is that the answers would not have been favourable. We emigrants await with interest the report of the team's work.—I am, etc.,

J. STANNERS.

Medical Centre,
Daysland, Alberta,
Canada.

SIR,—On 12 October I received a letter from the British Government Office in Edmonton notifying me that the British Ministry of Health board would be in Banff on the next two days, that is to say 13 and 14 October, and in Calgary on 15 and 16 October. The letter stated that the aim of the doctors' extensive North American tour "is to meet those doctors (with whom they have already established contact), who, as U.K. citizens, qualified in Britain and are now considering returning to that country to work." The letter continued: "They have not asked my assistance in that principal object, but they have asked me to 'pass the word around' that they would also be glad to have a chat and an exchange of views with any doctor (and his wife) in the above British category who would like to meet them—even though he has not the slightest intention of returning to Britain to practise."

Several questions arise from this letter: Why did not this board contact the British doctors in Alberta instead of leaving it to the Trade Commissioner to do so at the last minute?

Why was not adequate time given for the recipients to act?

Why should they meet in Banff, a town with a population of 3,000 people with nine doctors, only two of whom are British? Why not Edmonton, the provincial capital, 250 miles away, a city of 360,000 with many

British doctors, a teaching hospital, and several British residents who are not yet on the *Register*?

Surely the committee, had it taken the job at all seriously, would have visited Edmonton in central Alberta. As it was it moved 77 miles from Banff to Calgary on the only road out of the resort (other than the one to Jasper, which is 180 miles to the north and which has two British doctors). If this committee had been interested in discussing the whys and wherefores of immigration or re-immigration of doctors in Alberta it would have made more effort to contact us.

In short, Sir, we bring the activity of this committee (or lack of it) to your notice because we do not feel that it is getting as much information as could have been acquired by a carefully worded questionnaire. Also the poor geographical location, in Alberta at any rate, and the complete indifference in contacting people, would seem to us to suggest this expedition is little more than "window dressing" on the part of the Ministry of Health, and a very pleasant trip by the committee at the British taxpayers' expense.—We are, etc.,

C. D. ELTON.

I. W. M. WRIGHT.

University of Alberta Hospital,
Edmonton, Alberta,
Canada.

Acrylamide Poisoning

SIR,—In view of the recent paper by Drs. T. O. Garland and M. W. H. Patterson (21 October, p. 134) we feel we should report the preliminary results of a study of acrylamide neuropathy in baboons. Acrylamide was shown by D. D. McCollister and his colleagues¹ to be toxic to a variety of experimental animals, including monkeys, but pathological changes in the nervous system were not demonstrated. Only in rats, subsequently studied by P. M. Fullerton and J. M. Barnes,² has it been established that there is a toxic degeneration of the peripheral nerves. From the present work it is now clear that peripheral nerve degeneration also occurs in primates.

Six adult baboons (*Papio hamadryas*) were given acrylamide by mouth in a daily dose of 10–15 mg./kg. After six weeks the animals began to show mild weakness of the lower limbs. After eight weeks some clumsiness of the hands was noticeable, and the animals began to lose their normal cry. By 12–15 weeks there was severe bilateral weakness affecting the facial muscles and the muscles of mastication as well as the muscles of the limbs. Ataxia was usually so severe that an animal could sit upright in the cage only by propping itself up with its arms. At this stage the tendon reflexes were absent. Appreciation of pinprick in the hands and feet was never completely abolished, but some loss of tactile and joint sensation may be inferred from the fact that animals would drop objects from the hands without being aware of it. Sphincter disturbance of the type described in rats poisoned by acrylamide was not seen.

Electromyography confirmed the presence of widespread denervation in the distal muscles of the limbs. Maximal motor conduction velocity in the median nerve was reduced by 30 to 40%, and sensory action potentials from the fingers disappeared as the disease progressed.

Pathological studies have confirmed the presence of extensive peripheral nerve de-

generation involving both motor and sensory nerves, and affecting particularly the distal parts of the longest nerve fibres. Damage to the recurrent laryngeal nerves was conspicuous in all animals. While the pathological changes were mainly of the Wallerian type, occasional segmental demyelination was present and changes in paranodal myelin were relatively common. The brains of affected animals have not yet been examined, but preliminary studies of three spinal cords and their dorsal root ganglia have not shown significant neuronal loss or demyelination of fibre tracts.

Two animals are still alive one year after stopping poisoning, and both have greatly improved clinically. Electromyography and nerve biopsy are being used to follow the time-course of peripheral nerve regeneration and remyelination in these animals.—We are, etc.,

A. P. HOPKINS.

R. W. GILLIATT.

Institute of Neurology,
London W.C.1.

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Oral Contraceptives and Dental Care

SIR,—The hypertrophic gingivitis of pregnancy, which is thought to be due to hormonal changes, is also seen in the patient on the "pill." In dental practice it is normal to see the slightly puffy appearance of the gums and marginal soreness.¹ Lindhe and Björn² studied 115 women aged 18–35 who were taking oral contraceptives. They observed the same pattern of gum lesions which are reported by Orban.³ Following a study of 1,002 women Mohamed S. Gridly⁴ gave a full account of the gingival condition in pregnant women.

The dental problem is that the disordered arrangement of the delicate tissues round the necks of the teeth may progress to acute infection (Vincent's disease or trench mouth, now referred to as acute ulcerative gingivitis) or the changes may become chronic, leading to pyorrhoea. With proper oral hygiene and routine attention to diet the patient can usually prevent either of these conditions. Occasionally, the hypertrophy of the gum tissue leads to a tumour. This is benign and the epulis clears up when the menstrual cycle is re-established.

The proper care of the expectant mother is so important that this group of patients is given special priority by the National Health Service. They are given the same relief from statutory payments as children. Although I should not like to see the day when the question "Are you on the 'pill'?" is added to the dental estimates form (the existing footnote threatens persons who make false declarations with a fine not exceeding £100 or three months' imprisonment or both), I do now find myself looking for gingivitis in my young female patients.

There has been so much written about the side-effects of the oral contraceptive that I should like to have the opportunity to draw attention to the need for the pseudo-pregnant to take extra care of their teeth. The old wives' tale—"for every child a tooth"—has some truth, for, although the rate of dental caries may not increase severely, dental disease

becomes an acute problem in the neglected mouth. Interviewing 222 women who were attending the Queen Victoria Maternity Hospital at Adelaide, Fanning, Barrett, and Cellier found that of these 57% thought they had no trouble with their teeth or gums.⁵ In fact of this group of 125 patients 75 were in urgent need of treatment and 46 required treatment of a routine nature.

We should therefore add to our list of warnings given to the patient for whom oral contraceptives are prescribed that she will need regular dental care.—I am, etc.,

Manchester 21.

D. N. BARBER.

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Psychotropic Drugs

SIR,—We should like to reply to the criticism of our views which has been expressed by Dr. P. J. Dally (28 October, p. 233), and to extend more constructively the discussion on the place of controlled trials of treatment in psychiatry. In his criticism Dr. Dally accuses us of confusing and oversimplifying the subject by failing to differentiate between endogenous depression and other psychiatric conditions. If he re-reads our letter (14 October, p. 108) he will see that we specifically excluded such confusion by pointing out that the M.R.C. trial,¹ which showed phenelzine to be valueless in endogenous depression ("depression as defined in the terms of that trial") must not be taken to show that phenelzine was necessarily valueless in other conditions.

However, the essential problem which interests us, and is of considerable importance to all psychiatrists and to doctors generally, is the problem of the satisfactory evaluation of psychotropic drugs, particularly the antidepressants. The British taxpayer is currently spending something approaching £5m. per annum on antidepressants, and it would seem reasonable to suggest, as has been done by the Dunlop Committee, that scientific evaluation should be attempted before this figure is further increased. Uncontrolled observations, even by experienced clinicians, are not really enough; we know that most depressions get better anyway, regardless of the treatment used. Various studies have found rapid marked improvement in up to 83% of non-psychotic depressive persons given placebo tablets. One wonders how much higher this percentage might become if the placebo were backed by the faith and enthusiasm of some therapists. When the non-specific sedative effect of phenelzine is added also the figure may well go up to 95% or more. We put forward this view, not in any offensive spirit, but as a serious argument in favour of the controls which we feel to be essential in this difficult field. It might be relevant also at this point to recall that claims for other treatment techniques in non-psychotic depression—for example, those often made by experienced psychotherapists—may equal the claims made for the drugs. Psychotherapy has been used for over half a century without really satisfactory evaluation. Are we going to drift into the same

appalling position with respect to drugs such as the monoamine oxidase inhibitors?

We would agree with Dr. Dally that it may not be easy to carry out controlled trials of the necessary high standard. Blackwell and Shepherd² have recently clearly illustrated some of the difficulties, and one of us has reviewed³ the chaotic state of affairs which is resulting from the publication of many drug trials which are not of sufficient technical quality. But it must be clearly understood that this present chaos is not to be used as an argument against controlled trials, but rather as an argument for the carrying out, in psychiatry particularly, of better controlled trials.

We agree with Dr. Dally that the Medical Research Council could help considerably to improve the present unsatisfactory position. While it was far from perfect, the M.R.C. trial was perhaps the most reliable of the antidepressant drug trials carried out in this country, and several features of its design seem to us to recommend themselves for future trials of treatment in other psychiatric conditions. It would be presumptuous to attempt to advise the Council on finance, but it is known that the drug companies spend considerable sums on the financing of small and often unsatisfactory trials which are carried out by doctors acting individually or in small independent groups. We feel that there are several important arguments to be advanced in favour of larger, multi-centre, and more impersonal trials such as those run by the M.R.C. Perhaps the drug companies and the Council could co-operate over this. Certainly something needs to be done.—We are, etc.,

PETER LEYBURN,
A. O. A. WILSON.
PIERS C. ROBSON.
JOHN LE GASSICKE.

St. George's Hospital,
Morpeth, Northumberland.

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Q Fever Endocarditis

SIR,—Cardiac involvement in Q fever has been recognized in a number of cases reported in recent years from Britain. Although these reports indicate a growing awareness of Q fever as a cause of endocarditis, there is often considerable delay in reaching the diagnosis. We here report another case, diagnosed after death, which illustrates the clinical and pathological features and poor prognosis of the disease.

In March 1964 the patient, a gardener 44 years of age, presented with a mild febrile illness and dry cough. His family doctor detected signs at the left base and pulmonary disease was confirmed radiologically. No radiological evidence of cardiac abnormality was present either at this time or four weeks later, when there was clinical and radiographic clearance of the lung lesion. Malaise, lethargy, and increasing dyspnoea persisted. The ankles became swollen and transient rash was noticed during this period. At the end of May, when next seen, his condition had deteriorated to the extent that cardiac failure was beyond doubt. He was afebrile at this time and showed mild icterus with purpuric rash on the thighs. There was clinical and radiological cardiomegaly with manifestations of aortic incompetence. Slight hepatosplenomegaly was de-

tected, and air entry was diminished at the right base.

There was mild hypochromic anaemia (Hb 12 g./100 ml), leucopenia (2,600/cu. mm.), with neutropenia (364/cu. mm.), and thrombocytopenia (70,000/cu. mm.). The anaemia remained at this level throughout the course of the illness but there was considerable fluctuation of the leucocyte count (700 to 12,000/cu. mm.) and of the platelet count (5,000–67,000/cu. mm.). Multiple blood cultures were taken and failed to establish a bacterial diagnosis. Serum bilirubin varied between 1.2 and 2.7 mg./100 ml, serum alkaline phosphatase was constant at 20 K.A. units, serum protein 6.8 g./100 ml, serum albumin 3.0 g./100 ml, and serum globulin 3.8 g./100 ml, with electrophoretic evidence of hypergammaglobulinaemia. The maximum blood urea was 54 mg./100 ml, and moderate albuminuria was constantly present.

Because of the severity of the disease, intensive antibacterial therapy (penicillins and streptomycin) was started immediately after the first series of blood cultures had been taken. Death occurred on 14 June after progressive deterioration.

Since the diagnosis of Q fever endocarditis was considered possible, precautions were taken to minimize the danger of infection of personnel concerned in the necropsy. This revealed bilateral pleural effusions, each of 800 ml., and bilateral bronchopneumonia. The heart weighed 490 g., all chambers being dilated. The aortic valve was distorted and calcified, and several friable vegetations arose from the fused cusps and adjacent aortic sinuses. Histological examination of the vegetations showed many microcolonies of haematoxyphil bodies. The peritoneal cavity contained almost 2 l. of clear bile-stained fluid, and the liver (1,980 g.) and the spleen (290 g.) showed chronic congestion. The presence of renal and splenic infarcts was confirmed histologically, but the rickettsia-like bodies were not identified in these organs. These findings were considered to be consistent with rickettsial endocarditis, and serological and cultural verification was sought.

Complement fixation tests of serum collected before death showed high titres of antibody to *Rickettsia burneti* antigens (1,024, Phase 1; 2,048, Phase 2), but none (<8) to epidemic typhus or psittacosis-group antigens. *R. burneti* was isolated from 10⁻⁴ dilution of approximately 10% suspension of heart valve by intraperitoneal inoculation of guinea-pigs—that is, at least 10⁵ I.D.₅₀ per gramme tissue.

It seems probable that Q fever caused the febrile illness with pneumonia in March 1964, and that endocarditis was established at that time. The subsequent course of illness was fairly typical,¹ except in the absence of fever, until the final stages of disease. Thrombocytopenia was particularly severe. Hypergammaglobulinaemia was present, and is typically found in these cases of chronic Q fever. Serological tests provide the best method of diagnosing these cases during life, and should be performed when, as in our case, blood cultures are negative. As in the present case, rickettsiae may also be isolated from unfixed vegetations, but this is a hazardous procedure which should not be attempted without safe laboratory and animal-house facilities.

The usual source of Q fever in this country is domestic animals or their excreta or birth-products, inhalation being the common route of infection. In the present case a gardener had been using untreated farmyard manure as a fertilizer a short time before the onset

of symptoms. Because of the gravity of Q fever endocarditis, which may not reliably be eradicated by the available rickettsiostatic drugs, it would seem advisable for patients with known or suspected damage to heart valves, or who have undergone cardiac surgery, to avoid contact with fertilizers based on farmyard dung as well as more obvious contact with sheep and cattle.

Rickettsial antigens were kindly provided by Professor M. G. P. Stoker (Phase 1) and by Dr. C. M. P. Bradstreet (Phase 2).

We are grateful to Dr. A. W. B. Edmunds for permission to report this case.

—We are, etc.,

D. C. LAMB.
N. R. GRIST.

Darlington Memorial Hospital,
Darlington.

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Restrictions on Doctor in South Africa

SIR,—A copy of your leading article (26 August, p. 512) and the letter from Lord Adrian and others (p. 556) were sent to me by airmail, and I greatly appreciated the terms of both the leading article and the letter. I regard both as fair comment. It may therefore seem strange that I have not written to you.

In the first place I did not feel free to do so because I was awaiting the outcome of an interview between the Minister of Justice and a deputation consisting of the Chancellor, the Chairman of the Council, the Principal and Vice-Chancellor, and myself as head of the University department in which Dr. Hoffenberg is employed. This deputation had correspondence with the Minister, who requested several memoranda which took time to prepare. As a result the interview has only just taken place, as has been reported in the South African press.¹ I therefore now feel free to comment.

However, now that I can comment I find myself reluctant to wash South African linen outside the Republic, I propose, therefore, to limit my own comment to the public press of South Africa.²

I have chosen the public press because I believe this to be a matter of common justice. The extent to which it involves international principles such as academic, scientific, and professional freedom is very deep and important, but primarily it is a civic matter which reflects many centuries of the history of democracy.—I am, etc.,

J. F. BROCK.

Department of Medicine,
University of Cape Town,
South Africa.

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Case or Person?

SIR,—Emboldened by views expressed by Lord Adrian,¹ Sir Francis Fraser,² and recently by Lord Platt,³ I wish to comment on a case report from the Royal Postgraduate Medical School (28 October, p. 222) of a "case" of Crohn's disease in a patient with coeliac disease. Herein case No. 204058 is presented as an Irish housewife aged 34 at the time of her death. This non-person was

investigated with the thoroughness and brilliance that one expects and admires from this group of workers.

The absence of any personality profile of this patient, who spent some months in hospital, is, however, to be deplored not only on general grounds but for more specific reasons. Firstly, knowledge of her personality make-up would in my experience have exposed the personality characteristics so often described in psychosomatic disorders,⁴ and this would have produced a bias towards the correct diagnosis of Crohn's disease as opposed to the suspected intestinal lymphoma. Laparotomy might not then have been indicated. Secondly, it is conceivable that this patient had only one disease—Crohn's—for, on the one hand, there was no evidence pointing to the date of its onset, and, on the other hand, we already know that severe villous atrophy has been previously observed in Crohn's disease.⁵ Further, it is known that in dermatitis herpetiformis⁶ and in rosacea⁷ varying degrees of jejunal mucosal atrophy have been found in three-quarters of a series of the former and in one-third of a series in the latter. This association of skin and intestinal mucosal disorder would hardly surprise an embryologist. The discovery of these intestinal changes certainly enlarges the concept of these skin diseases, but no one would suggest that these patients had two diseases. Partial villous atrophy has been described in ulcerative colitis⁸ and in an increasing variety of conditions. The normal dynamics of mucosal replacement in the upper intestine presents an astonishing phenomenon, and a survey of its abnormalities in a greater number of conditions—including psychological stress and psychosis—could lead to a recognition of some of the determinants of these mucosal changes.

I certainly do not decry the importance of chemical and other organic studies at every level in diseases in which psychosomatic factors are present (Dr. G. L. Engel, 7 October, p. 56). Nevertheless, man is not the sum of his chemical processes. Case No. 204058 was a woman, and one must regret that her social and psychological history was not described.—I am, etc.,

London N.W.8. HUGH GAINSBOROUGH.

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Thyroid Hormone and Catecholamines

SIR,—Dr. E. Grunwaldt (14 October, p. 109) rightly points out that experimental evidence in man and animals is available which suggests that thyroid hormone does not augment the actions of catecholamines on the cardiovascular system. He does not point out, however, that there is a considerable body of opinion that is in favour of such a relationship between thyroid and autonomic activity, and which believes that the failure to demonstrate it in experimental situations is due to lack of a suitable model system.

Exaggerated responses to catecholamines in thyrotoxic patients have been demonstrated.¹ Peripheral manifestations of hyperthyroidism in the cardiovascular system and in the eyes (lid lag and lid retraction) have been shown to be reduced or abolished by sympathectomy and by sympathetic blocking drugs.^{2,3} The efficiency of a pure beta-adrenergic receptor blocking drug in reducing thyrotoxic tremor⁴ and tachycardia⁵ has also been demonstrated. There is no convincing evidence that thyroid hormone increases plasma or tissue levels of catecholamines, but Brodie *et al.*⁶ have shown that it produces a rise in tissue adenylyl cyclase activity. It is tempting to suggest that this would lead to increased stimulation of cyclic 3',5' adenosine monophosphate by catecholamines, and this would explain increased responsiveness to normal levels of catecholamines in hyperthyroidism. The possible relationships between catecholamines and cyclic 3',5' adenosine monophosphate especially on heart muscle has been extensively reviewed.⁷

This increased sensitivity in thyrotoxic patients to catecholamines might explain why certain beta-adrenergic receptor blocking drugs that possess intrinsic sympathomimetic activity may fail to reduce thyrotoxic tachycardia, whereas similar drugs that do not have this particular activity can be employed successfully in the same patient.⁸—We are, etc.,

R. C. HILL.
P. TURNER.

Department of Clinical Pharmacology,
St. Bartholomew's Hospital,
London E.C.1.

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Complication of Thyroid Cancer

SIR,—We were very interested to read the review by Dr. K. E. Halnan and Mr. P. H. Roberts of nine patients with paraplegia caused by spinal metastases from thyroid carcinoma (26 August, p. 534), and, as their search of the literature revealed very few cases, we thought it would be of interest to record another case.

A 13-year-old African male was admitted to hospital with a history that he had been in good health until three weeks prior to admission. He then developed pain in the lower lumbar region radiating into both knees. Accompanying this he noticed he was having increasing difficulty with walking and his gait was unsteady. He had no bladder or bowel symptoms. Examination showed a well-built boy with a keloid neck scar. No abnormality was noted in the systemic examination of any system except in the C.N.S., where there was a paraplegia in extension with weakness, increased tone, and bilateral extensor responses, but no wasting, fasciculation, or sensory loss was detectable. Investigation showed a normal blood picture, alkaline phosphatase 31 King-Armstrong units, E.S.R. 30 mm./hour, and normal chest x-ray. Lumbar

puncture showed clear fluid under normal pressure, with increased protein of 120 mg./100 ml., normal sugar, and a white cell count of less than 1/cu. mm. An x-ray of the lumbar spine was normal. A myelogram showed a complete block at the level of T8. The neck scar was the result of a thyroidectomy performed in December 1962, and the histology report at that time was reported as being possibly malignant.

This boy was operated on by Mr. L. F. Levy, and a laminectomy was performed at the level of T7, T8, and T9. An oval tumour measuring 1½ in. by 1 in. (3.5 cm. by 2.5 cm.), apparently extradural in site, was easily lifted from the dura with extensive bleeding. Postoperatively he made an uneventful recovery and is walking quite satisfactorily. Microscopy of this tumour suggested metastatic carcinoma from the thyroid gland.

Dr. Malcolm Ross reviewed the old sections and reported on the present one, and gave his opinion that both showed thyroid carcinoma.—We are, etc.,

A. C. B. WICKS.

G. K. T. HOLMES.

Department of Medicine,
University College of Rhodesia,
Salisbury, Rhodesia.

Warming Blood

SIR,—The letter from Dr. B. Philpott and Dr. I. P. Slee (14 October, p. 111) refers to Grant Laboratories' standard J.B.1 water bath. Several of your readers have had some difficulty in tracing us under this title, so I should like to confirm that we are the makers of the bath.—I am, etc.,

C. H. CHAPMAN,
Managing Director,
Grant Instruments (Cambridge) Ltd.
Cambridge.

SIR,—Dr. B. Philpott and Dr. I. P. Slee point out in their letter (14 October, p. 111), quite rightly, that there are other methods of warming blood besides that described by Mr. F. Alladine and myself (23 September, p. 787), and describe the use of a laboratory water bath.

Although primarily we were interested in producing a compact instrument which was convenient in use and unobtrusive in the theatre, there were essential considerations of safety, some of which should be mentioned. A second safety thermostat was thought to be essential to avoid overheating in the event of failure of the control thermostat, and this is lacking in the unadapted laboratory instrument. Moreover, the latter instrument, in a size convenient for theatre use, relies upon convection currents to mix the water, with the coil of blood overlying and very near the heating element. We decided that this was at least potentially hazardous, and so isolated the heating element and made use of a water impeller to reduce temperature gradients. Lastly, there was added a built-in thermometer, and the compartment to contain the coil was made of transparent material to permit continual observation of the blood in the coil. Of course, these considerations have added to the cost, but they have also added an essential element of safety.

We were aware of the potential hazards of vinyl plastic drip extensions, which are not normally warmed. Pharmax Ltd., who now market the Seeco Haemoguard, as the machine is now called, are also producing

the ready-made coils, and have been very helpful in providing the appropriate information on the British standard for testing this material—that is, B.S.2463, 1962. Animal tests for toxicity are carried out on the extracts of tubing heated to 85° C.—well above the temperature used in warming blood. So far we have no evidence of harmful effects on the blood, or on patients receiving warmed blood, though the results of further testing will be published in due course.—We are, etc.,

PATRICK J. BENNETT.

Middlesex Hospital, F. ALLADINE.
London W.1.

Fallacies in Four Fevers

SIR,—In your issue of 28 October (p. 237) Drs. J. P. Telling and J. M. Morfitt draw attention to the fact that the latest edition of the joint memorandum of advice to school medical officers was in 1956 and that the periods of exclusion given are now thought by some to be excessive. If an authority is required to support advice for shorter periods this may be found in that invaluable but too little known handbook *Control of Communicable Diseases in Man*.¹ An introductory note states that "The substance of this report has been accepted by the Ministry of Health for England and Wales, the Scottish Home and Health Department. . . ." The advice given for the four fevers is as follows.

Measles. Isolation: From diagnosis until 7 days after appearance of rash. . . . Schools should not be closed nor classes discontinued.

Rubella. Isolation: None, except where contacts include a woman in early pregnancy; then under direction of the attending physician for 5 days after onset.

Mumps. Isolation: For 9 days from onset of swelling; less if swelling has subsided.

Chicken-pox. Isolation: None; exclusion from school for one week after eruption first appears and avoid contact with susceptibles.

This advice cannot be regarded as unduly oppressive.—I am, etc.,

J. C. KELSEY.

Central Public Health Laboratory,
London N.W.9.

REFERENCE

- Gordon, J. E., *Control of Communicable Diseases in Man*, Report of American Public Health Association, 1963, 10th ed. New York.

Teaching the Behavioural Sciences

SIR,—Everyone, I am sure, will welcome the timely leading article entitled "Teaching the Behavioural Sciences" (21 October, p. 123), and will support the suggestion that this teaching should run as a thread throughout the preclinical and clinical courses. Much of the teaching will be focused upon the daily lives and activities of both the sick and the healthy where clinicians from various specialties are already engaged in the study and management of the behavioural aspects of health and disease. This is in fact the essence of paediatric practice.

The omission of child health from the list of clinical subjects concerned with the behavioural sciences was presumably unintentional; there have been many paediatric contributions to this topic. Examples readily come to mind: teaching about normal and abnormal development,¹ stimulating the prac-

tice of developmental paediatrics,² encouraging the visiting of children in hospital,³ and awakening concern for the welfare of the under fives.⁴

It is to be hoped that curriculum committees will not forget the contributions which child health has made, and will continue to make, to the study of the behavioural aspects of health and disease in childhood and the subsequent application of these lessons in practice.—I am, etc.,

KENNETH HOLT.

Institute of Child Health,
University of London,
London W.C.1.

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M.A.O. Inhibitors and Headache

SIR,—Perhaps I can throw some light on Dr. C. A. H. Watts's observation of monoamine oxidase inhibitor headache without hypertension (28 October, p. 238).

Severe headache, the result of acute but often short-lasting hypertension following monoamine oxidase inhibitor antidepressant drugs, is well documented.^{1,2} There is much evidence in these cases to suggest that the elevation of blood pressure and consequent headache are due to cumulative inhibition of intestinal amine oxidase, with a resultant "enhanced" pressor action of various biologically active amines (dopamine, and particularly tyramine), which occur naturally in certain foodstuffs³ (cheese, Marmite, broad beans, chicken livers, etc.). Although I believe that hypertension probably accounts for the majority of severe headaches following monoamine oxidase inhibitor drugs and cheese, it is clear that other mechanisms may be involved, since severe headache has occurred without such changes in the blood pressure.^{4,5}

During the natural maturation of cheeses, although conditions favour the formation of tyramine,⁶ histamine is occasionally formed⁷; histamine is present more constantly and in much greater concentrations in Marmite.⁸

Monoamine oxidase inhibitors are known to interfere with histaminase,⁹ an enzyme which inactivates histamine; for this reason the physiological actions of exogenous histamine derived from foodstuffs or endogenous histamine or both, the release of which is promoted by organic bases present in many foods, may be greatly augmented and produce clinically observable effects. The histamine hypothesis is supported by Mathov's¹⁰ observation that over 50% of a series of asthmatics he studied showed clinical deterioration following treatment with a variety of monoamine oxidase inhibitors.

Histamine may induce a variety of toxic manifestations in humans, including severe occipital headache, hypotension, anginal pain, blurred vision, colic, diarrhoea, urticaria, "asthmatic breathing," and excessive secretion of salivary, gastric, and lacrimal glands, etc. It is easy to see how one or several of these "toxic symptoms" could occur following monoamine oxidase inhibitors and cheese.

In the individual case the particular toxic symptoms following monoamine oxidase inhibitors and cheese, Marmite, or other foods probably represents the algebraic summation of the respective and often antagonistic physiological actions of tyramine or histamine and perhaps other biologically active amines (the concentrations of these naturally occurring amines in any foodstuff depends upon manufacturing processes, and has been shown to be subject to considerable variation), as well as the degree of gut amine oxidase inhibition, which if complete may allow comparatively large quantities of tyramine or histamine or both to be absorbed into the bloodstream and produce spectacular toxic effects.

In Dr. Watts's patients who experienced headache without hypertension histamine rather than tyramine seems the likely cause. The simultaneous clinical occurrence of other histamine-like effects, as enumerated above, would support such a contention. In these cases the logical antidote would be antihistamines.—I am, etc.,

ALAN J. COOPER.

Department of Psychiatry,
University of Edinburgh,
Edinburgh.

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Railroading in Retinal Vessels

SIR,—There has been considerable correspondence lately regarding the appearance of the retina at death. Mr. A. C. Gillies (28 October, p. 236) writes about the late Dr. Gulland, of Edinburgh, who made "discoveries," including railroading in the retinal vessels, around 1922.

To Mr. Gillies, and to others interested, I must state that Dr. C. Usher, who did so much original work in the eye department at Aberdeen, gave a full description of the fundus appearances in *Ophthalmic Review*, 1896.¹—I am, etc.,

CHARLES COCKBURN.

Department of Ophthalmology,
Royal Infirmary,
Aberdeen.

REFERENCE

- Usher, C. H., *Ophthalm. Rev.*, 1896, 15, 339.

Multiple Sclerosis in South Africa

SIR,—Dr. J. F. Kurtzke in his letter (16 September, p. 739) about my paper on multiple sclerosis in South Africa (17 June, p. 724) commented that it would be most helpful if I could provide a further table for the 72 European immigrants from Europe to South Africa who had their first symptoms of multiple sclerosis in South Africa, listing the ages at immigration, at onset of symptoms, and at prevalence day. He suggested that such a table might provide further information on the hypothetical "incuba-

tion" or latent period between presumed disease onset and symptom onset.

These are the details that Dr. Kurtzke requests:

Age at Immigration, Onset of Symptoms and at Prevalence Day of 72 European Immigrants (Multiple Sclerosis)

Age at Immigration	Age at Onset	Age at Prevalence Day	Age at Immigration	Age at Onset	Age at Prevalence Day
2	35	35	26	36	40
3	21	25	26	32	47
3	29	40	26	35	56
5	23	35	27	29	31
7	41	53	27	37	67
7	30	62	27	29	59
9	39	48	28	45	51
10	18	42	28	43	49
10	18	61	28	39	41
15	40	54	28	36	61
16	33	52	28	43	66
16	37	40	29	30	47
16	23	42	29	40	54
17	25	38	29	32	39
17	29	51	30	41	44
17	29	38	30	43	56
17	30	51	31	38	41
17	34	43	31	42	43
18	38	58	32	43	44
18	23	37	33	41	67
18	35	61	33	35	46
18	24	65	33	40	52
19	35	68	34	38	46
19	42	59	35	47	49
20	29	40	37	39	50
21	23	69	39	40	53
21	31	59	39	41	48
21	24	31	39	54	69
22	29	30	40	42	51
22	35	40	41	44	47
22	28	53	41	52	64
23	24	25	42	47	53
24	34	43	43	47	55
24	44	58	47	49	58
25	46	52	52	53	56
25	38	47	53	54	62

I hesitate to make any comments as to how the table should be interpreted.

Dr. Kurtzke is impressed, as I was myself, by the high proportion of English-speaking South African born multiple sclerosis patients who had visited Europe (46 out of 101), 39 of these before the onset of multiple sclerosis. Nevertheless, when the English-speaking South African born controls are matched by sex, age group, and by birthplace of parents the "expected" number to have visited Europe (40.5) is not significantly different from the actual number (46). The controls must be matched by birthplace of parents because a higher proportion of the English-speaking South African born multiple sclerosis patients (40 out of 101) than of the English-speaking South African born population at risk matched for age and sex only (23.5), had both parents who had been born in Europe.

It is not therefore correct for Dr. Kurtzke to take only the remaining 55 out of 101 English-speaking South African born and divide 55 by the total English-speaking population at risk, bringing the rate down from 11 per 100,000 (101 out of 925,000) to 6 per 100,000 (55 out of 925,000) as compared with the rate for the Afrikaans speaking of 3 per 100,000.

Dr. Kurtzke suggests that multiple sclerosis is perhaps caught in the high risk area and brought to the low risk area rather than vice versa. This, I agree, is a possible explanation—however, the low risk areas are those that particularly favour infection early in life. Furthermore the higher risk in the English-speaking than in the Afrikaans-speaking white South African born and the higher risk in the upper economic class that Kurtzke has shown occurs in the United

States¹ and which has also been reported in the United Kingdom^{2,3} suggests that multiple sclerosis is, like poliomyelitis, an infection which if caught early in infancy is not likely to cause neurological damage. If, on the other hand, the infection is delayed the pre-disposed may develop the syndrome we know as multiple sclerosis.—I am, etc.,

Port Elizabeth,
South Africa.

GEOFFREY DEAN.

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- 2 Registrar-General's Decennial Supplement, *England and Wales (1951). Occupational Mortality*, Part II, Vol. 1, Commentary, 1954, p. 33. H.M.S.O., London.
- 3 Miller, H., Ridley, A., and Schapira, K., *Brit. med. J.*, 1960, 2, 343.

Mushroom-worker's Lung

SIR,—I read the article on mushroom-worker's lung by Dr. A. Sakula (16 September, p. 708) with much interest, for mushroom production is a local industry. In particular, I was struck by the similarity of Case 3 to a patient I saw in 1965, and I am prompted to give details.

He was aged 55, and he had worked on a mushroom farm for three years in connexion with the spawning process. Late in April 1965 he developed troublesome breathlessness, together with non-productive cough, anorexia, tiredness, and weakness, and he had to stop work. A chest x-ray showed extensive fairly coarse reticulonodular shadowing throughout both lungs, with some coalescence but no hilar lymphadenopathy. The nature of his work raised the suspicion that these appearances were due to extrinsic allergic alveolitis, but precipitin tests with his serum were negative. A Mantoux test (1:100) was also negative. Biopsy of a scalene node, however, showed changes considered to require recognition as sarcoidosis.

The diagnosis in this patient was proved only by biopsy. Undoubtedly a few individuals with occupational lung disease do have negative precipitin tests, but in the present state of knowledge when this is so I suggest that sarcoidosis does need to be excluded, histologically if possible, either by examination of a scalene node or a Kveim test. As Dr. Sakula recognizes, both types of illness are not dissimilar, and one knows that in some instances they can be differentiated only by biopsy methods. I feel it would have been interesting to have studied tissue from his Case 3. Admittedly this patient was tuberculin positive, but, although tuberculin sensitivity is frequently depressed or absent in sarcoidosis, it is not invariably so.

Dr. J. Edgar Morison, of the department of histopathology, Belfast City Hospital, recently re-examined the scalene gland obtained from my patient (personal communication). He confirmed that it showed granulomatous lesions indistinguishable from Boeck's sarcoidosis. He points out that, in contrast with sarcoidosis, and as far as is known at present, granulomatous lesions in farmer's lung do not extend beyond the lung. Presumably this also applies to other forms of allergic alveolitis of similar aetiology. The occurrence of acute sarcoidosis in this mushroom worker probably was fortuitous and coincidental, but it is impossible not to speculate that it might have resulted from exposure to something at work, as in beryl-

liosis. However, there is no indication of what this could have been, and there have been no other comparable cases.

Finally, in Dr. Sakula's Cases 1 and 2 an association between their work with mushrooms and the respiratory symptoms certainly appears likely, although the precipitins in their blood might possibly have resulted from dust exposure during previous jobs. The indications are that serum precipitins, once induced, can persist for eight years at least.—I am, etc.,

C. T. B. ADAMS.

Coleraine,
Northern Ireland.

Stress Incontinence

SIR,—I have been interested to read the recent articles on the treatment of stress incontinence by electrical stimulation of the levator muscles by Mr. T. Moore (16 September, p. 740) and Mr. S. A. Vincent (19 August, p. 498).

Mr. K. P. S. Caldwell (21 October, p. 175) states that he has observed a "lift forward" of the bladder neck on stimulation and that "this fits in well with the theories of continence put forward by Jeffcoate and the Liverpool school."

I should like to draw these authors' attention to my own articles.¹⁻³ In these the development of the operation of colpo-fixation for the worst cases of stress incontinence in the female was based upon the physiological theories enunciated in Liverpool. This operation, which elevates and fixes the upper urethra to effect a permanent cure, was followed up in more than a hundred cases over periods of two, five, and ten years to show a symptomatic and anatomical cure rate of over 80% after 10 years.

The treatment of this condition by electrical stimulation of the admittedly weak and attenuated levator and perineal muscles must therefore stand the test of time such as this in order to show itself of more than temporary benefit and thus to prove its worth.—I am, etc.,

Manchester.

K. VERNON BAILEY.

REFERENCES

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- 2 ——— *ibid.*, 1956, 63, 663.
- 3 ——— *ibid.*, 1963, 70, 947.

Glycosuria in Pregnancy

SIR,—I would appreciate an opportunity of replying to Dr. T. Lind (24 June, p. 841).

Dr. Lind states that the glucose oxidase method of estimating glucose in urine is valueless for small quantities up to 5 mg./100 ml.

He will change his mind if he cares to dip a Clinistix paper into a 5 mg./100 ml. glucose solution and obtains a distinctly blue colour; he will also get a recognizable change with 2.5 mg./100 ml. The oxidase test is more sensitive than Clinistix, since the reaction continues to completion, and detection of colour change is enhanced by the use of a spectrophotometer with appropriate colour filter. He also criticizes the method because of the loss of glucose which occurs when urine is treated with charcoal. I observed this loss early in my study of the method, and solved the problem it involved by the two-tube

method described in my first paper (8 May, 1965, p. 1209). The first tube contained urine alone, the second had 10 mg./100 ml. glucose added. The difference in the extinction readings represented 10 mg./100 ml. glucose, whatever the glucose loss, which in any case rarely exceeds 20%.

This loss, incidentally, is partly due to charcoal adsorption and partly to residual antienzyme action. I agree that occasionally charcoal fails to remove the antienzymes, rendering it impossible to analyse the glucose in the urine. Such cases are excessively rare, and only a few specimens were discarded for this reason out of thousands examined. As for persistence of yellow colour in the filtrate, this can occur if a poor quality of activated charcoal is used, but in any case it does not invalidate the method provided the urine antienzymes are substantially reduced. The optical density of the yellow filtrate can be read and an appropriate deduction made from the final extinction readings. Variation in results due to time and temperature, and differences in results when identical samples are analysed, are in my opinion due to lack of experience in the technique. I have trained large numbers of technicians who all eventually emerged from the early stage of crudity of performance.

I think the best evidence of the remarkable ability of the glucose oxidase method to detect slight variations in urine glucose level is revealed in the glucose tolerance test studies described in Table VI of my first paper. In each of the eight cases a rise of a few mg. is demonstrated in the normal volunteers following ingestion of 50 g. glucose, and the suggestion that this is due to experimental error is less than tenable.

Dr. Lind thinks that the hypoglycemia and hyperglycemia of pregnancy are figments of my imagination born out of experimental error. I would therefore invite him to examine the chart (Fig. 4 in my second paper) illustrating the shift in the histogram values from pre- to post-delivery populations. Does he seriously consider that the raised incidence of hypo- and hyperglycemia in the pre-delivery group is due to technical errors which mysteriously evaporate after delivery?—I am, etc.,

Pathological Laboratory,
Kitwe Central Hospital,
Kitwe, Zambia.

J. FINE.

Aspirin and Gastric Bleeding

SIR,—It is surprising that in your recent leading article on aspirin and gastric bleeding (30 September, p. 810) there was no consideration of the role of gastric acidity in the pathogenesis of this troublesome side-effect.

It has been known for many years that the irritant effect of sodium salicylate can be reduced by the simultaneous administration of sodium bicarbonate, and more recently there have been a number of observations suggesting that the irritant effect of aspirin might be, similarly affected by changes in gastric acidity. Thus the incidence of bleeding from the stomach is reduced when aspirin is given with an excess of sodium bicarbonate,¹ and it has been found that patients with atrophic gastritis or achlorhydria are less susceptible to aspirin-induced bleeding (23 January, p. 137).

Aspirin is a relatively strong acid, and in the unbuffered gastric juice will be largely in the form of the undissociated molecule. At the pH of the plasma and in the intra-

cellular fluid the concentration of the molecule will be very small indeed, and the drug will be almost entirely in its anionic form. The pharmacological effects of the salicylates are related to the intracellular concentration of their anions, and by "non-ionic diffusion"; this is related to the pH gradient across the cell membrane. There is no reason to suppose that the gastric mucosal cells are different from other cells with respect to their intracellular pH, and so the pH gradient across the luminal membrane may be very high indeed. Even at moderate levels of gastric acidity, say pH 5, the concentration of the acetylsalicylate anion within the mucosal cell may be as much as 100 times the concentration of the anion in the gastric juice. With this in mind it is scarcely surprising that haemorrhage from the gastric mucosa may follow the ingestion of aspirin, even when this is given in the soluble form after meals.¹

If this interpretation is correct aspirin-induced gastric bleeding should be preventable by maintaining the gastric pH at or even higher than pH 7 while the drug is being absorbed. Merely to buffer the acetylsalicylate itself is not sufficient; the hydrochloric acid produced by the stomach must be neutralized as well to an extent beyond that normally achieved in the treatment of duodenal ulcer. The use of sodium bicarbonate for this purpose will render the urine alkaline and increase the excretion of salicylate. However, it may well protect the cells of the distal tubule and collecting duct from a similar pH gradient and destructively high intracellular concentration of salicylate anion as is found in the gastric mucosa.—I am, etc.,

Royal Infirmary,
Edinburgh.

JOHN M. BONE.

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- Wood, P. H. N., Harvey-Smith, B. A., and Dixon, A. St. J., *Brit. med. J.*, 1962, 1, 669.
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Conservative Treatment of Fractured Femur

SIR,—It is the practice in many centres to treat grossly comminuted fractures of the femur either in a Thomas splint or in some sort of sliding traction. This leads to many difficulties in nursing, pressure sores, bowel and urinary trouble, venous thrombosis, and hypostatic pneumonia. In addition, frequent adjustment of the splint, weights, etc., is necessary, and if the patient survives the leg may still be malunited and short. This is a genuine problem, especially in hospitals where such cases are perforce treated in busy general surgical wards.

For the past two years I have treated such cases, when over 70 years of age, as follows. Shortly after admission, once conservative treatment has been decided upon, a well-padded cast is applied from toes to mid-thigh. An antirotation bar (wood) is incorporated on the sole and just above the knee. Two plaster loops are also made just below the knee, so that traction can be easily applied. The limb is held, correctly rotated, and shortening of 1 in. (2.5 cm.) is accepted, and indeed attempted, thus allowing "controlled collapse."¹ The fracture is generally quite sticky in four weeks, when the plaster is converted to a below-knee one. Active

movement is insisted upon from the start. In six weeks the plaster is removed, and by the tenth week the patient is at home with partial-weightbearing crutches. The results achieved are gratifying, and both patient and nurses are spared time and trouble.—I am, etc.,

DOMINIC S. COLBERT.

Regional Hospital,
Galway, Ireland.

REFERENCE

- Charnley, J., *The Closed Treatment of Common Fractures*, 1961, 3rd edition, pp. 9 and 139. Edinburgh.

Vasectomy for Contraception

SIR,—In his letter (11 November, p. 354) Mr. Donald Young refers to the opinion of counsel which the Medical Defence Union obtained in 1949 regarding the legality of sterilization. The Union's legal advisers are no longer of the opinion that an operation for sterilization is unlawful, whether it is performed on therapeutic or eugenic grounds or for any other reason, provided there is full and valid consent to the operation by the patient concerned. It must be emphasized, however, that this opinion is not based on a statute or judicial authority, because the proposition has never been tested in the courts. Nevertheless, our legal advisers are confident that a surgeon who complies with a patient's request that he be sterilized would not be committing an offence.

Attention was drawn to this change in view in my letter published in your columns (25 June 1966, p. 1597) and on p. 14 of the Union's 1966 Annual Report.—I am, etc.,

PHILIP H. ADDISON,
Secretary, Medical Defence Union.

London W.C.1.

Fluoridation of Water Supplies

SIR,—Dr. R. L. Kerr (21 October, p. 176) takes the Minister of Health to task for doing his duty in trying to improve children's teeth and save them from unnecessary pain. Then followed the usual anti-fluoridation letters. The facts are that there are over 50 million people drinking fluoridated water (1 p.p.m.) in North America and about two million in Britain. Fluoridation is the official policy of the Ministry of Health, the Public Health Authority in the U.S.A., the World Health Organization, and, so far as I know, every reputable health authority in the civilized world. It also has the blessing of the law. In the Lower Hutt case, which was brought before the Judicial Committee of the Privy Council, Lord Upjohn, giving the judgement of the Board, said:

"The water of Lower Hutt was no doubt pure in its natural state, but it was very deficient in one of the natural constituents normally to be found in water in most parts of the world. The addition of fluoride added no impurity and the water remained not only water but pure water and it became a greatly improved and still natural water, containing no foreign elements."

—I am, etc.,

Beckley,
Rye, Sussex.

C. G. LEAROYD.

REFERENCE

- The Times*, 23 July 1964.

** This correspondence is now closed.—
Ed., B.M.J.

"No Change"

SIR,—In the recent ballot 1,783 votes have been cast in favour of stopping all merit awards, 1,670 voters are in favour of continuing the present system, 4,639 voters desire a change away from the present method of distributing these awards, and 5,272 voters support the continuation of some system of merit awards. The writer of your leading article on this subject (21 October, p. 128) interprets these figures as a mandate for "no change."

These figures indicate that there should be rewards for special merit within the hospital service, and that the present system is not acceptable. The Council of the Association has in fact been given a clear mandate to initiate reform of the merit awards system. The comments of the *B.M.J.* leader writer on this subject appear to me to conflict with the voting figures. Any Council member who has been tempted to accept a like conclusion should consider the effect that failure to tackle this problem resolutely may have on the substantial majority of the voters in this ballot who consider a change is necessary.—I am, etc.,

JOHN K. MCCOLLUM.

Newcastle upon Tyne.

SIR,—I have read your leading article (21 October, p. 128) "No Change" with great interest: I agree with you that it is a pity that there was only a 50% poll, but this is generally attributable to the confusion caused by the ineptness of the question pattern and to the fact that the poll was held at the height of the summer holiday season. There is no doubt that a public announcement by the Council to the effect that these defects arose by accident rather than design is called for and might do something to restore confidence in the Central Consultants and Specialists Committee.

With regard to the leading article it would appear that, concerning question five, 5,272 replies could be in favour of some revised system of merit awards, but in addition to this number a further 4,639 state definitely that the present system requires change. There can be no doubt whatsoever as to the statistical significance of the similarity between these two sets of figures.

From the figures quoted on the results of the ballot on the questions asked, there is no justification whatsoever for saying there is a mandate for "no change." To say that there is to be deliberately misleading, and I am most surprised that you should lend yourself to this sort of thing.—I am, etc.,

Winchester.

C. REMINGTON-HOBBS.

* The change most widely called for was for less or no secrecy. Only 1,532 of those who replied made this comment—about one-fifth—or about 10% of those to whom the questionnaire was sent.—ED., *B.M.J.*

Night Visits

SIR,—I was most interested to read of Dr. J. D. Wigdahl's failure to submit forms in respect of night visits to patients who

were very ill or subsequently died (23 September, p. 802). This of course will be common practice on the part of general practitioners who feel that to submit their one and only "bill"—especially for such a paltry sum—at perhaps the most worrying and harrowing time in a patient's life is somehow morally wrong, out of place, badly timed, and rather debasing to one's Hippocratic oath. Of course the Ministry of Health realizes this and it knows that such a form sent for signature to the patient is tantamount to telling the patient that his general practitioner is a bit of a rogue, completely untrustworthy, and not just the sort of fellow anyhow to be treating a near and dear relative, perhaps their only child, at such an important and dreadful crisis in life—and after all wasn't the Ministry right, because perhaps the patient died?

Similarly, in our area we have been having the most infuriating trouble over having "emergency treatment" paid for. Each form is scrutinized in minute detail, many letters are written to general practitioners asking why they didn't treat their patient four miles away, when they didn't even know their patient had lacerated his hand at work, or fallen over the cliff. This again has resulted in some practitioners stating that they are not going to submit another "emergency treatment" form; another victory for the Ministry.

The answer is a vastly different type of Health Service, where payment is by item of service, which will almost double the general practitioner's income; where there will be incentives to acquire new knowledge and skills, because he will be paid extra for using them; where he will be relatively free from the stupid petty frustrations of today; where he will have time to do his work, because those who are able to do so will have to pay to see him, and pay for part of the cost of their drugs (about 70% of the population); and where he will regain the respect of his hospital colleagues, because he will have time to do worthwhile work in view of the fact that much of the other kind of work will disappear.

Does all this seem like Utopia? Well, you can take it from me that it is; unless in desperation we have the courage to fight for what is worth while.—I am, etc.,

Peterhead,
Scotland.

G. I. LUMSDEN.

Service Overseas

SIR,—May I be permitted to comment on views expressed at the first meeting of the Committee on Overseas Affairs (*Supplement*, 21 October, p. 20)?

It will be recalled that many of these views, in so far as they relate to the emergent countries of Africa, formerly British Colonies or Protectorates, were admirably stated in your leading article under the title "Africa's Need."¹ These were commented upon subsequently.^{2,3} As regards service overseas after retirement, this proposal was raised in a private report⁴ passed to officials of the Department of Technical Co-operation in July 1964. For several reasons, some quite obvious, a period of two years abroad for a doctor aged 65 might be too exacting, though clearly the Medical Adviser to the Ministry of Overseas Development was wholly justified in remark-

ing that "three months would neither be useful nor economically feasible." This aspect of overseas aid offers some scope for further discussion, but the overall response among retired general practitioners or consultants from the United Kingdom is unlikely to be significant.

Consideration also by the Committee of a letter from the Ministry of Overseas Development raised points that might have far-reaching importance. They could ultimately permit a much more realistic approach to the urgent needs of clinical departments overseas and relate them far more closely to requirements in Britain within the National Health Service. Furthermore, it is well known that there have been instances, perhaps isolated, where doctors returning from overseas have been resettled at a disadvantage. Officials of the Ministry of Overseas Development know quite well it would always be very difficult to prevent disadvantageous resettlement inasmuch as advisory appointments committees at regional board level in this country could never be influenced directly in favour of a returning expatriate.

It seems therefore abundantly clear that doctors in all grades should in future go overseas only on secondment, and it is hoped the Committee will henceforward urge the establishment of central sources of supply of manpower for overseas to be administered at each regional level by a small standing overseas committee.—I am, etc.,

Liverpool 1.

H. VINCENT CORBETT.

REFERENCES

- ¹ *Brit. med. J.* 1965, 1, 939.
- ² Corbett, H. V., *ibid.*, 1965, 1, 1308.
- ³ *ibid.*, 1965, 2, 364.
- ⁴ A Report on a Private Visit to Uganda and Kenya during May, 1964.

Signs for Doctors' Cars

SIR,—I note that the Private Practice Committee (*Supplement*, 7 October, p. 9) intends to issue 2,000 self-adhesive signs for doctors' cars.

Having had a supply of these since the Annual Representative Meeting, I would urge that this plan be scrapped, as they are quite useless. Owing to the transparent background and small size the words are almost invisible beyond the car's bonnet. Please think again, Private Practice Committee, as a matter of urgency.—I am, etc.,

Edgware,
Middlesex.

A. D. MANNING.

Points from Letters**Menace of Smoking**

Dr. E. B. GROGONO (Woodford Green, Essex) writes: I read your leading article (23 September, p. 753) and hoped that so important a topic might provoke a lively correspondence. Twenty thousand avoidable deaths in Britain per year are surely more important than many of the rare topics we discuss in the *B.M.J.* I believe that, as a profession, we have set a moderately good example, and I have the impression that cigarette-smoking is far less common among students, medical students in particular, than it was 20 years ago.

Obituary Notices

M. DAVIDSON, M.A., D.M., F.R.C.P.

Dr. M. Davidson, a leading authority on diseases of the chest, and consulting physician to Brompton Hospital and the Miller General Hospital, London, died in hospital on 8 November. He was 84.

Maurice Davidson, son of the late Professor Alexander Davidson, emeritus professor of pathology in University College, Liverpool, was born in Liverpool on 30 August 1883. From Liverpool College he entered Trinity College, Oxford, where he graduated B.A. in 1905 with second-class honours in physiology in the final school of natural science.

He went to University College Hospital, London, for his clinical training, and graduated B.M., B.Ch. in 1908, taking the M.A. the same year. He held early appointments at University College Hospital, Huddersfield Royal Infirmary, and the Hospital for Sick Children, Great Ormond Street, before becoming medical registrar and tutor at St. George's Hospital. He proceeded D.M. in 1912 with a thesis on gastric secretion in anaemia and chlorosis, with reference to their relation to gastric ulcer. A year or so before the outbreak of the first world war he moved to Southsea, where he was honorary medical officer to the home for convalescent children. His service as a temporary captain in the R.A.M.C. during the war took him to Gallipoli, Sinai, Egypt, and Palestine.

After demobilization Davidson settled in London, taking the M.R.C.P. in 1919, and being elected F.R.C.P. in 1927. In 1920 he was appointed physician to the Miller General Hospital, where he became senior physician, and, ultimately, consulting physician. In the same year he was appointed physician to outpatients at the Royal Waterloo Hospital for Children. Appointed assistant physician at the Brompton Hospital in 1921, he became full physician a few years later and, subsequently, consulting physician. For five years he was dean of the medical school at the Brompton. He was also consulting physician to St. Luke's Hospital, Chelsea, St. Stephen's Hospital, and the Western Ophthalmic Hospital; honorary consulting physician to the Papworth Village Settlement and the Manor House Hospital; and associate physician to the Royal Marsden Hospital.

When the British Medical Association held its Annual Meeting at Oxford in 1936 he served as a vice-president of the section of tuberculosis. For a number of years he represented the section of medicine (of which he had been president) on the editorial committee of the Royal Society of Medicine, being for a time honorary editor of the *Proceedings*.

He was a senior member of the Thoracic Society.

In 1952-3 Davidson delivered the FitzPatrick Lectures before the Royal College of Physicians of London on "Medicine in Oxford, a Historical Romance." The lectures were subsequently published in book form. He was the author of *Cancer of the Lung and other Intrathoracic Tumours*, published in 1930; *A Practical Manual of Diseases of the Chest*, which appeared in 1935 and ran through several editions; and *The Diagnosis and Treatment of Intrathoracic New Growths*, printed in 1951. He also wrote in 1954, jointly with Mr. F. G. Fouvray, *The Brompton Hospital: The Story of a Great Adventure*, and in the following year he produced a handsome volume entitled *The Royal Society of Medicine: The Realization of an Ideal, 1805-1955*, a book written to commemorate the 150th anniversary of the founding of the Medical and Chirurgical Society of London, now the Royal Society of Medicine. *Memoirs of a Golden Age* appeared in 1958, and *Destiny and Freevill* in 1962. He was editor and contributor of *Medical Ethics: A Guide to Students and Practitioners* (1957). He also contributed articles on diseases of the lung to the second edition of the *British Encyclopaedia of Medical Practice*.

In 1913 Davidson married Gretchen Lucy, youngest daughter of the Rev. H. Bolton Smith, vicar of Wymering, Hampshire, and they had a daughter and three sons. His wife died in 1963.

F.H.Y. writes: If during the period after the war a ballot had been taken among the staff of the Brompton Hospital, both medical and lay, to decide who was the most-loved member, Maurice Davidson would undoubtedly have headed the poll. He was a good physician of the old school, careful and kind, slow to criticize and quick to praise. No one could have been quicker to condemn, and, if possible, remedy an injustice. His hospital patients adored him. His appearance was always neat, but he affected an old-fashioned type of dress, and his square bowler hat was familiar to us all. Before he was ill he was often seen walking along Harley Street wearing a speckled straw hat and a pair of sponge bag trousers. I remember well being telephoned by him in the 'fifties to ask if I could lend him a pair of white canvas spats, which he wished to wear at a wedding. He had searched London unsuccessfully to find a pair to replace those which were worn out. In some respects he was unlucky, as owing to the long period in which there were no vacancies on the staff he did not become a physician at St. George's; but this was to the advantage of the Brompton Hospital and the Royal Society of Medicine, as it gave him more time to devote himself to their welfare. He was devoted to Oxford, his Alma Mater, and this led him to choose Oxford as the subject of his FitzPatrick Lectures. The Royal Society of Medicine owed much to him, and in 1965

showed its appreciation by electing him an honorary Fellow. His home life was very happy, but saddened by the death in an accident of a much-loved daughter, and later by the loss of his wife. During the last few years he was dogged by ill-health, losing a leg by amputation, and subsequently had trouble with his eyesight; this latter was a sore trial to him as he was a voracious reader. But he took misfortune bravely, and was always cheerful. With his death we have lost an English gentleman in the best sense of the word.

F. BOYES KORKIS, M.B., CH.B.
F.R.C.S., F.R.C.S.ED.

Mr. F. Boyes Korkis, consultant surgeon to the Metropolitan Ear, Nose and Throat Hospital, Hillingdon Hospital, and Hayes and Uxbridge Cottage Hospitals, died as the result of an accident at sea on 7 November. He was 53.

Frederick Boyes Korkis was born in England at Rickmansworth, Hertfordshire, on 21 December 1913, but on the death of his father was taken at an early age to live in New Zealand, and hence became known to many of his friends and associates as a New Zealander.

He received his early education at King's College, Auckland, before entering Otago University medical school, where he graduated M.B., Ch.B. in 1937. The following year he came to England, where he trained under Lionel Colledge at the Throat, Nose and Ear Hospital, Golden Square, and obtained his Edinburgh Fellowship in 1941 and the D.L.O. in 1940. During this time he also met and worked with Scott Stevenson. He then returned to New Zealand, where he joined the 2nd New Zealand Expeditionary Force and served as otologist in Egypt, Palestine, and Italy, attaining the rank of major.

After demobilization Korkis was appointed registrar to the Metropolitan Ear, Nose and Throat Hospital before returning to New Zealand to start practice as assistant ear, nose, and throat surgeon at the Auckland General and Green Lane Hospitals. He soon established a busy and successful practice, and it seems likely that he would have remained in New Zealand had it not been for his earlier association with Scott Stevenson, who encouraged his return to England when a vacancy occurred on the staff of the Metropolitan Ear, Nose and Throat Hospital. He was appointed shortly before the National Health Service was inaugurated in 1948, and he continued to serve the hospital until his



(Elliott & Fry)



death, although its identity was lost within a regional organization when amalgamated with St. Mary Abbot's Hospital. Indeed, he was a most ardent and loyal supporter of the "Met. B.N.T.," and in his capacity as dean never ceased to work and plan for its future, even though many considered that officially its death certificate had been signed. He took the F.R.C.S. in 1949, and became consultant-ear, nose, and throat surgeon to a number of hospitals, including Whittington and Hillingdon, and was also appointed honorary otolaryngologist to the Royal Academy of Dramatic Art and the Royal Society of Musicians.

Fred Boyes Korkis was a man of exceptional ability with a wide range of interests, many of them outside surgery. As a surgeon he was quick, dexterous, and undaunted even by the most fearsome conditions, and his exceptional skill and remarkable *sang-froid* enabled him to impart great assurance and confidence to all within the operating-theatre. His surgical interests were wider than those often associated with his specialty, and embraced the "ear, nose, and throat" in its widest sense. The surgical treatment of malignant growths of the larynx and pharynx was a field in which he demonstrated remarkable skill. His performance of these intricate operations was admired and envied by the many visitors who came to watch him operate. But most of all he will be remembered for his kindness and consideration to all who sought his advice, and for the care and devotion so freely given to his patients.

The same exceptional talents were apparent in his other activities. Thus he showed the most remarkable ability to learn even the most complicated subjects with apparent ease. He never failed an examination for which he studied—his most recent achievement being in wireless telegraphy, in which he obtained the certificate of the City and Guilds radio amateurs examination. He taught himself photography and became an outstanding amateur photographer, using his talent to provide material to illustrate some of his books and articles. He was a prolific and lucid writer, publishing many papers on a wide variety of subjects, but he will be remembered more particularly for his book on *Bar, Nose and Throat Nursing*, published in 1955, and for his latest edition of *Recent Advances in Otolaryngology*, published in 1958, previously edited by Scott Stevenson.

Of recent years he became interested in sailing, and with characteristic enthusiasm set out to master the difficulties and to face the challenge of the sea. He became an enthusiastic member of the Rochester Cruising Club, and it is sad that this activity led to his tragic death.

He is survived by his widow and two young daughters, and an older daughter of a previous marriage, to all of whom we extend our sincerest sympathy.—G. E. H. E.

D. K. ADAMS, M.A., B.Sc., M.D.
F.R.C.P., F.R.C.P.GLASG.

Dr. D. K. Adams, honorary consulting physician to the Western Infirmary, Glasgow, died at his home on 6 November, aged 76.

Douglas Kinchin Adams was born on 29 August 1891. He was educated at Kelvin-side Academy and Glasgow University, and

after a brilliant academic career graduated M.A. in 1910, B.Sc. in 1912, and M.B., B.S. a year later. He became a house-surgeon at the Western Infirmary, Glasgow, with that great pioneer of surgery Sir William Macewen, whom he admired and frequently quoted. During the first world war he served in the Royal Navy, and on demobilization in 1919 he became an assistant to the late Professor T. K. Monro at Glasgow University, and also an extra dispensary physician at the Western Infirmary.

Outstanding among his colleagues in stature and intellect, he acquired a well-merited reputation as a clinical teacher. Keenly interested in diseases of the nervous system, he clarified many of the problems associated with that difficult branch of medicine for graduates and postgraduates alike. Disseminated sclerosis provided a life-long study and the subject for his M.D. thesis, which he was awarded with honours and a Bellahouston gold medal in 1921. He took the F.R.F.P.S.Glasg. in 1919 and the M.R.C.P. in 1926, and rapidly acquired an extensive consultant practice in the west of Scotland. He was elected F.R.C.P. in 1937 and became F.R.C.P.Glasg. in 1964. He was appointed visiting physician at the Ministry of Pensions hospital at Bellahouston, physician in charge of wards at Stobhill General Hospital, and later visiting physician in charge of wards at the Western Infirmary, Glasgow, which post he held until he retired from hospital work at the age of 65, when he was appointed an honorary consulting physician to the Western Infirmary.

"D.K." wrote little, but his few articles were of a high order and always commanded attention. His impact upon the Glasgow School of Medicine came mainly from clear and brilliant clinical teaching, and, as one of the great teachers of his time, he helped countless students over examination hurdles, and won for himself a lasting place in their admiration and esteem.—W. B. K.

C. D. GRANGE, O.B.E., M.B., B.S.
F.R.C.S.

Mr. C. D. Grange, formerly a surgeon at Harrogate and District General Hospital, died on 19 October at his home at Angmering-on-Sea, Sussex. He was 80.

Charles D'Oyly Grange, the son of a doctor, was born on 29 August 1887, and was educated at Leeds University and St. Bartholomew's Hospital, London, qualifying in 1910 with the Conjoint diploma, when he was awarded the Willett silver medal for operative surgery, and graduating M.B., B.S. two years later. After early house appointments at St. Bartholomew's Hospital he took the F.R.C.S. in 1913, and went to Newcastle upon Tyne, where he worked under Professors Morison and Grey Turner. During the first world war he served with the R.A.M.C. as major in charge of the surgical division of the Northumberland War Hospital, and was awarded the O.B.E. for his services. After demobilization he went to Harrogate, where he became surgeon to the Harrogate and District General Hospital (then known as the Harrogate Infirmary), and to the Royal Bath Hospital, Harrogate. He was also consultant surgeon to the Ripon and District Hospital. In 1932-3 he was chair-

man of the Harrogate Division of the British Medical Association. He retired in 1947.

G. N. B. writes: Grange was a versatile surgeon and a kind and charming man who endeared himself to both colleagues and patients. His juniors knew they could always rely on his help and unfailing good humour, and many of them have much to thank him for. He was a genial host, and he and his wife were well known for the warmth of their hospitality. His retirement in 1947 after many years of very hard work gave them both virtually twenty years of well-earned relaxation and happiness. To Mrs. Grange we send warmest sympathy.

E. BURSTAL, M.A., D.M.

Dr. E. Burstal, a Bournemouth general practitioner, died at his home on 12 October, at the age of 88.

Edward Burstal was born in Derby on 23 August 1879, and was educated at Dulwich College and Trinity College, Oxford, graduating B.A. In 1901 he obtained a Commoners Exhibition with honours in natural science and physiology, and for his clinical studies went to St. Bartholomew's Hospital, graduating M.B., B.Ch. in 1904. After early house appointments at St. Bartholomew's and the West London Hospital, he set up in general practice at Staines in 1909. He also held the post of assistant surgeon at the King Edward VII Hospital at Windsor. During the first world war he joined the R.A.M.C. and was major in charge of the medical division 82nd General Hospital, serving for some time in Salonika. After demobilization he proceeded D.M. in 1918, and the following year he left his practice in Staines to take up a practice at Bournemouth, in which he remained until his retirement in 1963. An active member of the British Medical Association, in 1931-2 he was chairman of the Bournemouth Division, and from 1939 to 1948 was president of the Dorset and West Hants Branch.

For recreation he was very fond of walking, especially in the Alps. He took a great interest in English numismatics, and served as president of the Wessex Numismatic Society. In 1908 he married Winifred, daughter of Worsley Battersby, who predeceased him in 1965. They had a son and two daughters.

N. F. A. writes: Dr. Burstal's death removes one more link with what may be considered as the more gracious days of living in Bournemouth, when medicine was practised at a leisurely pace and with a very personal relationship between doctor and patient. He did not value his patients at so many shillings a head—well or ill—and was essentially a family doctor, concerned almost as much with the personal as with the strictly medical problems of his patients. Though not given to suffering fools gladly, he yet possessed great charm and courtesy. He was a true general practitioner, with keen clinical judgement—rightly confident in his own ability, yet ready to seek help from colleagues when need arose. Though not prominent in medical politics, he was active in attendance at clinical and scientific meetings. He will be sorely missed for his bonhomie, clear thinking, and high standard of ethics.

V. G. BEST, M.D.

Dr. V. G. Best, formerly in general practice at Cleethorpes, Lincolnshire, died at his home in Northwood, Middlesex, on 18 July. He was 80.

Victor Greer Best was born at Ballinahinch, Co. Armagh, on 27 June 1887. He was educated at Lurgan College and at Trinity College, Dublin, graduating M.B., B.S. in 1911 and proceeding M.D. shortly afterwards. He served as ship's doctor on the Blue Funnel Line to the Far East before taking up an appointment as house-surgeon at the Grimsby and District Hospital. In 1914 he joined Dr. Walter Fisher in general practice in Cleethorpes. During the first world war he served in the R.A.M.C., and after demobilization with the rank of captain he rejoined the practice in Cleethorpes in 1918, remaining there until his retirement in 1957.

For 30 years he acted as honorary surgeon to the Cleethorpes Division of the St. John Ambulance Brigade, and was a past master of St. Albans Masonic Lodge in Grimsby. A member of the British Medical Association, he was chairman of the North Lincolnshire Division in 1925-6, and president of the Lincolnshire Branch from 1955 to 1957.

Dr. Best was respected and loved in Cleethorpes. He was a good family doctor who not only cared well for his patients but was interested in them as people; his patients were his friends, and for them nothing was too much. I joined him in the practice in 1925, and worked with him in partnership until his retirement. We worked in complete harmony; he was always good tempered, and I recall the years I worked with him with affection and pleasure.

He was a good family man, and took great joy in his daughter and her two children. To his widow, Maude, and to their family we extend our sincere sympathy.—M. C. L.

E. FRASER BROWN, M.B., CH.B.

Dr. E. Fraser Brown, formerly a general practitioner in Moseley, Birmingham, died on 18 September. He was 70.

Elliott Fraser Brown was born in Salisbury on 6 February 1897, and was educated at Monkton Combe School. He received his medical education at the University of Birmingham, qualifying with the Conjoint diploma in 1920, and graduating M.B., Ch.B. in 1924. In the first world war he saw active service as a surgeon probationer sub-lieutenant in the Royal Navy. On being invalided out he joined the First War Hospital at Rubery, Birmingham, after which he continued his training at the university. After qualification he held resident posts at the Queen's Hospital, Birmingham (now the Accident Hospital), and the Birmingham General Hospital. During the second world war he served again as a medical officer in the Royal Air Force. Dr. Fraser Brown was a family doctor in the old tradition who took a very personal interest in all his patients. He was a surgeon in the St. John Ambulance Brigade, and became county surgeon of Birmingham. He was an active member of the B.M.A. and the Christian Doctors Group.

After a life of strenuous service he was forced to retire in 1962 following a serious illness. He moved to South Devon, but still

maintained his interest in medicine, joining the local branch of the B.M.A., sitting on medical boards, and helping his local colleagues.

He will be missed by many, and the sympathy of his patients and of his many friends will go out to his widow, son, and daughter.—M. H. O.

S. S. DATTA, M.D.

Dr. S. S. Datta, for many years senior medical officer at Manor Park Hospital, Bristol, died on 3 November after a short illness. He was 77.

Sukha Sagar Datta was born in Calcutta on 23 May 1890, and came to Britain in 1910. Deciding to take up medicine, he entered Bristol University, graduating M.B., Ch.B. in 1920 and proceeding M.D. in 1931. After early appointments at Bristol General Hospital and Southmead Hospital, he was appointed resident medical officer at Stapleton Hospital (now Manor Park Hospital), where he remained until his retirement in 1956.

Dr. Datta was an active member of the St. John Ambulance Brigade, and taught first aid during and after the second world war. In 1956 he was made an Officer Brother of the Order of St. John. He was elected chairman of the Bristol Borough Labour Party in 1943 and became president of the Bristol Trades Council in 1946. After the second world war he became founder president and life member of the Bristol Indian Association, an organization to promote understanding between students and immigrants from the Subcontinent and members of the British public.

He leaves a widow and two sons, one of whom is a member of the medical profession.

D. D. writes: Dr. Datta was above all a man dedicated to the service of others; he was an idealist with a strong practical streak. He early became a follower of Freud, and after his retirement from Manor Park Hospital continued to keep abreast of post-Freudian developments in psychiatry, particularly in the fields of research in which purely chemical explanations of mental sickness are being pursued. With his death Bristol loses a very remarkable and much-loved man.

W. F. D. BENTON, M.R.C.S., L.R.C.P.

Dr. W. F. D. Benton, clinical assistant in the skin department of Croydon General Hospital, died at the hospital on 10 October after a short illness. He was 66.

William Frederick Douglas Benton, elder son of the late Dr. William Benton, was born at East Ham on 17 February 1901, and received his early education at Chatham House, Ramsgate, and Eastbourne College. For his medical studies he went to St. Bartholomew's Hospital, qualifying with the Conjoint diploma in 1926. He held appointments at Queen's Hospital, Hackney; the Albert Dock Hospital; City Hospital, Nottingham; City Hospital, Plymouth; and was ship's surgeon to s.s. *Queen of Scots*, before settling in general practice at Thornton Heath in 1934. Here he worked for 33 years, except during the second world war, when he served as captain in the R.A.M.C. in India and else-

where. At the time of his death he held the appointments of clinical assistant in the skin department, Croydon General Hospital; medical officer to Waddon Hospital, Croydon; and honorary medical officer to the British Red Cross Society.

He was a member of the local medical committee and of Croydon Executive Council. A member of the British Medical Association, he was chairman of the Croydon Division in 1955-6, and representative at the Annual Meeting in 1956, 1959, and 1962.

His hobbies were many and varied: travel, literature, and the arts, archaeology, swimming, tennis, and golf. Eleven years ago he became a member of the Roman Catholic Church. He was a man of high principles and high ideals. His colleagues and his many patients have lost a friend.

We extend our deepest sympathy to his widow, Delia, and to his brother, who is also a member of the medical profession.—C. R. N.

T. H. McLEOD, M.R.C.S., L.R.C.P.

Dr. T. H. McLeod, a well-known north Norfolk general practitioner, died suddenly on 8 October. He was 74.

Thomas Hawks McLeod, the second son of Professor Herbert McLeod, F.R.S., was born in Englefield Green, Surrey, on 5 April 1893, and was educated at Aldenham School. He studied medicine at St. George's Hospital, London, qualifying with the Conjoint diploma in 1917. He then served in the R.A.M.C. in Mesopotamia until the end of the first world war. On demobilization with the rank of captain he joined the Iraq Health Service, and continued to work in Iraq until 1935, at which time he held the post of civil surgeon, Mosul. In 1936 he came to North Walsham, Norfolk, and settled in general practice, and here he remained until his retirement in 1964. He took a great interest in the St. John Ambulance Association, and was divisional surgeon to the Order of St. John of Jerusalem.

His practice was a busy, single-handed one, and he was helped considerably by his wife, who is also a doctor. "Peter" McLeod devoted all his energies and thoughts to his patients, who held him in high regard. His interests outside his work were shooting, riding, and gardening; and during his later years what leisure time he had was spent in his beautiful garden. He was held in great esteem by his medical colleagues, who could always go to him for advice or help.

Our sympathy goes out to his widow and three children, one of whom is also a doctor.—C. D. H.

P. H. B. writes: Many people—friends, patients, and colleagues—were saddened by the sudden death of "Peter" McLeod. He and his wife, Peggy, had worked in North Walsham for so many years, and with such devotion that they had won the deepest respect and affection. This was amply shown when they retired two or three years ago to the neighbouring village of Worstead. Peter McLeod's dedication to his work left him little time for other distractions. He knew all his patients as only a doctor in a small town can, and his letters to hospital contained not only a careful history and his own clinical findings but human details which made every patient unique. He

regarded his own physical disabilities with detachment and dry humour, and with a loyal confidence in his advisers. We salute the passing of a compassionate man and a greatly loved doctor.

G. LANG, M.B., CH.B.

Dr. G. Lang, formerly in general practice at Potters Bar, Herts, died at the Holloway Sanatorium, Virginia Water, on 27 October, after a long illness. He was 61.

Gerard Lang was born on 8 November 1905, and received his medical education at the University of Edinburgh, graduating M.B., Ch.B. in 1930. After holding house appointments at Edinburgh Royal Infirmary and Leicester Royal Infirmary he settled in Potters Bar, where for over 30 years he was in partnership in general practice, retiring at the end of last year owing to ill-health. He was on the staff of the local district hospital, and was chairman of the Medical Advisory Committee. During the second world war he remained in civilian practice, accepting responsibility for the patients of other doctors on an agreed temporary basis.

He was an active member of the Enfield and Potters Bar Division of the British Medical Association and of Catholic Societies, including that of SS. Cosmas and Damian and the Guild of St. Luke. He leaves a widow and four daughters.—E. W. W. E.

D. P. THOMAS, M.R.C.S., L.R.C.P.

Dr. D. P. Thomas, a former general practitioner in Conway, Caernarvonshire, died in hospital on 18 September. He was 77.

David Page Thomas was born on 13 March 1890, and received his medical education at St. Bartholomew's Hospital, qualifying with the Conjoint diploma in 1915. Shortly after qualification he joined the R.A.M.C., and went to France. During the Battle of the Somme he was gassed, and was invalided home. Later he was posted to Palestine, where he was wounded, and after returning home he was transferred to the Ministry of Pensions Hospital in Bangor. After demobilization with the rank of captain he joined the staff of this hospital in Bangor. In 1921 he entered practice in partnership with the late Dr. M. J. Morgan in Conway. During the second world war, owing to the shortage of doctors and the large number of evacuees in the area, his work was arduous, but he gave his services throughout with courage and devotion.

I first met him in 1950 and was at once enchanted by the warmth of his personality. The better one knew him the more one appreciated his deep knowledge of medicine and his constant interest in modern trends. A skilled obstetrician, he was proud of having received his training at Queen Charlotte's. He had the gift of giving confidence to babies and young children, who always greeted him with affection. Dr. Thomas was a man of great integrity, with a deep sense of his responsibilities and an unfailing love of justice. He was a magistrate, a founder member of the Conway Rotary Club, and a Freemason, being a past master of the Royal Leek Lodge in Bangor. His sterling qualities were combined with a delightful sense of humour, and, what is perhaps rare in many of us, an ability

to laugh at himself. His conversation was always stimulating and easy. A real countryman, he took a keen interest in all country matters, and was recognized as an expert angler and marksman. He will be sadly missed in many homes in Caernarvonshire and Denbighshire, and will always be remembered as the "beloved physician."—G. H.

K. B. JONES, M.R.C.S., L.R.C.P.

Dr. K. B. Jones, who was in general practice in Sheffield, died of leukaemia on 26 July at the age of 42.

Keith Bromfield Jones was born on 28 November 1924, and qualified with the Conjoint diploma in 1951. He set up in general practice in Sheffield, and was also medical officer to several large factories and to the Sheffield College of Education, and was the appointed factory doctor to Sheffield East. He was vice-president of the Yorkshire Liberal Federation and ex-chairman of the Sheffield Liberal Party, as well as serving on the executive council of the British National Temperance League. He also did a great deal of work for the Boy Scout movement. Much of his limited spare time was spent in caravanning, of which, like everything else he took up, he was an enthusiastic supporter.

Those of us who knew Keith Jones as a colleague and neighbour remember his unfailing cheerfulness and good humour, unaffected by his dismay at the state of medicine under the N.H.S., and by his full knowledge of his disease which progressed so rapidly.

To his wife and two children we extend our deep sympathy.—G. R. B. W.

G. C. C. WHARTON, M.R.C.S., L.R.C.P.

Dr. G. C. C. Wharton, a general practitioner in Gloucester for 19 years, died on 3 September while on holiday in Norway. He was 57.

Geoffrey Charles Clegg Wharton, son of a doctor, was born in Oldham on 11 March 1910, and was educated at Malvern College, Manchester University, and Charing Cross Hospital, London, qualifying with the Conjoint diploma in 1939. After holding the post of casualty officer at Charing Cross he set out to gain experience of general practice by taking assistantships successively in Northampton, Hitchin, and Maidenhead. During the second world war he joined the Royal Air Force, and in 1946—the year after his demobilization—he became a partner in a practice in Gloucester, where he remained until 1965. At that time he felt that he could afford to resign from the National Health Service, but he greatly enjoyed clinical work, and continued to exercise his skill by assisting colleagues and in other medical work. Since 1958 he had been secretary of the local medical committee.

Geoffrey Wharton was a genial person who easily made friends. Foremost among his hobbies were golf and travelling, but he was a man of wide interests, including music, wines, antique furniture, railways, and ships. He will be remembered by all who knew him for his sense of humour, his infectious enthusiasm when talking of countries and places he had visited, and above all his happy and kindly outlook.

To his wife, Jennie, and to his two sons we tender our deepest sympathy.—H. G. D.

A. BOWIE, M.M., M.B., CH.B.

Dr. A. Bowie, a general practitioner in Newcastle upon Tyne, died on 2 October at the age of 68.

Andrew Bowie was born in Bonnybridge, Stirlingshire, on 29 October 1898, and was educated at Falkirk High School, whence he joined the 7th Black Watch, 51st Highland Division. He saw service in France during the first world war, and was awarded the Military Medal. After demobilization he entered Glasgow University, graduating M.B., Ch.B. in 1924, and went into general practice in Jarrow, Co. Durham. A year later he moved to Newcastle upon Tyne, where he remained in practice until his retirement in July 1966.

Andrew Bowie was a most human and dedicated doctor with a ready sense of humour. His home was an open door to his patients, who regarded him as a friend and counsellor. It was a privilege to work alongside a man to whom his patients' needs were of paramount importance, and who could always find time to listen to their problems.

He married in 1930, but lost his wife during the second world war after a long and tragic illness. His many friends and colleagues extend their sincere sympathy to his son and daughter, who both nursed him with great affection and courage during the last year.—G. S. A.

Sir JAMES LEARMONTH, K.C.V.O.

C.B.E., LL.D., M.D., CH.M., F.R.C.S.

F.R.C.S.ED., F.R.A.C.S., F.A.C.S.

F.R.F.P.S.GLASG.

A. W. R. writes: Sir James Learmonth's (obituary, 7 October, p. 58) students will remember him as a master of the art of teaching, a teacher without peer. His lectures, obviously prepared with scrupulous care, were delivered with clarity and conciseness, and adorned by his dexterity on the blackboard. His clinics at the bedside were models of the professional art. There was no room for levity in the presence of a sick person, and he insisted on the basic principles of politeness and respect for human dignity. On being called forward to examine a patient, woe betide the student who plunged straight into the traditional "What are you complaining of?" If he did not already know the patient's name he was instructed that a glance at the chart would provide this information. These basic principles of introduction to the medical profession were impressed on the students from the first day in his ward, and were the result of his determination to emphasize that the patient, the central important character on the stage, was a human being and not just another case. He championed the underdog, never failing to encourage the weaker student, never embarrassing him in front of his colleagues. So long as that student was industrious and doing his best, then he regarded it as his bounden duty to produce in him a sound and understanding practitioner. Teachers of the calibre of James Rognvald Learmonth are met only once in a lifetime, and those who were fortunate enough to come under his spell will remember him with gratitude and affection. He was indeed the great master with many disciples.

News and Notes

EPIDEMIOLOGY

England and Wales in Second Quarter

The abridged life table for 1964-6 in the quarterly report for June gives the expectation of life at birth for males as 68.5 years and 74.7 years for females. During the past 10 years the figures have increased by 0.9 years for males and by 1.6 years for females.

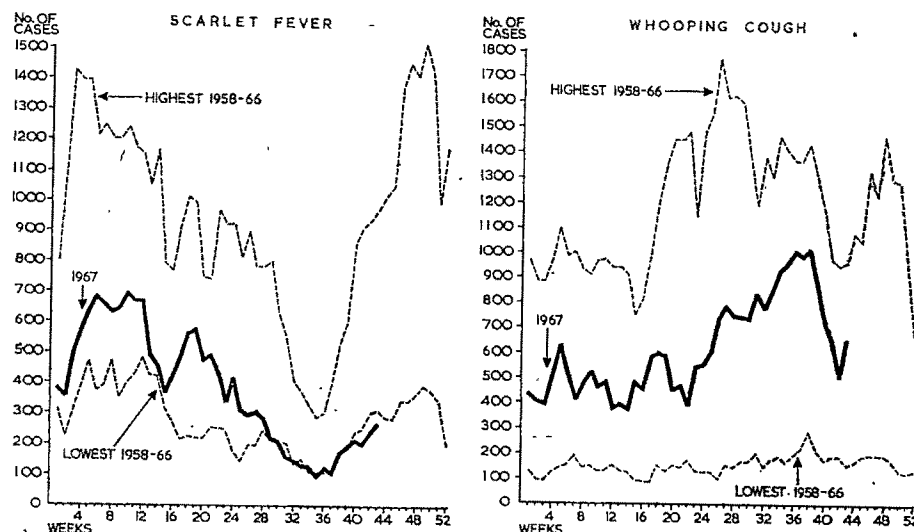
No cases of diphtheria were notified in the second quarter of 1967, but 7,053 cases of whooping-cough were notified. Measles was epidemic, with 130,190 notifications. Other large returns were 7,094 for dysentery, and 5,638 for scarlet fever. Only 6 cases of acute poliomyelitis, 5 paralytic and 1 non-paralytic, were notified. These figures are uncorrected.

The rising trend of emigration to Australia, Canada, and New Zealand continued. The numbers rose from 28,700 persons in the second quarter of 1964 to 43,100 persons in the second quarter of 1967 (Australia 25,600, Canada 13,100, and New Zealand 4,400). In the professional and managerial category the numbers of emigrants rose and those of immigrants fell in comparison with the previous second quarter, giving an estimated loss of 3,000 in the first quarter of 1967 compared with a net gain of 200 in the corresponding quarter of 1966.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of scarlet fever and whooping-cough in England and Wales.

Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 28 October (No. 43) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		1	0	0	0	
Dysentery ..	263	40	157	2	3	307	46	113	8	9
Encephalitis, acute..	6	0		0		0	0		0	
Enteric fever:										
Typhoid ..	6	3	3	0	1	1	1	0	0	
Paratyphoid..	0	0	0	0	0	2	1	0	0	
Food-poisoning	176	32	6	0		98	23	3	0	
Infective enteritis or diarrhoea under 2 years				43	39				25	54
Measles*	1,346	77	34	9	48	8,200	1031	263	178	61
Meningococcal infection ..	3	1	3	0		10	2	4	0	
Ophthalmia neonatorum..	6	0	1	0		21	3	0	0	
Pneumonia† ..	83	7	83	4	3	100	14	133	0	
Poliomyelitis, acute:										
Paralytic ..	0	0	0	0		1	0	0	0	
Non-paralytic	0	0	0	0		0	0	0	0	
Puerperal fever‡	71	28	0	0		63	24	10	0	
Scarlet fever ..	272	39	21	17	4	406	55	32	8	4
Tuberculosis: Respiratory ..	221	58	34	3		199	44	32	6	
Non-respiratory ..	47	10	7	1		25	4	6	2	
Whooping-cough	660	67	48	3	27	501	53	68	6	19

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute..				0						0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	7	0	0	0	0	6	2	1	0	
Influenza ..	7	0	1	0	0	8	0	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..				0				1		
Pneumonia ..	589	106	15	17	3	568	98	23	16	4
Poliomyelitis, acute..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	31	5	2	0	3	40	8	5	1	3
Non-respiratory ..				0	0				0	1
Whooping-cough	1	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	267	53	14	7	10	266	59	21	7	3
Deaths (excluding stillbirths)	9,838	1583	546	113	201	9,896	1660	582	82	154
LIVE BIRTHS	15,092	2528	853	282	439	15,716	2702	900	231	349
STILLBIRTHS	234	27	11			224	43	15		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

‡ Includes puerperal pyrexia.

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

Dysentery	Week Ending	
	27 Oct.	3 Nov.
Cheshire	6	16
Bredbury and Romiley U.D.	0	15
Essex	11	20
Chigwell U.D.	8	10
Gloucestershire	6	11
Bristol C.B.	5	10
Greater London	40	31
Lancashire	46	36
Walton-le-Dale U.D.	0	11
Yorkshire West Riding	53	47
Saddleworth U.D.	6	29
Glasgow	83	63
Edinburgh	20	10
Selkirk County	0	18
Angus County	10	15

Food-poisoning	Week Ending	
	27 Oct.	3 Nov.
Dorsetshire	0	17
Dorchester M.B.	0	17
Greater London	32	29
Lancashire	39	47
Liverpool C.B.	6	12
Glasgow	4	33
Diphtheria		
Stirling Burgh	0	4
Typhoid Fever		
Luton C.B.	0	1
Haverling (London)	0	1
Bradford C.B.	1	1
Glasgow	0	1

Smallpox at Wandsworth

The Medical Officer of Health for the London borough of Wandsworth has sent us the following report on a case of smallpox there:

"On the evening of 16 October a 3-year-old Pakistani girl, recently arrived in this country, was seen in the receiving-room at St. George's Hospital, Tooting, and clinically diagnosed as a case of smallpox.

"The duty doctor notified his consultant physician and subsequently the medical officer of health, and in the early hours of the following morning the child, together with her mother, was admitted to Long Reach Isolation Hospital, Dartford, smallpox having been confirmed by the gel-diffusion test. The mother subsequently developed several small skin lesions from which smallpox virus was grown. She had no constitutional disturbance and her condition was regarded as a highly modified form of smallpox.

"On 20 October the father of the child was also admitted to Long Reach after having become pyrexial. No skin lesions developed and the pyrexia subsequently settled and smallpox has not been confirmed. The little girl is now recovering and both parents are well. Surveillance of contacts in Wandsworth has not so far revealed any further cases."

PARLIAMENT**Ministerial Assurances on Artificial Sweeteners**

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The argument for deferring the permissive use of artificial sweeteners was answered by the Parliamentary Secretary to the Ministry of Agriculture, Fisheries and Food, Mr. J. HOY, in the House of Commons on 9 November.

Use in all foodstuffs except ice-cream is permitted by the Artificial Sweeteners in Food Regulations, which come into force on 1 December. Mrs. JOYCE BUTLER (Wood Green, Lab.) sought to annul the regulations and have the use of cyclamates deferred until further studies were completed.

Mr. Hoy, taking seriatim the objections which were raised in the debate, said the simple answer about the exclusion of ice-cream from the regulations was that artificial sweeteners were forbidden in the ice-cream regulations, 1959; it was part of the compositional requirements and had nothing to do with the safety of cyclamates or saccharin. It was not true that the European Economic Commission had decided that cyclamates had not to be used. All that had been decided was that they would delay harmonization. Four countries would continue to use them, as they were doing now. There had been no announcement that the Food and Drugs Administration in the United States was doing further work on cyclamates, except in the normal process of their work. In this country the Food Additives and Contaminants Committee's recommendation for further work was a common recommendation for all types of additives; it was what was normally done to keep the Government aware of what was happening on a continuous basis.

Mr. Hoy assured the House, on the advice of the Ministry specialists, that cyclohexylamine was not a cancer-causing agent. M.P.s, he said, should not use terms which frightened people. Dicyclohexylamine did not metabolize from cyclohexylamine; it had been looked for but had not been found.

Specifications were laid down in the regulations by reference for the various types of cyclamate, and also—for the first time—for the various types of saccharin. A minimum content of saccharin and cyclamate respectively was laid down for mixed tablets.

Since fresh evidence about the safety of cyclamates was submitted, the question of their use had been twice referred back to the Food Additives and Contaminants Committee. Both reports from the committee recommended that there was no hazard to health in permitting the use of cyclamates—conforming to satisfactory specifications—in food. Since the advice of the Government's experts had been almost exactly echoed by that of the Joint Expert Committee of the Food and Agriculture Organization and of the World Health Organization, the Government were on fairly safe ground.

The use of cyclamates was likely to be limited. They would chiefly be employed with sugar or saccharin? Apart from soft drinks—in which they had been permitted since 1965—their main use was likely to be in canned fruit and vegetables, jellies, pickles and sauces, and some types of sweet confectionery. To people who must avoid too much sugar cyclamates would be of great benefit and would greatly improve the attractiveness of food, particularly cooked food. They represented a technical advance, and the experts were satisfied there was no health risk.

The motion to annul the regulations was withdrawn.

Accidents in Industry

Dr. SHIRLEY SUMMERSKILL (Halifax, Lab.) asked the Minister of Labour on 13 November what steps he was taking to reduce the increasing number of industrial accidents and deaths.

Mr. R. GUNTER stated that he had recently

appointed the Industrial Safety Advisory Council, both to advise him on measures to be taken centrally and to encourage and co-ordinate action throughout industry to promote safety. Priority was being given to work on safety training in close co-operation with the machinery set up under the Industrial Training Act; joint consultation on safety; research needs and the improvement of statistical information as a basis for action.

Government financial support was being given to the work of the regional organization for industrial safety of the Royal Society for the Prevention of Accidents.

Legal requirements were continuously under review, and within recent months a start had been made on a major revision of the safety, health, and welfare legislation for which he was responsible. In addition, steps were being taken to increase the strength of H.M. Factory Inspectorate.

"While legislation and enforcement have an important part to play in accident prevention," he said, "there will only be an effective reduction in the number of accidents if managements and employees fully understand and accept their own responsibilities."

Immigrant Medical Staffs

Sir DAVID RENTON (Huntingdonshire, Nat. Lib. and Con.) asked the Minister of Health how many Commonwealth immigrants and aliens, respectively, were employed in hospitals, maternity homes, and similar establishments in England and Wales as doctors, nurses, and student nurses, respectively, on the latest date for which figures are available. Mr. K. ROBINSON stated that at 30 September 1965 there were about 6,150 doctors, other than locums, holding posts in National Health Service hospitals, who were born outside the United Kingdom and the Irish Republic. This represented about 30% of the total. More detailed information about doctors was not available.

MEDICAL NEWS

Royal Society Medals

The Copley medal has been awarded to Professor B. KATZ, F.R.S., professor of biophysics at University College, London, for contributions to knowledge of the fundamental processes involved in transmission across the neuromuscular junction.

The Buchanan medal has been awarded to Sir GRAHAM WILSON, director of the Public Health Laboratory Service of England and Wales from 1941 to 1963, for work on the medical aspects of bacteriology and immunity and for the Public Health Laboratory Service.

Appointment to Professorship

The title of professor of clinical immunology has been conferred on Dr. J. PEPYS in respect of his post at the Institute of Diseases of the Chest. Professor Pepys graduated at the University of Witwatersrand in 1935. Coming to England in 1948, he held appointments at the Royal National Ear, Nose, and Throat Hospital, the department of pathology of Guy's Hospital, and the Wright-Fleming Institute, St. Mary's Hos-



[W. Churcher]

pital. In 1955 he was appointed senior lecturer, and in 1964 reader in clinical immunology at the Institute of Diseases of the Chest. He is honorary consultant in clinical immunology to the Brompton Hospital. From 1960 to 1967 he was director of the M.R.C. Research Group in Clinical Immunology at the Institute. His research activities during this time have concerned reactions to inhaled organic dusts. The elucidation of the antigen-antibody reactions underlying farmer's lung and the identification of thermophilic actinomycetes as the source of the antigens led him to the study of other diseases resembling farmer's lung, in that similar reactions to inhaled organic dusts were occurring in the gas-exchanging part of the lung. He has also contributed to knowledge of the immunological basis of diseases associated with the common mould *Aspergillus*. These studies have involved a general interest in precipitin-mediated hypersensitivity reactions in man. His earlier interests included the mechanism of the tuberculin reaction.

Academic Posts in Psychiatry

In 11 medical schools, including Oxford and Cambridge, there is no professorial department of psychiatry, said Sir GEOFFREY VICKERS in the annual address last week to the Mental Health Research Fund. Sir Geoffrey, a former treasurer of the Medical Research Council, retired this year as chairman of the fund's research committee. In medicine generally, he said, professors and medical teachers numbered over 1,500, of whom 450 were professors. The corresponding numbers for psychiatry were 80 and 20. "There are more than six academic posts for

every 100 doctors in the hospital service, less than four for every 100 psychiatrists; more than two professors for every 100 doctors but less than one for every 100 psychiatrists." Sir Geoffrey stressed three basic needs: to create more established posts in the academic departments; to increase, both within and outside the universities, the posts in which research is the main responsibility; and to expose medical students and young doctors to more psychiatry and psychiatric research before they take their first registrarship.

Centre for Postgraduate Medical Students

The Lister Institute of Postgraduate Medical Education and Research was opened in Edinburgh last week by LADY FRASER, wife of the late Sir JOHN FRASER, a former principal of Edinburgh University. It provides teaching accommodation and completes the development of the postgraduate education complex. The first stage was the Pfizer Foundation building, opened in July 1965 (see *B.M.J.*, 17 July, p. 179). LORD FLOREY, O.M., F.R.S., delivered the Lister Oration.

Commonwealth Fund

The 1967 report of the Commonwealth Fund records a grant of \$534,800 to Oxford University faculty of medicine to help to finance the construction and equipping of a clinical sciences instructional laboratory and the addition of academic and technical staff. Commenting on the University's reform of education, the report says that the new curriculum when fully implemented will represent "a model of strong university commitment to medical learning" and will have considerable application to problems of United States and Canadian medical schools. During the year ended 30 June Harkness fellowships were awarded to 26 candidates in the United Kingdom, three in the medical and biological sciences.

Early Diagnosis and Surveillance

The Office of Health Economics is sponsoring a series of pamphlets on the early diagnosis and surveillance of disease, written with the general practitioner especially in mind. The first two pamphlets are now available, price 2s. 6d. each from the Office, at 162 Regent Street, London W.1. Their titles and authors are *The Early Diagnosis of Raised Arterial Blood Pressure*, by Dr. W. W. HOLLAND, and *The Early Diagnosis of Visual Defects*, by Mr. P. A. GRAHAM.

Multiple Screening Clinic

From 21 November to 1 December a multiple screening programme will be carried out at Rotherham (see *B.M.J.*, 1965, 30 October, p. 1034). This year's clinic has 10 test stations, eight of which are suitable for men and eight for women. The tests will cover blood and urine, arteries and heart, chest x-ray, lung function, breast and cervical cancer, vision, glaucoma, and mental health. There will be no open sessions, the tests being taken by appointment.

Hospital Research Project

An investigation into the organization and administration of hospitals and the hospital service is to be undertaken during the next three years by the School of Social Sciences at Brunel University. It forms part of the hospital efficiency programme of research

sponsored by the Ministry of Health, and will be conducted in collaboration with regional hospital boards and other units of hospital administration. Mr. MAURICE KOGAN, formerly secretary to the Central Advisory Council for Education, has been appointed director of the project, which will be under the general supervision of Professor ELLIOTT JAKES. The research team will be assisted by appropriate departments of the university.

Oncologists Association

The Association of Head and Neck Oncologists of Great Britain has been formed to make contributions to the progress of all aspects of oncology relating to the head and neck by research into and discussion of medical, surgical, radiotherapeutic, pathological, chemotherapeutic, and other problems. Membership of the association is open to those interested in head and neck oncology. Further details and forms of membership will be supplied on application to Mr. R. W. RAVEN (chairman, steering committee), Department of Surgery, Royal Marsden Hospital, Fulham Road, London S.W.3.

Casualty Surgeons Association

After the meeting of senior casualty officers at Luton in March a committee was nominated which met in London on 12 October and formally established the Casualty Surgeons Association. The following were elected officers: *president*, Mr. M. ELLIS; *secretary*, Mr. E. P. ABSON; *treasurer*, Dr. D. B. HINDLE.

British Computer Society

The medical specialist group of the British Computer Society, which was launched about a year ago, holds meetings every six weeks from October to July at the Hospital Centre in London. Inquiries should be sent to Dr. J. M. FORSYTHE, chairman of the group. His address is 1A Sandy Road, Norton, Stourbridge, Worcestershire.

Nutrition of the Elderly

A survey of nutrition of the elderly in the Rutherglen area, Lanarkshire, is to be conducted by Professor W. FERGUSON ANDERSON, of the David Cargill chair of geriatric medicine at Glasgow University. The aim of the project, which will be based on random sampling, is to find out whether old people are getting enough food, and food of the right type, to maintain health. The Ministry of Health, jointly with the Scottish Home and Health Department, will cover the cost of the survey up to £1,500.

Doctor Appointed Managing Director

Dr. G. E. PAGET has been appointed managing director of Smith Kline and French Laboratories in Britain. He succeeds Mr. STANLEY FENWICK, who is taking up an appointment with the parent company in Philadelphia, U.S.A. Dr. Paget, who is 45, graduated at Durham in 1944 and proceeded M.D. in 1954. He was lecturer in pathology at Manchester University before going to the pharmaceuticals division of Imperial Chemical Industries, where he was head of the section of pathology. In 1963 he joined Smith Kline and French Laboratories as director of research and development.

Awards Scheme for Overseas Students

A new scheme of awards for students from the developing countries, with effect from the academic year 1968-9, was announced in the Commons on 9 November by Mr. R. PRENTICE, Minister of Overseas Development. The awards, he said, would be for fees at universities and other institutions but not maintenance or travel or other costs. They would be held for an average period of two years. He expected about 1,000 students a year would qualify; when the scheme was in operation it might cover about 2,000 students in Britain. The cost would be approximately £500,000 in a full year.

People in the News

► Mr. CYRIL ROBERTS, former member of the National Coal Board responsible for staff, has been appointed chairman of the Institute of Cardiology.

► Mr. JOHN A. LUMLEY, chairman and managing director of Riker Laboratories, has been elected president of the Association of the British Pharmaceutical Industry.

News in Brief

A second training centre for young adult spastics has been completed by the Spastics society at Slydales Road, Lancaster. The Society's first training centre, Sherrards, at Welwyn, Hertfordshire, was opened in 1957.

The Standing Technical Committee on Synthetic Detergents has reported to the Minister of Housing and Local Government (Ninth Progress Report, H.M.S.O., 2s.) that the quantity of detergents in sewage effluents and rivers has been reduced by two-thirds since the change-over to soft detergent material—that is, material more easily decomposed in water. The search for even softer materials is to continue.

Recent Publications

A new handbook *Pneumoconiosis and Allied Occupational Chest Diseases*, with a foreword by the chief medical officer of the Ministry of Social Security, replaces previous publications of the Ministry on the subject. There is a section on the work of the pneumoconiosis panels. H.M.S.O., 3s. 3d. net.

Clean Air Act 1956: *Chimney Heights*. This is a revised edition of the memorandum published in 1963. H.M.S.O., 2s. 6d.

Everybody's Guide to Social Security, with a foreword by Mrs. JUDITH HART, Minister of Social Security. H.M.S.O., 1s. (postage 4d.).

A hospital admission leaflet for parents has been prepared by the National Association for the Welfare of Children in Hospital (74 Denison House, 296 Vauxhall Bridge Road, London S.W.1). Single copies 1s. 6d. post free.

Preparation for Retirement is the first brochure in a health education series published

for the Medical Association of South Africa by the *South African Medical Journal*.

Coming Events

Postgraduate Medicine, 1967 (T.V. Programme).—"Advances in Reconstructive Surgery," Scottish Television, 20 November (11.50 p.m.), repeat 22 November (1.10 p.m.). "Advances in Cardiology," Tyne Tees Television, 21 November (1.15 p.m.), repeat 26 November (10.15 a.m.).

College of Pathologists.—At Royal College of Physicians of London, 22 November, 11 a.m., annual general meeting; 5.45 p.m., Foundation lecture, "Immuno-pathology," by Professor R. R. A. COOMBS, F.R.S. (admission free without ticket); 7 for 7.30 p.m., annual dinner.

Royal Marsden Hospital.—Centenary open day, 22 November. Details from Mr. T. WEST, Lonsdale Information Ltd., Commonwealth House, London W.C.1.

Medical Society for the Study of Venereal Diseases.—Meeting, "General Infection in Women," 24 November, 7 p.m. for 7.30 p.m., 11 Chandos Street, London W.1.

Medical Association for the Prevention of War.—Symposium (jointly with Conflict Research Society), "The Politics of Research into Peace and War," 25 November, 10 a.m., Gustave Tuck Theatre, University College London, Gower Street, London W.C.1.

Royal Society of Medicine.—Lloyd Roberts lecture by Baroness Wootton, "Crime and the British Penal System—Reflections of a Long-service Magistrate," 30 November, 6 p.m. Admission without ticket.

Institution of Electrical Engineers.—Faraday Lecture, "Medical Electronics," by Dr. D. W. HILL, 30 November, 6 p.m., Central Hall, Westminster. Admission free. Applications for tickets to Secretary (Dept. LC), Institution of Electrical Engineers, Savoy Place, London W.C.2.

Newcastle upon Tyne University in conjunction with Royal College of General Practitioners (North-east England Faculty).—Symposium, "Sex Problems and Contraception," 3 December, in Newcastle. Details from Postgraduate Sub-dean, The Medical School, The University, Newcastle upon Tyne 1.

Kent Postgraduate Medical Centre at Canterbury.—Conference, "Brucellosis," 3 December, 2 p.m., Kent and Canterbury Hospital. Details from Mr. M. D. KAY at the hospital.

Worshipful Society of Apothecaries of London.—350th anniversary of the foundation of the Society, 6 December. Celebrations, 3 to 8 December, include a symposium, "Medicine and the City of London (1617-1967)," 5 December, in the Great Hall of St. Bartholomew's Hospital.

King Edward's Hospital Fund for London.—Conference, "The Patient in the Community—Co-ordination Examined," 5 December, Hospital Centre, 24 Nutford Place, London W.1. Applications by 27 November.

Lister Commemoration.—Symposium, "Operating Rooms a Century After Lister," arranged by the British Medical Association, 8 December, 2 p.m., B.M.A. House. The Minister of Health will open the symposium. There will be an exhibition of modern theatre designs, also a portable operating theatre. Admission by programme obtainable from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London W.C.1.

Institute of Urology.—Week-end course on "Recent Advances in Urology," 8-10 December. For details see advertisement on p. xxxiii.

British Society of Audiology.—Meeting, 8 December, 2 p.m., Department of Audiology and Education of the Deaf, Manchester University. Programme will consist of lecture demonstrations. Details from Mr. A. BOOTHROYD, Department of Audiology, Manchester University.

Biochemical Society.—Joint meeting with Society for General Microbiology, 14-15 December, Leicester University. The programme will include a symposium on "Control of Gene Function in Micro-organisms." Details from Executive Secretary, Biochemical Society, 7 Warwick Court, Holborn, London W.C.1.

Glasgow Postgraduate Medical Board.—The programme for 1967-8 is available. Details of courses can be obtained from Professor C. M. FLEMING, Director of Postgraduate Medical Education, The University, Glasgow W.2.

Societies and Lectures

For attending lectures marked Ⓢ a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 20 November

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.
HUNTERIAN SOCIETY.—At Apothecaries' Hall, 8.30 p.m., "Fee for all is better than Free for all."
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. A. Jarrett: Process of Keratinization.
INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Dr. K. B. Jefferson: Radiology of Coronary Artery Disease.
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., combined staff consultation clinical meeting

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

ABSTRACTS OF WORLD MEDICINE

The November issue (Volume 41, No. 11) contains, as well as abstracts of papers from current world medical literature, a review article entitled

Clinical Aspects of Diabetes Mellitus

By M. G. Fitzgerald, M.D., M.R.C.P.

A wealth of current thinking has been assembled in this authoritative article on a subject which is of continuing interest and importance. Sections deal with factors predisposing to diabetes, atherosclerosis and diabetes, diabetic retinopathy, nephropathy and neuropathy, coma in the absence of ketoacidosis, treatment with the newer insulins, the sulphonylureas, and the diuretics, and finally insulin antagonism. There is an extensive bibliography for those who wish to pursue the subject still further.

Published monthly Annual subscription £6 6s., U.S.A. \$18. Single number 12s. 6d.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. B. Cheng: Basic Genetics; 6.30 p.m., Dr. P. Flute: Fibrinolysis. ●
LEEDS AND WEST RIDING MEDICO-LEGAL SOCIETY.—At Clinical Theatre, General Infirmary at Leeds, 8.30 p.m., speaker, Lord Merthyr.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark lecture on perspectives in health planning—III by Dr. A. Engel (Sweden): Mass Screening for Asymptomatic Disease as a Public Health Measure.
ROYAL FREE HOSPITAL.—5.15 p.m., Dr. Barbara Evans: A Visit to South Vietnam.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. Stuart Mason: Epidemiology of Addison's Disease.
SCOTTISH TELEVISION LTD.—11.45 p.m., Advances in Transplant Surgery. (Sponsored by Glasgow Postgraduate Medical Board.)

Tuesday, 21 November

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. F. H. Doyle: Radiological Measurements in Endocrine and Metabolic Diseases.
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. M. Feivel: The Skin and the Adrenals.
INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Dr. J. Insley: Chromosomal Abnormalities in Gynaecological Practice. ●
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Heath Clark lecture on perspectives in health planning—IV by Dr. A. Engel (Sweden): The Swedish Regionalized Hospital and Health System.
NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., Mr. D. K. Sambrook: My Recent Visit to the United States.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Professor R. B. Welbourn: Cushing's Syndrome.
SOCIETY OF APOTHECARIES OF LONDON: FACULTY OF THE HISTORY OF MEDICINE AND PHARMACY.—5.30 p.m., Sydenham lecture by Professor C. D. O'Malley: John Evelyn and Medicine. ●
SURREY UNIVERSITY.—At Great Hall, 5.30 p.m., Professor J. Waterlow: The Body's Need for Protein—a Challenge for Research.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. N. G. Hulbert: clinical demonstration.
WESTMINSTER MEDICAL SCHOOL.—At Keene Theatre, 5.15 p.m., Dr. J. D. Swales: Observations on Renal Hypertension.

Wednesday, 22 November

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Professor F. A. Whitlock: Psychosomatic Disease—I.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Scadding: Management of Patients with Asthma.
INSTITUTE OF NEUROLOGY.—6 p.m., Dr. A. M. Jelliffe, and 7 p.m., Dr. P. T. Lascelles: The Use and Misuse of Ionizing Radiation in Neurology.
INSTITUTE OF UROLOGY.—5 p.m., Mr. J. E. A. Wickham: Surgery of Renal Calculi.
MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University Medical School, 4.30 p.m., Telford memorial lecture by Professor E. B. Chain, F.R.S.: Recent Developments in Bacterial Chemotherapy.
OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Dr. J. Chayen: Measurement of Metabolic Function in Biopsies.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—5.30 p.m., postgraduate museum demonstration by Mr. J. B. Blakley: A Surgeon's Comments on the Pathology of Carcinoma of the Cervix Uteri.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conferences by Professor R. Fraser: Renal Failure; Dr. E. D. Williams: Hyperparathyroidism. (2) 2 p.m., Professor J. A. Strong: Obesity.
SCOTTISH TELEVISION LTD.—1 p.m., Advances in Transplant Surgery. (Sponsored by Glasgow Postgraduate Medical Board.)
STOKES MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. C. S. Pitcher: clinical cases. (2) 6 p.m., Air Vice-Marshal W. P. Stamm: Amoebiasis.
WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Dr. J. Marshall: Dementia as a Presenting Symptom.

Thursday, 23 November

ABERDEEN UNIVERSITY FACULTY OF MEDICINE.—At Large Lecture Theatre, University Medical Buildings, Foresterhill, 5 p.m., Professor D. D. Reid: International Studies in Cardio-respiratory Disease.
BIRMINGHAM UNIVERSITY MEDICAL SOCIETY.—At Medical School, 5.15 p.m., B.M.A. lecture by Professor D. A. K. Black: "Life With and Without Kidneys".
BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. H. K. Weinreb: Control of Growth and Regeneration in the Liver.
DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Professor H. C. Miller

(Kansas): Psycho-Biological Approach to Problems of the Newborn.
INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. J. S. Pegum: Apocrine Glands.
LEAMINGTON MEDICAL SOCIETY.—At Warneford Hospital, 8.30 p.m., Mr. M. P. Ward: Man at High Altitude—Mountain Physiology.
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8.30 p.m., Dr. Letitia Fairfield: Pioneer Medicine.
NORTHAMPTON GENERAL HOSPITAL.—12.30 p.m., Dr. J. J. Walsh: Domestic Resettlement of Tetraplegics and Paraplegics.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Professor J. V. Dacie: Recent Advances in the Knowledge of Haemolytic Anaemias.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 4 p.m., Dr. D. G. Melrose: Heart Lung Machines. (2) 5 p.m., lecture on medical history by Dr. E. S. Clarke: The Anatomical Basis of Medicine—II.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Mr. V. R. Tindall: Thromboembolism in Obstetrics and Gynaecology.

Friday, 24 November

BROOK GENERAL HOSPITAL.—(1) 2 p.m., clinical cases by Dr. W. E. Mahon. (2) 5.30 p.m., Dr. W. Tillman: Use of Steroids in Dermatology.
KINGSTON-UPON-THAMES MEDICAL CENTRE.—At gynaecological outpatients department, Kingston Hospital, 2.30 p.m., medical case demonstration.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—At Nuffield Hall of the College, (1) 3.30 p.m., William Blair-Bell memorial lecture by Miss E. Blanche Butler: Effect of Iron and Folic Acid on Red Cell and Plasma Volume in Pregnancy; (2) 5 p.m., J. Y. Simpson oration by Mr. A. Gunn: James Young Simpson, the Complete Gynaecologist. ●
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Dr. G. A. Rose: Some Aspects of Osteoporosis.
WEST MIDDLESEX HOSPITAL.—4 p.m., Professor P. Huntingford: Early Detection of Foetal Distress.

Appointments

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—Enid C. Evans, O.B.E., M.R.C.S. (honorary curator, Museum of Pathology at the Medical Academic Unit, Chelmsford).
GRAHAM, N. G., M.B., F.R.C.S., F.R.A.C.S. (consultant general surgeon to the Huddersfield Royal Infirmary and associated hospitals).
MANCHESTER REGIONAL HOSPITAL BOARD.—V. D. Dalal, M.B., F.R.C.S. (whole-time or maximum part-time consultant traumatic and orthopaedic surgeon, Rochdale and District group of hospitals); D. McIntyre, M.B., F.R.C.S. (whole-time or maximum part-time consultant urologist, at the Salford Royal Hospital, Crumpsall Hospital, Manchester, and the Royal Manchester Children's Hospital, Pendlebury); N. MacDonald, M.B., F.R.C.S. (whole-time or maximum part-time consultant surgeon, Wythenshawe Hospital, Manchester); Maira P. Jonas, M.B., D.P.M. (whole-time or maximum part-time consultant child psychiatrist, Bolton and District and Wigan and Leigh groups of hospitals).
MINISTRY OF OVERSEAS DEVELOPMENT.—Sheila A. Benningfield, M.B., M.R.C.P., D.C.H. (registrar, Children's Hospital, Saigon).
NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—J. H. Baron, D.M., M.R.C.P. (consultant physician in general medicine to Tottenham group of hospitals); A. F. Davy, M.R.C.S. (medical assistant in accident and orthopaedic surgery at St. Helena group of hospitals); H. W. G. Loudon, M.B. (consultant chest physician to Ilford and District group of hospitals); Margaret H. Tripp, M.B., D.P.M. (medical assistant with special interest in drug addiction at St. Clement's Hospital).
NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—Bridget A. Jepson, M.B., F.F.A.R.C.S. (consultant anaesthetist at Wilkesden General Hospital); F. G. Ellis, M.S., F.R.C.S. (consultant surgeon at Royal Northern Hospital); A. D. Atkinson, M.B. (assistant geriatrician (medical assistant grade) to the Hillingdon group and Harefield and Northwood group of hospitals); G. Snape, M.B., D.P.M. and R. Ravden M.B., D.P.M. (assistant psychiatrists (medical assistant grade) at Shenley Hospital); N. J. Doherty, M.D., M.R.C.P., D.C.H. (consultant paediatrician at West Middlesex, Ashford, Hounslow, and South Middlesex Hospitals); I. D. Archibald, L.R.C.P.S. & Sd. (assistant surgeon (medical assistant grade) in traumatic and orthopaedic surgery at West Middlesex Hospital); Sybil M. Cockersell, M.R.C.S. (assistant in Accident/Emergency Department (medical assistant grade) at Watford General Hospital (Peace Memorial Wing)); M. F. Stranc, F.R.C.S. (consultant plastic surgeon at West Middlesex, Hillingdon, Wexham Park and Mount Vernon Hospitals); J. W. Blandland, M.B. F.R.C.S. (consultant general surgeon to the Windsor group of hospitals); Bridget A. Jepson, M.B. F.F.A.R.C.S. (consultant anaesthetist at Royal Northern and City of London Maternity Hospitals); E. W. G. Davies, M.B., F.R.C.S. D.O.M.S. (consultant ophthalmologist at West Middlesex, South Middlesex, and Teddington Memorial Hospitals); Md. M. Ali, L.M.S.S.A.,

D.O. (assistant ophthalmologist (medical assistant grade) at Edgware General Hospital and School Eye Clinics).

Universities and Colleges

ROYAL COLLEGE OF PHYSICIANS OF LONDON

On 1 November the following candidates, having satisfied the Censors' Board, were admitted Members of the College:

B. D. Apthorp, B. M. O. Arbab, N. Arumugam, J. T. Baker, D. B. Bannerjee, J. B. G. Benedikt, A. Bernstein, M. Black, A. A. D. Blair, J. A. Blankson, P. R. Bradley-Moore, I. D. L. Brewis, D. A. Canavan, J. Candy, W. R. Chapman, J. A. Child, Barbara A. Clarkson, S. B. Cohen, A. E. Collins, G. O. Cowan, B. R. M. Crook, L. R. Da Costa, A. J. David, B. Davies, P. A. Du Plessis, M. C. Dutta, J. U. Egere, R. S. Elkeles, Anne G. Ferguson, N. D. C. Finlayson, L. M. Flacks, O. J. Follows, P. H. Frank, C. C. Frears, J. S. Geddes, A. L. Gibson, C. Godber, D. P. B. Goldberg, P. L. Golding, T. J. Goodwin, A. McL. Gordon, M. A. Halim, I. W. F. Hanham, A. M. M. Haq, A. Ul Haq, H. Harris, J. B. Hawkins, H. J. Heggarty, R. C. Hickman, M. T. Hossain, Florence A. Howell, R. C. Hughes, K. R. Hunter, Elizabeth R. K. Imrie, K. J. Ivey, P. C. Jain, V. K. Jayaram, S. R. Jayasuriya, D. M. Johnston, G. Jones, B. R. Kanyerezi, D. L. Kennard, S. Kumar, G. N. Kundaje, L. C. Lau, D. McCall, G. P. McMullin, W. J. McNeilly, A. P. Manasse, A. R. Marsh, J. C. Marshall, B. Mason, J. D. Maxwell, S. C. D. Mehta, A. B. Monro, W. R. Moore, A. G. Morgan, S. K. Mukherjee, Janet Murray, P. C. H. Newbold, Charnian R. Newton, S. H. Ng, A. C. Nigam, M. Perlman, J. O. M. Pobe, R. Rao, M. P. Ravindranathan, Pamela A. M. Rendell, J. F. Rivers, A. Robinson, M. J. Rose, Alison Ross, P. R. Salmon, N. K. P. Singh, D. C. Sinha, B. N. Somayaji, B. W. Somerville, J. B. Stoker, R. W. Stout, W. Warren, R. L. Willing, A. C. MacD. Windsor, D. L. Wingate, G. Withers, P. F. M. Wrigley, V. Wynn, D. W. Young, F. Q. Uz Zaman, H. Zeitlin.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council held on 9 November, with Sir Hedley Atkins, president, in the chair, Professor J. F. Nunn was admitted to the Board of Examiners for the Fellowship in the Faculty of Anaesthetists.

A resolution of condolence was passed on the death of Mr. L. E. C. Norbury (past member of Council and vice-president).

The Hallett prize for 1966 was presented to Dr. Omer Mohamed Beilel (University of Khartoum).

Handcock prizes were presented to Dr. P. J. Leopard (Guy's Hospital Medical School) and Dr. R. T. Watson (St. Thomas's Hospital Medical School and Macloghlin scholar 1961).

The appointment of Dr. G. B. Arden (Institute of Ophthalmology) as the Edridge Green lecturer for 1967 was reported.

The Begley prize was awarded to Dr. M. M. Bowen (St. Bartholomew's Hospital Medical College).

The award of the Nuffield prize to Dr. Jennifer A. Jones was reported.

The appointment of Dr. J. D. Robertson as Frederic Hewitt lecturer for 1969 was reported.

Diplomas of Membership were granted to P. S. Bennett, R. C. Bucknall, I. M. Hutton, and F. T. S. Loh.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Atiology*, London W.C.1. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 25 NOVEMBER 1967

Pointers

Advancement of Learning: Lord Platt voices some salutary home truths about clinical research and warns against trying to prove everything by contrived experiments (p. 439). Leader this page.

Relieving Infertility: Clomiphene therapy is more efficacious in patients with amenorrhoea of short duration who have normal-sized ovaries (p. 444). Similar findings reported in large series from Israel (p. 446). Leader at page 434.

Porphyria in Sweden: Variegata type in three families totally unrelated to families with sufferers from acute porphyria intermittens (p. 449).

Peanuts and Bleeding: Controlled study does not bear out clinical impression that haemophiliacs have fewer bleeding episodes on diet which includes peanut extracts (p. 453).

Gastric Acid Secretion: Pentagastrin may supersede histamine in testing for complete vagotomy as results are comparable and side-effects minimal (p. 456).

Effects of Cold Storage: Red cells and intracellular enzymes appear to survive five years at minus 196° C. satisfactorily (p. 458).

Haemorrhagic Enterocolitis: Association with heart failure, rather than with disease of splanchnic vessels, is postulated, and condition may be precipitated in certain climatic conditions by proliferation of normally harmless organisms in the bowel (p. 460).

Case Reports: Prevention of traumatic Bell's palsy (p. 464). Sarcoid myopathy improved with corticosteroids (p. 465). Transfusion malaria (p. 466).

Postgastrectomy Syndrome: Concluding the review of complications (p. 467).

Clinicopathological Conference: Cushing's syndrome with misleading urinary steroids (p. 472).

Employing the Computer: Inpatient statistics more accurately derived by taking the person rather than the hospital discharge as the unit (p. 476).

Television Medicine: Role of television in medical education discussed at B.M.A. lecture (p. 479).

Hospital Administration: Functions of hospital boards and their composition questioned in first letter (p. 482).

Christmas Cards: Christmas cards purchasable from B.M.A. House: profits to medical charities (p. 490).

Public Health Medical Officers: Firm offer received in response to salary claim (*Supplement*, p. 58).

Cui Bono?

William Harvey was by contemporary accounts a brilliant scientist but an indifferent medical practitioner. The antithesis is not altogether unexpected, because the cool, objective approach to ideas and hypotheses—the scientific method—is not always compatible with the emotional involvement of caring for sick people. Until recently a doctor could choose between laboratory and clinical practice, but with increasing technological advance and emphasis on man as the most suitable experimental model in which to study the effects of disease the division between scientist and practitioner has become blurred. The medical profession is thus faced with a new dilemma—the need to preserve human dignity while ensuring that medical advance is not retarded. Its manifestations have not gone unnoticed. Hospitals have been attacked for alleged indignities to patients used for teaching purposes, and research institutions have been accused in a celebrated *exposé* of carrying out questionable experiments on human patients. Doctors would be less than human if they did not attempt to minimize these criticisms as rare exceptions to the general rule of high ethical standards. But when a former professor of medicine and member of the medical establishment voices similar doubts about the path along which academic medicine is travelling our attitudes towards the role of scientific research and teaching must be re-examined.

Lord Platt, in his Harveian oration, which we print at p. 439, accepts that the application of the scientific method has brought much benefit to the investigation of bodily function and of disease. But he points out that academic clinical departments have hardly been responsible for any of the revolutionary advances in therapy in the last 40 years. The sort of clinical research which they teach may indeed be detrimental to the advancement of treatment and prevention of disease. In general they are concerned increasingly with the chronic and rare diseases for which treatment is not yet available, and the research physician becomes a physiologist with a passion for measurement. Given ever more sophisticated apparatus it is necessary to find something to measure, and research becomes more and more dictated by the tools available, with the result that time, energy, and money are too often squandered on "the trivial, the irrelevant, and the obvious."

The need for thought, observation, ideas, and hypotheses—the hard work of science—recedes, and the clinical scientist is relieved of the even harder task of practising medicine. Moreover, we are apt to forget that clinical research is applied research, and in carrying out experiments on human beings we should first pause to ask whether the research is likely to be wholly beneficial or actively detrimental. *Cui bono?* Do academic clinical departments absorb too many of our brightest young graduates who would be better employed in solving the pressing problems that confront humanity? Is the yield in ideas and results sufficient to justify

their existence, or do they merely provide, as Professor Martin Roth has put it, "occupational therapy for university staff"?

The pursuit of research has, of course, its own merit in creating an atmosphere of intellectual inquiry, and the able physician will be constantly stimulated by the problems posed by the individual patient. But his research must be relevant and it must be directed with the needs of the patient in mind. The beneficial collaboration between physician and surgeon in the accurate investigation and treatment of cardiac disease is a case in point, and advances in other fields are to be expected with the increasing partnership between doctors and technologists. But Platt's chief plea is to break the bonds imposed by measurement (which implies that man is merely a machine) and to repair what he believes to be the greatest failure of clinical science—the almost complete neglect of psychological factors in disease.

From earliest times man has built up elaborate defences against the analysis of his subconscious mind, and this is apparent in the medical schools of today. Patients are interrogated and examined in open outpatients and wards in the presence of numerous students, or are presented as "cases" at grand rounds. Clinical research is directed almost entirely towards organic disease, and until recently the mentally ill, together with psychiatrists, were conveniently segregated in separate institutions. And there are the additional defences that psychological medicine cannot be taught objectively and that the time is not ripe for serious

research. Yet no one denies the importance of such factors as heredity, emotional development, social, environmental and cultural influences, chemical changes, and organic cerebral disease in the causation of psychological illness. Each of these can be studied by modern techniques, and even the psychiatric interview is amenable to analysis by computer. Measurement and controlled experiment may not be possible, but "the unbiased collection and verification of observations"—the central feature of the scientific method—can still be satisfied. Human behaviour is surely a subject worthy of the clinical scientist.

Platt does not expect everyone to accept his views on the shortcomings of academic medicine nor his attempt at a solution. Nevertheless, he is really only reiterating what has been said before in other contexts—that in our effort to teach medicine as a scientific discipline we are in danger of losing those very qualities of understanding, compassion, and a carefully practised technique which are the essence of the good doctor. Science is in danger of becoming the master rather than a servant to be dismissed on the many occasions when the patient is better without its services. Man is presented to medical students today as a corpse or as a machine, and it is natural that their approach to illness should be largely mechanistic. A change in emphasis towards the scientific study of psychological factors in health and disease might well be the bridge to close the gap between the differing qualities of mind that often seem to separate the clinical scientist from the practising physician.

Clomiphene for Ovulation

The two articles on the artificial induction of ovulation in the *B.M.J.* this week come at a time when treatment with clomiphene citrate is passing from the research to the clinical stage. Preparations of human pituitary gonadotrophin are at present available for very few patients and under restricted circumstances. They are more dangerous than clomiphene, and their safe use necessitates elaborate facilities for hormone assay. Few would dispute that in the foreseeable future treatment with gonadotrophin preparations should be restricted to a few highly specialized units. Clomiphene, on the other hand, is available on prescription, and its untoward side-effects are slight.¹ Thus it is appropriate to consider the indications for prescribing the drug.

The first reports on treatment with clomiphene appeared nearly seven years ago,² and there is now general agreement on the indications for its use, its dosage, its side-effects, and the changes in ovarian hormone production which follow.³⁻⁵ The means by which its effects are brought about are not clear, so that some caution in prescribing it is wise. It is suitable only for the treatment of infertility associated with anovulation. In disorders of menstruation such as amenorrhoea it seldom brings any prolonged amelioration of the disorder.

In a woman having periods of amenorrhoea for more than three months it may be presumed that ovulation is sufficiently rare to be regarded as absent for clinical purposes. Among the questions that need to be determined before treatment for infertility is begun are whether she has a pituitary capable of producing gonadotrophins, ovaries capable of ovulating, and a uterus able to sustain a pregnancy. Clinical common

sense can do much to clarify the diagnosis before elaborate laboratory investigations need to be undertaken. A considerable proportion of patients with primary amenorrhoea have genetic defects such as Turner's syndrome or testicular feminization, or anatomical defects such as congenital absence of the uterus. None of them can be expected to respond to clomiphene. Primary amenorrhoea should therefore be investigated thoroughly before clomiphene therapy is undertaken. Secondary amenorrhoea poses more difficult questions. Some women have signs of low production of ovarian hormone, such as underdeveloped breasts, scanty pubic hair, and a flat vulva. Often this is due to deficient secretion of gonadotrophin by the pituitary. Treatment in this group is apt to be unsuccessful, as Dr. E. Rabau and colleagues show in their paper on page 446 this week. But enough of such women have a pituitary capable of response to make treatment worth trying, particularly if the results of laboratory tests are favourable. If the secondary sex characters are fully developed the outlook is more hopeful, particularly if ovarian enlargement can be detected or some virilization is evident.⁶

Infertility associated with secondary amenorrhoea can often be successfully treated with clomiphene. In carefully selected patients the success rate approaches 50%, but this can be achieved only after exacting preliminary laboratory investigation. Probably the most useful single test in selecting those amenorrhoeic patients who are suitable for clomiphene is an

¹ Lamb, E. J., and Guderian, A. M., *Obstet. and Gynec.*, 1966, 28, 505.

² Greenblatt, R. B., Barfield, W. E., Jungck, E. C., and Ray, A. W., *J. Amer. med. Ass.*, 1961, 178, 101.

³ Bell, E. T., Loraine, J. A., Harkness, R. A., and Foss, G. L., *J. Obstet. Gynaec. Brit. Cwlih.*, 1966, 73, 766.

⁴ Whitelaw, M. J., *Fertil. and Steril.*, 1966, 17, 584.

⁵ *Brit. med. J.*, 1966, 1, 1436.

⁶ Kistner, R. W., *Obstet. gynec. Surv.*, 1965, 20, 873.

assay of the urinary excretion of oestrone. Women who excrete more than 5 μ g. of oestrone per 24 hours have evidence of some residual ovarian activity and are likely to respond to the drug. A nonspecific method for assaying oestrogen, such as that successfully employed by Dr. D. Ferriman and his colleagues (page 444), gives some indication of ovarian response, but its sensitivity in distinguishing between those patients who are likely to respond to clomiphene and those who are not may be questioned. They found that patients with menstrual cycles of less than six months were more likely to respond successfully to clomiphene than those with longer cycles.

Women whose endogenous ovarian activity is sufficient for them to have fairly regular menstruation but who do not ovulate are the most rewarding group for clomiphene therapy, but they are also the most difficult to identify with any assurance. Endometrial biopsy and assay of urinary pregnanediol are more reliable means of detecting ovulation than basal temperature charts. Even for a nulliparous woman an endometrial biopsy should not entail more than a few hours in hospital and does not require an anaesthetic. The assay of urinary steroids like pregnanediol and oestrone is a different matter. These procedures have been out of the research stage for more than a decade, but few teaching hospitals have initiated specific techniques for carrying them out, most clinical centres lack facilities for doing them, and some use simplifications which are inadequate for clomiphene therapy.

There is little point in starting clomiphene therapy unless it can be established that the woman does not ovulate, is capable of ovulation, and has a fertile husband. To this end gonadotrophin assays are helpful, but they are available to few patients. Oestrogen and pregnanediol assays are well-nigh essential, and a semen analysis is mandatory. To determine whether a woman responded at all to clomiphene and when she ovulated requires nearly continuous 24-hour collections of urine for steroid assays over two to three weeks. This can be done on an outpatient basis; the diagnosis and therapy can be undertaken only with the aid of a specialist clinic. Without the collaboration of such services the use of clomiphene in general practice is clearly unwise. It is a fine example of a situation where the skilful use of laboratory resources can be of great benefit to a few people while a failure to use them can do harm to a larger number.

Blue Blood

In these days of egalitarianism blue blood is no longer the much sought after prerequisite of the nobility; indeed, it has of late become fashionable to disclaim such an inheritance. Nature unfortunately cannot be so denied; we are all the inheritors of blue blood, or almost all. Those of us who are not so endowed are certainly severely underprivileged members of the community, though it will take more than an Act of Parliament to put things right. Normal plasma contains a blue copper protein, caeruloplasmin, first isolated by C. G. Holmberg and C. B. Laurell^{1,2} in 1947 and 1948 and so named because of its colour. In 1952 I. H. Scheinberg and D. Gitlin³ showed that in patients with Wilson's disease this protein was markedly deficient or even entirely absent from the plasma, and they suggested that this was the primary metabolic defect in the disease.

The Scheinberg hypothesis was entirely reasonable; failure to elaborate this normal plasma protein resulted in the plasma copper remaining diffusible so that it entered the tissues in abnormal amounts. This led to basal ganglia degeneration in the brain and consequently to the bizarre sequence of motor disturbances which are so characteristic of the disease. In the liver excess copper led to necrosis and fibrosis, in the kidneys to defects of tubular reabsorption, and in the eyes to the typical Kayser-Fleischer pigment rings which are diagnostic of the disease. Unfortunately, as G. E. Cartwright and his associates⁴ have pointed out, in their experience—which mirrors that of most workers in this field—there is a poor correlation between caeruloplasmin concentration and the duration and severity of the clinical course of the illness. In fact, patients are occasionally seen with perfectly normal levels of this protein in their blood, as was early reported by A. G. Bearn and H. G. Kunkel⁵ and also by Cartwright's group.⁶

One possible explanation of this discrepancy, and a very attractive one at that, was the hypothesis that the caeruloplasmin present in some patients with Wilson's disease was structurally and therefore functionally abnormal. Thus there might be two different alleles mediating the disease, one leading to failure of protein synthesis and one to abnormalities of protein structure, either of which could give rise to the same disastrous functional derangement in the transport of copper in the body. This theory was discussed by a number of delegates at the London meeting on Wilson's disease held at the National Hospital in 1960,⁷ but we have had to wait for seven years before further light has been thrown on this aspect of the problem. Now N. A. Holtzman and his colleagues⁸ working at the Johns Hopkins Hospital in Baltimore have isolated and crystallized caeruloplasmin from a patient with Wilson's disease in whom the concentration of this protein in the blood approached normal levels. Their findings of a normal tryptic peptide map go a long way to disproving the theory of a structurally abnormal caeruloplasmin in Wilson's disease. These workers note, as others have done, that when treatment with penicillamine is instituted caeruloplasmin disappears from the plasma, and they postulate the occurrence of a reduced rate of synthesis of caeruloplasmin in their patient; when the excess copper stores were removed by penicillamine the stimulus to further synthesis of the protein became inadequate. This may well be true, but unfortunately it takes us no further in our understanding of the disease. Indeed, one of the main stumbling-blocks to our understanding of the pathogenesis of this mysterious illness is the complete absence of clues to the normal function of caeruloplasmin.⁹ L. Broman¹⁰ has even described it as "just an ineffective oxidase, in the wrong place, lacking a suitable substrate," but he himself believes that it represents a transport form of a copper-containing prosthetic

¹ Holmberg, C. G., and Laurell, C. B., *Acta chem. scand.*, 1947, 1, 944.

² ——— *ibid.*, 1948, 2, 550.

³ Scheinberg, I. H., and Gitlin, D., *Science*, 1952, 116, 484.

⁴ Cartwright, G. E., Markowitz, H., Shields, G. S., and Wintrobe, M. M., *Amer. J. Med.*, 1960, 28, 555.

⁵ Bearn, A. G., and Kunkel, H. G., *J. clin. Invest.*, 1954, 33, 400.

⁶ Markowitz, H., Gubler, C. J., Mahoney, J. P., Cartwright, G. E., and Wintrobe, M. M., *ibid.*, 1955, 34, 1498.

⁷ *Wilson's Disease: Some Current Concepts*, ed. J. M. Walshe and J. N. Cumings, Oxford, 1961.

⁸ Holtzman, N. A., Naughton, M. A., Iber, F. L., and Gaumnitz, B. M., *J. clin. Invest.*, 1967, 46, 993.

⁹ Holmberg, C. G., in *Wilson's Disease: Some Current Concepts*, ed. J. M. Walshe and J. N. Cumings, Oxford, 1961, p. 64.

¹⁰ Broman, L., *Acta Soc. Med. upsalien*, 1964, 69, suppl. No. 7.

¹¹ Osborn, S. B., and Walshe, J. M., *Lancet*, 1967, 1, 346.

¹² Aisen, P., Morell, A. G., Alpert, S., and Sternlieb, I., *Nature*, 1964, 203, 873.

group which acts as an oxygen-activating unit in cytochrome oxidase. Unfortunately this theory too falls foul of the facts, which have an unpleasant habit of invalidating all the theories about this disease as fast as they are put forward. As S. B. Osborn and J. M. Walshe¹¹ pointed out earlier this year, it is possible for a patient with Wilson's disease, treated with pencillamine, to live a perfectly normal life with no symptoms of disease and with no detectable copper or caeruloplasmin in his serum—always provided that the drug is continued and the patient maintained in copper balance. So this would suggest an excretory function for caeruloplasmin. But this theory comes up against the work of the Albert Einstein group of workers,¹² who have shown, at least for rabbits, that the copper of catabolized caeruloplasmin "is not directly or preferentially excreted by hepatic, pancreatic, intestinal, or renal routes." Blue blood may be all very well in preventing Wilson's disease, but the way in which it mediates this function is as obscure as its role in ennobling the nobility.

Obstructive Airways Disease

The clinical features of the bronchial and emphysematous types of obstructive airways disease have been defined by A. C. Dornhorst¹ and T. Simpson² and their physiological characteristics by C. Ogilvie³ and by W. A. Briscoe and A. Cournand.⁴ The careful and detailed studies of C. M. Fletcher, B. Burrows, and others^{5, 6} firmly established the criteria whereby these two types can be distinguished. These workers have also tackled the semantic problem posed by the indiscriminate use of the terms "chronic bronchitis" and "emphysema," the first being favoured in Britain and the second in America. Using standardized clinical, radiographic, and physiological techniques, they compared 50 patients from a "bronchitis" clinic in London with 50 patients attending an "emphysema" clinic in Chicago.⁷ Apart from a rather greater incidence of disabling chest illness in London, there was no real difference in the pattern of obstructive airways disease for the two cities. In particular, the frequency of the bronchial and emphysematous forms was the same.

N. L. Jones, Burrows, and Fletcher⁸ have now extended this study by carrying out an annual review of the original 100 patients over a period of three years. During this time progress and mortality were remarkably similar in the two cities, but the incidence of disabling chest illness was higher among the London patients. However, a detailed questionnaire showed that bronchitic exacerbations were not in fact more frequent in London than in Chicago but only more disabling in terms of the time spent in bed or off work. The authors attribute this to differences in working conditions, sickness benefits, and cost of treatment between the two cities rather than to differences in the behaviour of the disease process itself.

This recent survey also gives valuable information on the

relative prognosis of the two types of obstructive airways disease. The mortality was higher in the bronchial (36%) than in the emphysematous group (15%), and this was related to the greater incidence of hypercapnia among the bronchitic patients. It might have been thought that the complications of bronchitis (infection, hypercapnia, and right heart failure) would prove more amenable to treatment than the irreversible lung changes of emphysema. The actual finding of a much higher death rate for bronchitis surely points to the need for a reappraisal of therapeutic methods used in this formidable disease. The thorough techniques of investigation evolved by Fletcher and his co-workers could well provide the basis for a study of this kind.

Realism and Addicts

The Ministry of Health is facing increasing criticism because of its alleged dilatoriness in responding effectively to the threat of epidemic heroin addiction in Britain. A brief inquiry published by the *Guardian*¹ last week certainly gives a picture more of disarray than preparedness so far as hospital services are concerned, while a speaker at a recent meeting of the General Medical Services Committee² denounced "a typical Ministry paper scheme," which he alleged was simply putting forward proposals which could not be implemented owing to lack of facilities. To what extent are such strictures justified?

The latest "paper scheme" is a memorandum dealing with the rehabilitation and aftercare of heroin addicts.³ The G.M.S. Committee has already drawn attention to the inappropriateness of the use of the allocation procedure to place an addict on a general practitioner's list, but otherwise the ideas put forward in this memorandum deserve nothing but praise. It presents a humane and intelligent approach to the problem of drug addiction, stressing that detoxification by itself is not enough, and picturing narcotic addiction as requiring comprehensive integrated services—clinics, hospitals, hostels, work-training—rather than mere drug-handout centres. The memorandum supplements the model for hospital treatment which was put forward earlier this year.⁴

The trouble comes when turning from the Ministry's memoranda to the realities. Those in Alexander Fleming House seem to have some of the characteristics of the kind of student who writes alpha papers but muffs the practicals. To take an example: one of the most important proposals in the new circular concerns the role of hostels in the aftercare of addicts, and the benefits that can result from grouping patients are discussed with a degree of sympathy and insight which is admirable: "Although the establishment of a disciplined atmosphere is essential this alone is insufficient to prevent drug taking. It is necessary to build up an atmosphere of co-operation between staff and residents and in this task the psychiatrist can give valuable assistance. . . . The expectation of the hostel must not be set too high and staff must accept the probability that relapse will take place and be ready to contend with its effects on other residents and themselves." A splendid answer in a written paper, but then take the example further and look at the performance in the practicals.

¹ Dornhorst, A. C., *Lancet*, 1955, 1, 1185.

² Simpson, T., *Tubercle (Lond.)*, 1958, 39, 307.

³ Ogilvie, C., *Thorax*, 1959, 14, 113.

⁴ Briscoe, W. A., and Cournand, A., *Ciba Foundation Symposium on Pulmonary Structure and Function*, ed. A. V. S. de Reuck and M. O'Connor, 1962, p. 304. Boston.

⁵ Fletcher, C. M., Hugh-Jones, P., McNicol, M. W., and Pride, N. B., *Quart. J. Med.*, 1963, 32, 33.

⁶ Burrows, B., Fletcher, C. M., Heard, B. E., Jones, N. L., and Wootliff, J. S., *Lancet*, 1966, 1, 830.

⁷ Fletcher, C. M., Jones N. L., Burrows, B., and Niden, A. H., *Amer. Rev. resp. Dis.*, 1964, 90, 1.

⁸ Jones, N. L., Burrows, B., and Fletcher, C. M., *Thorax*, 1967, 22, 327.

¹ *The Guardian*, 16 November 1967.

² *Brit. med. J. Suppl.*, 1967, 4, 47.

³ *Ministry of Health Memorandum*, H.M. (67) 83.

⁴ *Ibid.*, H.M. (67) 16.

⁵ *Brit. med. J.*, 1967, 3, 692.

⁶ *Ibid.*, 1967, 4, 366.

How many hostels for addicts of the sort which the Ministry envisages are now functioning in London? Not one. Who is going to pay for these no doubt very expensive facilities? The Ministry makes hopeful murmurs about local health authorities footing the bill, but anyone with experience of that method of financing will know that ratepayers are always eager for new ventures to be sited in any borough but their own. Where are the staff of the hostels to be found? These and every other question which bears on reality meet with no answer.

The earlier suggestions on hospital care were of course similarly worthy and invited a volley of equally unanswered questions. Where are the consultant sessions to be found for the new treatment centres? Are new psychiatrists to be manufactured, or will they be withdrawn from other services? What training courses have been arranged? What laboratory facilities are being provided? Will extra psychiatric social workers be hired? How much money will be spent?⁵

It would not be fair to place all the blame on the Ministry for failing to find an immediate solution to this extremely difficult problem. To a large extent the solution (and responsibility) lies in the hands of local health authorities and hospitals, general practitioners and voluntary bodies: imagination, energy, and good organization are needed in the many local communities where drug addiction is established or beginning to be seen. All the blame may not be the Ministry's, but it is reasonable to ask for more practical action and more evidence of a sense of urgency. In 1954 there were 57 known narcotic addicts, while in contrast the present official count is 1,349.⁶ With a situation as threatening as this today's minor blunders, procrastinations, or meanness are the stuff out of which tomorrow's disasters are likely to be made.

Surfer's Nodules

All that some people ask is not a tall ship and a star to steer her by but a board that measures ten feet by two, has a core of polyethylene foam with springers of spruce or redwood, is jacketed in fibreglass and resin, and coated in paraffin wax to provide adhesion for its rider. J. G. Erickson and G. R. von Gemmingen¹ have described some of the hazards of surfboarding as it is practised in Southern California. It sounds much less comfortable than riding on a dolphin's back. The devotee "paddles in the kneeling position with his feet extending back and his body weight balanced on the tibial prominences, the middle of the top of the feet, and the dorsum of one or more metatarso-phalangeal joints . . . over months of surfing, at four to six hours a day." In this attitude he travels seaward in search of the perfect wave upon whose back he can ride shoreward in triumph and delight.

In these days of increased leisure it is becoming harder to draw any sharp distinction between work and sport as an occupation on the one hand and as a relaxation on the other. Indeed, some people would say that the point has been reached at which work has become a relaxation from the obsessive pursuit of a hobby. The surfers of Southern California seem a case in point. They pay for their devotion with nodules, ulcers, ganglia, and bony changes—attributable mainly to the effects of long-continued pressure—and, more hazardously, by taking the chance of being run down by their colleagues in the open sea. Though the pressure effects are avoidable

by temporary abstinence or by spreading the load, there is little enthusiasm for avoiding what is acknowledged to be a badge of distinction, since "the prestige of the surfer is proportional to the size of his nodule." "Abstinence," said Blake, if his shade will forgive this use of his words, "sows sand all over the ruddy limbs and flaming hair, but desire gratified plants fruits of life and beauty there." It seems unlikely that modern Britons will try to rule the waves so obsessively, if only because Pacific rollers offer better sport, but even so we could perhaps find examples of surfer's nodules upon our own shores, and students of occupational marks would no doubt like to add this new piece to their collections.

Platelets in Uraemia

The tendency of patients with advanced uraemia to bleed is associated with a defect in their platelets.¹⁻³ The more severe this abnormality in the platelets, the more marked are the clinical manifestations of bleeding.^{4,5} Thrombocytopenia may also occur, particularly in patients with acute renal failure, but the platelet count is normal in most patients with chronic uraemia. The impaired function of the platelets is manifested by an increase in the bleeding time, defective platelet adhesiveness, reduced platelet aggregation in the presence of adenosine diphosphate, impaired clot retraction, reduced prothrombin consumption, and poor availability of platelet factor 3. The earlier report of A. J. Hellem and his colleagues⁶ that intravenous infusion of urea prolonged the bleeding time and reduced platelet adhesiveness has not been confirmed by P. A. Castaldi, M. C. Rozenberg, and J. H. Stewart.^{7,8} Substances other than urea are now presumed to cause the functional platelet defect in uraemia.

Recently, Stewart and Castaldi⁷ have reported that platelet function in uraemia was considerably improved by dialysis (either peritoneal or haemodialysis), though complete correction—particularly of the bleeding time and platelet aggregation—was not achieved. The clinical improvement in haemostasis paralleled that in platelet function. Dialysis usually improved clot retraction, prothrombin consumption, and platelet adhesiveness. In most patients there was a rise in the platelet count after dialysis. Improvement in platelet function was found as early as one day after dialysis, and occurred in two cases with little fall in the level of urea in the blood. Successful renal transplantation was more effective than dialysis in restoring completely normal haemostasis.

Stewart and Castaldi used measurements of platelet aggregation, availability of factor 3, and clot retraction to estimate platelet function in vitro. No adverse effects were observed after the addition to plasma rich in platelets of urea, dextrose, mannitol, creatinine, urate, phosphate, potassium, or magnesium; or after changes of pH or osmolarity within the range which might be found in severely uraemic patients.

¹ Lewis, J. H., Zucker, M. B., and Ferguson, J. H., *Blood*, 1956, **11**, 1073.

² Cahalane, S. F., Johnson, S. A., Monto, R. W., and Caldwell, M. J., *Amer. J. clin. Path.*, 1958, **30**, 507.

³ Cheney, K., and Bonnin, J. A., *Brit. J. Haemat.*, 1962, **8**, 215.

⁴ Willoughby, M. L. N., and Crouch, S. J., *ibid.*, 1961, **7**, 315.

⁵ Castaldi, P. A., Rozenberg, M. C., and Stewart, J. H., *Lancet*, 1966, **2**, 66.

⁶ Hellem, A. J., Ødegaard, A. E., and Skälhegg, B. A., in *Proceedings of the Xth Congress of the European Society of Haematology*, in Basel, 1966.

⁷ Stewart, J. H., and Castaldi, P. A., *Quart. J. Med.*, 1967, **36**, 409.

⁸ Horowitz, H. L., Cohen, B. D., Martinez, P., and Papayianou, M. F., *Blood*, 1967, **30**, 331.

¹ Erickson, J. G., and von Gemmingen, G. R., *J. Amer. med. Ass.*, 1967, **201**, 134.

The abnormality in the platelets in plasma rich in platelets taken from uraemic patients could not be corrected in vitro by dialysis or by adding normal plasma poor in platelets. However, the failure of dialysis in vitro does not exclude a direct effect; restoration of function may not occur until the platelets have been returned to the circulation or have been in a normal environment for a longer time than the period of the in vitro test.

From their observations Stewart and Castaldi conclude that the qualitative platelet defect in uraemic patients is caused by the retention of a dialysable substance which would normally be excreted by the kidney. The impairment of function may be due to the net effect of many substances, but it is possible that a single agent is solely or largely responsible. More recently H. L. Horowitz and his colleagues⁸ have reported a defect in the activation of platelet factor 3 by adenosine diphosphate in blood from uraemic patients. Further studies pointed to the presence of an inhibitor of this reaction in the plasma of these patients, and preliminary observations suggest that the inhibitory factor may be a newly described intermediate of urea metabolism, guanidosuccinic acid. If this can be confirmed we may look forward to further advances in the knowledge of the physiology and pathology of platelets.

Chicken-pox Pneumonia

Chicken-pox is generally a trivial infection in children, but it tends to be more severe in adults and may be accompanied by pneumonia caused directly by the virus. Various surveys¹⁻³ in the U.S.A. have placed the incidence of chicken-pox pneumonia in adults between 16 and 33%, but it is found less frequently in Britain. The disease varies greatly in severity.⁴ At one extreme it can be a catastrophic illness characterized by severe dyspnoea, cyanosis, haemoptysis, and prostration, at the other a condition so mild that it can be detected only by routine radiography.

In a typical attack the patient is an adult with a heavy rash, which has usually been present for two to five days, in whom the spread of the disease to the lungs is heralded by a dry cough followed by increasing breathlessness and cyanosis. Abnormal signs are seldom present initially, but as the patient's condition deteriorates air entry diminishes and adventitious sounds are heard. The classical signs of consolidation are not found. After 48 hours the cough becomes productive of scanty mucoid sputum, which may be streaked with blood. Occasionally there is a more severe haemoptysis. Culture of sputum gives a sparse growth of bacteria, mainly commensals. The white blood cell count is usually normal but may show a polymorphonuclear leucocytosis. The sedimentation rate is rarely raised. After a week the patient's condition begins to improve and towards the end of the second week he emerges from the critical phase to face a prolonged period of convalescence. The cough and abnormal chest signs quickly disappear, but breathlessness may persist for

several weeks. If the illness is associated with neoplastic disease or pregnancy the prognosis is poor.

During the acute phase x-ray examination shows widespread nodular opacities in both lung fields. The lesions vary in size from several millimetres to more than one centimetre. In most patients resolution occurs within eight weeks,⁵ but occasionally a coarse reticular pattern of small, very soft nodules persists for years.⁶ J. B. Mackay and P. Cairney⁷ first drew attention to the association between chicken-pox in adult life and miliary calcification of the lungs. Their observations have been confirmed by A. F. Knyvett,⁸ who followed three patients from the early stage of soft nodular shadowing to calcification.

Chicken-pox pneumonia should be suspected if respiratory symptoms develop during the acute eruptive stage. When mild no special treatment is required, but patients with respiratory distress need skilled nursing in hospital. Though antibiotics have no obvious effect, they are usually prescribed for seriously ill patients in the hope of controlling secondary bacterial infection. The value of corticosteroid drugs is controversial. Rapid improvement may sometimes follow their administration, but on other occasions they fail to avert disaster. However, they do not appear to be harmful when given for the first time during the acute stage of chicken-pox. Beneficial results have been reported from the use of hyperimmune gammaglobulin,⁹ but further experience is required before its value in severe chicken-pox can be assessed, and supplies are extremely limited. Oxygen should always be given to patients with chicken-pox pneumonia who show deep cyanosis; should this persist tracheostomy and intermittent positive pressure respiration may prove life-saving.⁹

The Royal Society

The new premises of the Royal Society at 6 to 9 Carlton House Terrace were formally opened by the Queen on Tuesday this week. It was the first time that the Monarch, as Patron, had personally opened a new home of the Society. Her Majesty was accompanied by Prince Philip, Duke of Edinburgh, and Earl Mountbatten of Burma, both Fellows of the Society.

In the three centuries of its existence the Royal Society has occupied homes in Gresham College in the City of London, in Crane Court in Fleet Street, in Somerset House, and for the past century in Burlington House, Piccadilly. At Burlington House the Society's activities greatly increased in response to the growing importance of science in the community. The office staff of two in 1873 is now nearly 80, and not all of them could be accommodated in the building.

The new premises provide more than twice the space the Society had before. They have been formed by adapting four separate houses, the work of conversion being financed by an appeal fund launched by Lord Florey when he was president. Their situation, finely illustrated in a commemorative booklet, is unusually attractive. Not only do they face St. James's Park and the Mall but they are on the main pedestrian route between Parliament Square and the centre of the West End.

In congratulating the Society as it embarks on another stage of its development, we are sure that its new headquarters in the heart of the metropolis, made possible by the efforts of many people over a period of years, will be a source of pride and inspiration to the Society as it continues to play an increasingly significant part in the world of science.

¹ Weinstein, L., and Meade, R. H., *Arch. intern. Med.*, 1956, 98, 91.

² Krugman, S., Goodrich, C. H., and Ward, R., *New Engl. J. Med.*, 1957, 257, 843.

³ Mermelstein, R. H., and Freireich, A. W., *Ann. intern. Med.*, 1961, 55, 456.

⁴ Carstairs, L. S., and Emond, R. T. D., *Proc. roy. Soc. Med.*, 1963, 56, 267.

⁵ Bralley, A. G., jun., and Husebye, K. O., *Minn. Med.*, 1958, 41, 695.

⁶ Knyvett, A. F., *Quart. J. Med.*, 1966, 35, 313.

⁷ Mackay, J. B., and Cairney, P., *N.Z. med. J.*, 1960, 59, 453.

⁸ Loeb, W. Y., and Taylor, C. E. D., *Lancet*, 1966, 1, 1037.

⁹ Tidstrom, B., *Scand. J. resp. Dis.*, 1967, 48, 40.

Papers and Originals

Medical Science: Master or Servant?*

Lord PLATT, M.D., M.Sc., F.R.C.P.

Brit. med. J., 1967, 4, 439-444

Harvey and the Scientific Method†

If any testimony were needed to the unique position of William Harvey in the development of modern medicine, it would be sufficient to note that after more than three centuries new researches into his life and work continue to be made and have yielded in the last few years a quite astonishing harvest. Notable among them are the recent volume by Keynes (1966), so rich in learning yet so delightful to read, and that unique triumph of erudition and insight, the new transcription of Harvey's *Prælectiones* by Gweneth Whitteridge (1964, 1966), together with her interpretation of the manner and sequence in which they were written, so that we are now almost able to follow the trains of thought which led to the gradual revelation of the secrets of the circulation of the blood, in Harvey's mind.

As to his methods, there is no better source than *De Motu Cordis et Sanguinis* itself, and perhaps Harvey's own writings in reply to Riolan. Harvey described his work as proving the circulation of the blood "by reason and experiment." It is indeed the charm of *De Motu* to the present-day scientist that reason and experiment go hand in hand throughout, the experiment being carefully devised to prove or refute the hypothesis, the hypothesis having been derived from experience and the contemplation of data carefully observed, the perfect scientific method, in fact.

In spite of this, Harvey knew that in his day his methods and his conclusions were so unorthodox that they would be criticized and rejected by many of his contemporaries, and he said: "I fear lest I have mankind at large for my enemies, so much doth wont and custom become a second nature. Doctrine once sown strikes deep its root, and respect for antiquity influences all men. Still the die is cast and my trust is in the love of truth and the candour of cultivated minds."¹

Harvey's contemporaries and successors, nevertheless, generally accepted his teaching, but failed to find any way of making it relevant to medical practice. This was inevitable at that time, but they might have been quicker to adopt his experimental methods in the pursuit of the further knowledge of physiology.

As to his practice of medicine, Harvey was considerably criticized during his lifetime, and it is interesting that Lord Conway warned his daughter, who was a patient of Harvey's, against him, in spite of his obvious esteem for Harvey's scientific merit.

John Aubrey said of Harvey: "All his profession would allow him to be an excellent Anatomist, but I never heard of any that admired his therapeutic way. I knew several

practisers in this Towne London that would not have given 3d. for one of his Bills and that a man could hardly tell by one of his Bills what he did aime at." Dr. Broun, a generation after Harvey, said that his discovery had "seemed to illustrate the theorie of Medicine, yet it made no improvement in the practice thereof" (Clark, 1964). Sydenham, in his various writings on clinical subjects, did not mention Harvey's work at all.

But before we pursue the results of Harvey's experimental work, let us end with John Aubrey's comment on his character. He tells how Harvey made him "sitt by him two or three hours together in his meditating apartment discoursing.

"He was very far from bigotry. Why, had he been stiffe, starcht and retired, as other formall Doctors are, he had known no more than they. From the meanest, in some way or other, the learnedst man may learn something. Pride has been one of the greatest stoppers of the Advancement of Learning."

Aubrey clearly recognized Harvey as a great man.

Fruits of Science

There was, in fact, a period of more than 200 years before experimental physiology on Harveian lines can be said to have begun. Müller, Helmholtz, and, above all, Claude Bernard on the Continent, William Sharpey and Marshall Hall in England, and later Starling, Bayliss, and J. S. Haldane are names which come to mind, but the introduction of the methods of experimental physiology to clinical medicine is something which really belongs to my own time. Its development has been rapid and productive, so that today, all over the world, universities have their academic clinical departments, staffed for the most part with the descendants of Harvey, Bernard, and Starling, rather than the descendants of Sydenham and Osler, and engaged almost entirely in the application of the Harveian method to the investigation of bodily function and the manifestations of disease, in the course of which they have, as Harvey predicted, gained much from the study of nature's own experiments.

This has led to a new understanding of the scientific basis of medicine, comparable in its significance with Harvey's discovery of the circulation. The physiology and functional pathology of disorders of metabolism, of the heart, lungs, and kidneys, and of the digestive system, have all proved to be rich sources of study by these methods, and in some areas the physician has virtually taken over the role of physiologist.

Large and increasing funds from public and private sources have been devoted to medical research of this kind, and more and more persons have been attracted into careers in clinical science. The impact of science and technology has brought new skills and refinements into diagnostic methods.

On the therapeutic and preventive side of medicine we have, in my time, seen the virtual conquest of bacterial disease,

* Harveian Oration delivered to the Royal College of Physicians of London on 18 October 1967.

† This introductory section is somewhat abbreviated from the spoken version, which contained more material concerning Harvey's relation with the College of Physicians.

¹ The wording is my modification of Richard Asher's modification of Bowie's revision of Willis's *Transcription* and is near enough to a translation of Harvey's Latin in chapter VIII of *De Motu*.

including tuberculosis, and the prevention of poliomyelitis. Fatal diseases such as pernicious anaemia and severe diabetes are now controlled; cancer of the lung is known to be largely preventable. Modern anaesthesia and antibiotics, along with new technical cunning, have combined to make cardiac surgery a reality. Except in the most primitive parts of the world, plague is a thing of the past, and if malaria is not already eradicated it is for want of resources and not for want of knowledge. The overpopulation resulting from the conquest of disease could now be countered by modern means of contraception, which with little doubt will soon be further improved.

To this audience there is no need, and no time, for a full catalogue of the victories. One has only to think back to quite recent history, the plagues of the seventeenth century, the infant mortality of the eighteenth and nineteenth centuries, the deaths of Chopin and Keats and the Brontës from tuberculosis, to be grateful for the achievements of scientific medicine.

Critical Survey

The adoption of the scientific method in the Harveian tradition by clinical medicine has been recognized by the appointment of about 43 wholtime professors of medicine or of therapeutics in the United Kingdom alone.² The growth of departments of academic medicine in the United States has taken place at the same time on an even larger scale. Their contributions to the understanding of disease are established, real, and secure, and they have helped to make possible the deployment of the discoveries of modern medical science, both in relation to treatment and in diagnosis. Yet we must face the fact that these departments have not been responsible for, nor even seriously involved in, any of the discoveries in therapeutics or preventive medicine which I have just enumerated.

The antibacterial action of the sulphonamides was wholly worked out in the laboratories of pharmaceutical industry, starting with Mietsch and Klarer and taken up by Domagk, though the original idea that dyes could be antibacterial stems from Ehrlich. From the sulphonamides, hypoglycaemic agents such as tolbutamide have developed, and a whole series of diuretics of the chlorothiazide class.

The antibiotics originally sprang from an observation of Pasteur and Joubert of 1867, but Fleming's findings of 1929, which he left undeveloped for 10 years, were then taken up by Florey and Chain, who isolated penicillin and demonstrated its effectiveness. Attempts at synthesis were an expensive failure, but better culture methods developed in American Governmental laboratories and by the Pfizer drug company made penicillin a practical success. From the penicillin idea comes streptomycin, discovered by Waksman and his colleagues in a university department, and developed by Merck. All the subsequent antibiotics have originated in industrial laboratories. None has depended on clinical scientific departments or on the kind of clinical science which they teach.

Isoniazid and para-aminosalicylic acid have arisen from the combined work of academic and industrial departments. The new penicillins have come from the Beecham Laboratories.

Poliomyelitis vaccines have been developed by non-clinical scientists.

Liver treatment of pernicious anaemia was an exception, coming as it did from Minot and Murphy in an academic medical unit, taking a rather long shot from animal work by Robschert-Robbins and Whipple, which could have been quite irrelevant. These latter workers had suggested that there might be some "parent pigment substances" normally stored

in the liver. In spite of this lucky and favourable beginning the hard scientific work of isolating vitamin B₁₂, the active principle, was accomplished by scientists in the pharmaceutical industry in Britain and the United States.

Insulin, as everyone knows, was first extracted in a physiology department, and almost stands alone as having resulted from good scientific reasoning. The discovery that carcinoma of the lung was caused by cigarette smoking was due to clinical observation, followed by a first-class study by the techniques of epidemiology.

The synthesis of cortisone was combined work between an academic non-clinical scientist and a drug firm—namely, Merck—done as part of a wartime programme sponsored by the United States Office of Scientific Research and Development. But Hench, of the Mayo Clinic, made a clinical contribution to the cortisone story which was of great importance, especially as he had to some extent predicted the results by clinical observation. Stilboestrol came from an academic non-clinical laboratory.

To continue the recital would be tedious, but the findings are essentially the same when we look into the origins of anaesthetics, tranquilizers, vitamins, antimalarials, antihistamines, hypotensives, sex hormones, and oral contraceptives. Not one originated in a department of academic medicine or therapeutics. Even D.D.T., so important to preventive medicine, was discovered by Müller, working for the Geigy company.

I must acknowledge here my debt to Dr. William Bain for helping to ensure that my information is accurate and for calling my attention to Professor Ernst Chain's Trueman Wood Lecture of 1963, which contains most of the relevant information.

Ideas and Resources

If we are to draw any tentative conclusions from this survey of the origins of the control of human disease in our time, we might wonder whether the establishment of scientific clinical units interested in the exact study and measurement of the phenomena of disease has, like Harvey, succeeded in illuminating "the Theorie rather than the practice of Medicine," for the phenomenal success of modern medical treatment seems to have depended almost wholly on non-clinical, often non-medical, scientists, frequently working in, or in close collaboration with, the pharmaceutical industry. And it would be a serious mistake to think that the role of industry has been largely in the field of commercial development. A great deal of the basic scientific work, especially chemical isolation, analysis, and synthesis, has taken place there.

Ideas come from lucky accidents or from the inspiration of men of imagination. At the next stage, where the idea needs to be worked out, there seems to be a strong case for directing resources deliberately to the achievement of an objective, rather than devoting so much of our research potential to the investigation of observed phenomena of academic interest. In fact, both the Ministry of Health and the Medical Research Council have in recent years called together conferences and working parties with the object of seeing how money and manpower may best be applied to the achievement of specific objectives; for instance, in intensive coronary care, recurrent dialysis, leukaemia, and pyelonephritis. This may need resources not always to be found in academic and Research Council laboratories, and might require a major redeployment of Research Council funds. Where ideas have originated in the academic laboratory, collaboration with industry, not necessarily only the pharmaceutical industry, if required, should be sought early and willingly, not reluctantly and belatedly.

Some real discoveries have been made in academic clinical departments, often in the field of rare disease, such as primary aldosteronism, but the accurate study of function in chronic destructive disease of the lungs, the kidneys, and the liver has

² This includes the occupants of personal chairs in medicine and related subjects, such as neurology and cardiology, but does not include psychiatry, paediatrics, or preventive medicine, nor surgery, nor gynaecology, nor laboratory medicine, such as pathology.

sometimes seemed more akin to an absorbing hobby than a therapeutic exercise, though occasional and temporary relief to the patient may be a by-product.

It was predictable that the prevention of silicosis would not derive from refined studies of pulmonary function, and that lasting benefit in chronic renal failure could only come from something which would replace the kidneys—that is, transplantation—or take over their function—that is, repeated dialysis. These methods are now being developed and basic scientific work on the consequences of renal failure has been an important preliminary to their proper use.

Methods of resuscitation occasionally save lives worth saving, as in the treatment of cardiac arrest, but are all too often employed in keeping alive those who would by any possible standard be better dead.

Perhaps the most important therapeutic gains in which clinical scientific departments have played a part have been in the electrolyte field and in endocrinology (though few of these latter have been initiated there), and in cases where physician and surgeon collaborate in the accurate investigation and subsequent surgical treatment of defined conditions, as in cardiac surgery.

Perhaps it does not matter that the academic clinical departments of medicine and therapeutics have not contributed as much as one might have hoped to the treatment and prevention of disease. So much has been done by the non-clinical scientists, together with the drug firms, that the clinical departments have been left with the hard core of chronic disease in an ageing population, which is rather barren soil to cultivate.

A Paradox

But here we come across what Rustein (1967) has called the paradox of modern medicine. The expectation of life in the United States has remained almost stationary for the last 15 years or so and has in fact fallen well below that of other countries, such as Sweden and the United Kingdom. Yet this is not just a phenomenon of the aged, for in males of 15 to 44 years, for instance, the death rate is notably higher in the United States than in Sweden for every major cause of death except suicide. At the same time the infant mortality has failed to improve as compared with other countries, and all this is despite the fact that federal expenditure on biomedical research in universities and hospitals³ in the United States has increased during the last 20 years from \$1m. to \$1,000m.

To return to the clinical scientific departments, I have already acknowledged their contributions to the application of scientific discovery at the bedside. The very pursuit of research, moreover, provided that it is relevant, has merit in its own right in creating an atmosphere of intelligent inquiry; but in medicine the practising physician who is intensely interested in the diagnosis and treatment of the individual patient and responds to the challenge which every fresh patient brings has his own constant stimulus to intellectual inquiry and need not be ashamed if he finds the added burden of organized scientific research something of a distraction. A great deal of modern practice in medicine and surgery has been evolved by men whose researches were part of their daily clinical tasks. Cardiology and neurosurgery are good examples.

The situation in clinical research is bound to be different from that in the laboratory sciences which contribute to medicine. All clinical research is, and must be, applied research. To ask a protein chemist what use his work is going to be to mankind would be an impertinence, but we are entitled to ask *Cui bono?* of a clinical scientist carrying out investigations on patients. And we have a duty to pause from time to time and ask whether clinical science is wholly beneficial, or whether there could even be instances in which its influence was

actually detrimental. For instance, has the obsession for measuring what are now called *parameters* in chronic organic illness led to the neglect of other and more important problems? Do the scientific clinical departments absorb almost all the research potential of our best graduates and thereby deplete the pool available for research directed towards current problems of really pressing nature, such as drug addiction, neurosis, oral contraception, delinquency, alcoholism, aggression, and the prevention of lung cancer?

Is the Harveian method, as interpreted by clinical science, ever really likely to yield therapeutic results? Has it already reached a point of diminishing returns? Does medical science, as taught in academic clinical departments, really develop the prepared mind? If so, why have not more of the ideas behind modern therapy sprung from these departments? Finally, is medical education too much dominated by the clinical scientists at the present time? Some of these questions it will be my endeavour to examine.

Further Heresy

The demands of the clinical scientists for ever more expensive and sophisticated apparatus are justifiable if the things to be measured by the apparatus are relevant and important to the study of human health and disease, and if they cannot be equally well assessed by simpler methods, but no one who has been involved in the disbursement of funds for clinical research can come away without misgivings about whether time, talent, and money are sometimes squandered on the measurement of the trivial, the irrelevant, and the obvious. Given a new and expensive tool such as a gas chromatograph, an electromagnetic flowmeter, or a multichannel recorder of some kind, it becomes all too easy to find a subject for research; for there is bound to be something which has not yet been measured by these means. The need for thought, observation, ideas, and hypothesis, which form the hard work of research, recedes comfortably into the background for a year or two, while the research worker, supported by a grant and relieved of the much harder task of practising medicine, collects his results and has them analysed for him by a computer. One has the impression at times that the thought process starts with "What experiments can be done with these tools?" and that the "imaginative episode of thought" so essential to good scientific discovery has been bypassed. Medawar on scientific method should be required reading in all clinical scientific departments. And Harvey's *De Motu Cordis*.

It is only a very slight exaggeration of the truth to say that I have seen applications for an electroencephalograph to tell whether the subjects of the experiment are awake or asleep, and for a recording device to tell whether a baby is crying; and that I have recently listened to an account of scientific work which seemed to demonstrate beyond reasonable doubt that getting hot is closely correlated with sweating. No wonder that a friend of mine who has a gift for felicitous expression has distinguished between "ideas" research on the one hand and "occupational therapy for the university staff" on the other, and once referred to a research project as "squeezing the last drop of blood out of a foregone conclusion." I am afraid I am not one of those who would count it a triumph of modern medical science that it is possible to measure the blood-flow through the liver in a patient with mitral stenosis who is being exercised on a bicycle ergometer. There is no special significance in this particular example, which is only one of many that could be chosen. At its best this kind of experiment makes a trivial addition to human knowledge, at its worst another contribution to the already bulging archives of the Pappworth (1967) collection.

Research is supposed to train the mind into channels of scientific (and therefore respectable) thought, but does not this kind of research sometimes encourage the erroneous belief that

³ Distributed through the National Institutes of Health.

only that which can be measured is worthy of serious attention? "Not everything we count counts. Not everything that counts can be counted," was wisely said by Dr. Stephen Ross (Jason, 1966). And what kind of impact does the human guinea-pig make on medical students?

But if we are seriously and in all sincerity to try to assess the debit side of clinical science, then unhesitatingly I would put among its greatest failures its almost complete neglect of psychological factors in disease, and this is my next theme.

The Mind

The proper study of mankind is of eternal and absorbing interest, not because man is a chemical engine, as one scientist has told me, for that is an attribute which man shares with the amoeba, but because of the endless variety of the interplay of human personality, intellect, emotion, and motivation. That is what all great literature and great poetry have been about; it is the raw material of nearly every interesting conversation, whether in the senior common room or on the Clapham omnibus.

Yet what is acceptable to read in literature is not always acceptable if it threatens to become an analysis of our own unconscious mind, and man has from earliest times built up an elaborate series of defences lest his carefully sublimated emotions and motivations come disturbingly into consciousness. The defences have taken various forms: the material walls of monasteries, nunneries, and colleges, for instance, where the intelligentsia could isolate themselves from the undesirable and disturbing contacts of everyday life. Sir Arthur Thomson, in his Harveian Oration of 1961, recounted how that wealthy scientist, Henry Cavendish, once met a housemaid on the stairs of one of his mansions and promptly had another staircase built so that this encounter could not recur.

Taboos have been built up and rationalizations and fantasies, of which the legend of the Garden of Eden is surely one of the supreme and most ingenuous of examples.

Freud tried to bring us up against stark reality, but, in spite of him, these defences are as clear in a medical school today as in any other seat of learning.

Walls have been built to segregate those who are mentally ill, but they had the great advantage of isolating not only the patients but also the psychiatrists, who, until the second world war, were almost never allowed in a teaching hospital.

Sex education was taboo until quite recently, and still is in many—perhaps most—medical schools, unless one includes under that term the anatomy of corpses, the study of venereal disease, and the chemistry of hormones. Not my idea of an acceptable introduction to the biology, psychology, sociology, and aesthetics of sex.

"Clinical Material"

Patients, often hideously called the "clinical material" of teaching and research, have been drawn so far as possible from the lower social classes (everyone well brought up knows that the lower social classes have no emotional needs or feelings), and were, and still are, interrogated either in an almost open outpatient department in the presence of numerous students or recumbent in a hospital bed in an open ward; conditions chosen with unerring insight to ensure that the psychological factors in disease, even if present, cannot obtrude and disturb the proper pursuit of scientific medicine. But to make assurance doubly sure, the ward round is conducted as a ritual, the chief followed by his numerous attendants.

The advent of the professorial medical departments, which should have brought with it new attitudes towards patients consistent with the new understanding of interpersonal relations, has in some instances merely reinforced the defences by

a more refined and narrow choice of the "clinical material," by the abhorrence of private practice (thus ensuring that the patient cannot call the tune), and by the development of grand rounds to replace the ritual visits of former years. I have seen a patient wheeled in and demonstrated to a large meeting and wheeled out again without a single word being said to her—not even a word of thanks. Finally, the study of anything except organic disease is dismissed as unscientific. I have heard a research worker who has studied rheumatic disease for many years confess without apparent shame or embarrassment that the idea of investigating psychological factors had never been seriously considered.

Psychological Factors

The advent of the psychiatrists, so long as they can continue to be classed as eccentrics and therefore isolated from the main stream of clinical teaching and research, allows for the continued segregation of personality and emotional problems.

If challenged with neglect of psychological factors in disease, the usual defence mechanism of the clinical scientist is strangely and illogically three-phased: "In psychological medicine there is no corpus of proved knowledge to teach; if there is, there is no way of teaching it; in any case, I teach and practise it myself." Believe me, I am not describing something out of my distant student days, but recounting, without exaggeration, facts and opinions which have come to me through personal contacts during the last two years.

And yet the extent to which the mind and personality influence all illness must be obvious to any who do not close their eyes to the realities around them. One has only to observe two diabetics, for instance, scientifically indistinguishable, both requiring diet and insulin, to see how one will retreat into neurotic invalidism, abetted by his wife in the building of an elaborate and protective ritual, while the other regards his daily life as almost uninfluenced by a few minor inconveniences.

Of course clinical teachers vary greatly in their approach to these problems, and psychiatrists vary too in the amount of help and collaboration they are prepared or, let us admit, equipped to give; but even those who, like myself, have always delighted in the study of people do not, I think, sufficiently realize the amount of our neglect and the full extent of our conformity—"so much doth wont and custom become a second nature"—for we have not asked ourselves the essentially Darwinian-cum-Freudian question—to what end and for what purpose and in response to what selective pressures have the teaching hospitals evolved in this way?

From a research point of view, the defence which requires most serious thought is that "the time is not yet ripe for serious research into psychological medicine. Like infective disease before Pasteur, it awaits a break-through in knowledge." This view, which is rather a favourite at the present time, seems to me quite untenable today. The nature of infectious disease before Pasteur was quite unknown. Though the causes of psychological illness are multiple, varied, and infinitely complex, no one doubts that they are to be found in interactions between heredity, emotional development, social, environmental, and cultural influences, chemical changes (including drug action), and organic cerebral disease. Every one of these can be studied today by methods far more rigorous than existed even a few years ago. Indeed, they are being studied already to great advantage.

New Approaches

Important in this is the study of symptoms revealed by the psychiatric interview aided by modern knowledge of observer error and computer techniques of information storage and analysis, and the validation of methods and conclusions. There

is room for new approaches to the study of human behaviour in health and disease, on the lines of Tinbergen, Lorenz, and Desmond Morris.

"The central features of scientific method," says Martin Roth (1967), "are the dispassionate observation, recording and analysis of data aimed at deriving reliable answers to clearly formulated theoretical and practical questions. The advantages of quantification and controlled experiment are undeniable. But they may be inappropriate or applicable only to a limited extent at certain stages in the development of systematic inquiries in some fields of knowledge. This need not disqualify a discipline from scientific status, provided that the essential criterion, the unbiased collection and verification of observations can be satisfied."

Or, as Gaylord Simpson (1963) has said, the multiplication of relevant observations will not prove a hypothesis, but the more that they fail to disprove it the more confidence we have in the hypothesis; but the proviso is that the observations must be relevant, and to be relevant they must be capable of disproving the hypothesis. These surely were the methods of Darwin, of which we have no need to be ashamed.

There is enough in psychological medicine to keep an army of research workers fully employed for many years, but we shall not attract enough of the right men and women into the study of the mind if we continue to give medical students in their early and formative years no contact with man except as a corpse or a machine, and continue to build up elaborate defences between ourselves and the minds of our patients.

Should anyone doubt whether human behaviour is a fit subject for study, let him make observations on his colleagues, especially in committee. He will soon find behaviour patterns as specific as the song of the thrush; and let him inject noxious stimuli in the form of unwelcome concepts from time to time, and he will find that defence mechanisms springing direct from the unconscious, uninhibited by the rules of logic, surface promptly to the appropriate summons. But perhaps I have been overzealous in what probably amounts, for me, to replacement therapy in my period of bereavement for the loss of clinical medicine, my constant companion for about 45 years, and I had better turn rather hastily to my last subject.

Medicine versus Science

The real distinction between medicine and science is not, of course, a matter of method, nor is it the recognition that man is something more than a machine. It is a matter of aims. The object of the true scientist is discovery; the object of the doctor is to plan the method of action judged to be of best value to the individual. That the aims are different is undeniable; fortunately they do not have to be invariably in conflict.

The first need of the doctor is to have knowledge of the human body and mind in health and disease. Clinical science in medical departments has contributed greatly to knowledge of the body and almost not at all to knowledge of the mind. Given that he has this basic knowledge, the doctor's next task is to find the facts and to evaluate the clinical situation as it develops from day to day throughout the illness. In this he has science and technology among his tools, and he must know how to use them, but he will often find that the evaluation and judgment of the human mind far outweigh the value and accuracy of scientific measurement; and, of course, he requires other qualities, of understanding, insight, interpretation, compassion, and a carefully practised technique, without which the very facts on which he can base a reasoned plan of action will elude him, for they will not cross the barrier between him and the patient's mind. There is, of course, nothing which denies the clinical scientist of these qualities.

In the enthusiasm for teaching principles, the fact that much of medicine depends on the acquisition of technique is some-

times overlooked. Technique can be crucial where academic knowledge is useless. I wonder if Paganini ever realized that he was playing on a logarithmic scale; or cared.

To use the new aids which science has now put at his command the doctor does not have to know the scientific principles from which they have developed; and as science advances and becomes more complex it becomes increasingly impossible for him to do so. This should be accepted by medical educators without guilt or shame. The modern physician does not have to learn the engineering and physical principles on which an x-ray machine is constructed or the chemical nature of the emulsions used on the film in order to interpret an x-ray picture. (Even the interpretation is usually done for him.) He does not have to be a physicist to read an electrocardiogram. Almost none of the physicians who daily prescribe the tetracycline group of drugs knows anything about their chemical structure; or cares. Science is throughout the servant, not the master, a servant to be used with understanding and called on unsparingly in the patient's interest, but dismissed peremptorily and without remorse on all those many occasions when the patient is better off without its services; not only when science becomes a mere intruder in private affairs, but when it has led only to false clues, and the imperative need is to go back to the intimate confrontation of the patient for the information which he alone can give.

This should not mean that the doctor is disinterested in discovery, in the use of new remedies, or in the proper scientific appraisal of all that he does. Indeed, he should welcome the opportunities which scientific medicine presents in these respects; but I believe it to be more difficult to teach the true aims and values of the practice of medicine to undergraduate students from a department in which the primary aim is too obviously research and discovery, in which science has become the master. I know that there will be many who do not agree with me and who see no conflict and no antithesis between the aim of the good doctor and that of the good scientist. They will make the point that when a patient is seriously ill his foremost need is to be under the care of whoever has most knowledge of his kind of illness. This ingenuous view, which at first seems self evident, implies that someone else has first selected the right patient for the right department, and, secondly, that the illness is amenable to treatment or relief by modern medical science and not solely to diagnosis and investigation. "Guérir quelquefois, soulager souvent, mais rechercher toujours."

What is, of course, true is that the same man may wear the mantle of the doctor or that of the scientist with equal grace at different times and occasionally at the same time. Nevertheless, I think that this does not come easily to all people at all times, and such evidence as we have from John Aubrey and Lord Conway and other sources strongly suggests that Harvey himself found the compromise a difficult one. Lord Conway's letter of 1651 to his daughter, who was Harvey's patient, says: "I hear that you have a great opinion of Doctor Harvey. I thinke you doe well to love and respect a person of his merite for I thinke he hath deserved extremely well of all learned men for what he hath found out . . . but in the practice of Physicke I conceive him to be to much governed by his Phantasy . . . To have a Physician abound in phantasie is a perilous thing. . . ."

Conclusions

You will see, Mr. President, that I think the clinical scientist has certain difficulties which do not present themselves to the non-clinical scientist in medical research. I also believe that clinical science in its present state of development has neglected some of its opportunities, and has shown an unfortunate tendency to follow only the methods of physical science, which try to prove everything by contrived experiment, to the neglect of discovery by deliberate and relevant observation and the kind

of evolutionary—or, if you like, teleological—thinking so necessary to the study of biology. For in biology, because of Darwinian selection, we are entitled to ask not only "What?" and "How?" as in physical science, but also "Why?" and "What for?"

Because in clinical science we pride ourselves that we are building up medical knowledge we should not complacently assume that we are always doing it the right way, or making the best use of resources which in any society are bound to be limited. We should remember with John Aubrey that "Pride has been one of the greatest stoppers of the Advancement of Learning."

The defects may be only part of a temporary chapter in the history of medicine, and a symptom of a more widespread ailment. For man has put most of his efforts into improving the material state of society (and perfecting the engines of war), and has given scant attention to the ills of the mind of man and woman, and the study of their behaviour in health and disease and in society.

I know that I have spoken some heresies. If they are rather disturbing ones, my personal researches lead me to believe that the defences of the clinical scientists will be equal to them. Perhaps for another few years.

Nevertheless, with Harvey, "I fear lest I have mankind at large" (or at any rate some of my colleagues) "for my enemies, so much doth wont and custom become a second nature. Doctrine once sown strikes deep its root . . . Still the die is cast and my trust is in the love of truth and the candour of cultivated minds."

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Factors Affecting the Response to Clomiphene Therapy

DAVID FERRIMAN,* D.M., F.R.C.P.; ANTHONY W. PURDIE,† M.R.C.P.GLASG., F.R.C.S.GLASG., F.R.C.O.G.
 MICHAEL CORNS,‡ M.SC.

Brit. med. J., 1967, **4**, 444–446

It has been well established that clomiphene citrate (Clomid), a compound allied to chlorotrianisene (Tace), is capable of inducing ovulation in a substantial proportion of patients suffering from anovulatory infertility, with consequent relief of infertility in a significant number. In the present study we attempt to determine factors concerned with the outcome of such therapy.

Material and Methods

Fifty-five patients attending one gynaecological and one endocrine clinic with amenorrhoea, severe oligomenorrhoea, or mild oligomenorrhoea with anovulatory cycles have been treated with clomiphene. Forty-one of them were also suffering from infertility or amenorrhoea of more than two years' duration. All the patients had a full medical and gynaecological examination to exclude medical or gross gynaecological disorders likely to be associated with menstrual disturbance or infertility. All kept a basal temperature chart for at least six months, often much longer, before treatment, and continued to do this throughout therapy. Gynaecography was performed in 51. In those with infertility endometrial curettage and culture for *Mycobacterium tuberculosis*, hysterosalpingography, and analysis of the husbands' seminal fluid was carried out. Follicle-stimulating hormone assays were not done, but primary ovarian disorder is thought to have been unlikely on clinical grounds.

Oestrogen excretion assays were carried out on 39 patients, both under basal conditions and after treatment with clomiphene. At first, assays were done at weekly intervals for one

month after the start of treatment; experience showed that oestrogen responses tended to be maximal between the second and third weeks, and in the later stages of the investigations assays were performed only on specimens obtained during this period. Total oestrogen assays were made with a modified form of Ittrich's method (Corns and James, 1967), which had a non-specific fluorescent background of 10 µg./24 hours.

Various dosage schedules have been used, ranging from 50 mg. b.d. for five days to 100 mg. b.d. for two weeks. No obvious advantages were found for the longer schedules, and eventually a standard dosage of 100 mg. b.d. for five days was used. All patients were given at least three courses of treatment before it was concluded that no benefit was to be obtained.

Results

Criteria Used in Evaluation of Results.—Three types of response to clomiphene were distinguished: (1) no response, (2) menstruation without ovulation (as evidenced by absence of progestational temperature rises), and (3) ovulation and menstruation. Examination of our data suggested that the most meaningful classification would be into those with and those without evidence of ovulation. The criterion used for the diagnosis of polycystic ovaries was a gynaecography index exceeding 21 (Ferriman and Purdie, 1965).

Ovulatory Response in Relation to Duration of Cycles.—Consideration of our findings suggested that a significant division would be into patients with menstrual cycles less than or exceeding six months. The data have been analysed accordingly and the results are shown in Table I. Clearly patients with cycles of less than six months' duration fared better than those with cycles exceeding this figure. The difference is highly significant at the 0.1% level ($\chi^2 = 12.40$).

* Physician, North Middlesex Hospital, London N.18.

† Senior Obstetrician and Gynaecologist, North Middlesex Hospital, London N.18.

‡ Steroid Chemist, North Middlesex Hospital, London N.18.

TABLE I.—Relation of Ovulatory Response to Duration of Cycles

Cycles	Patients	
	Ovulated	Total
> 6 months	14	29
< 6 "	24	26

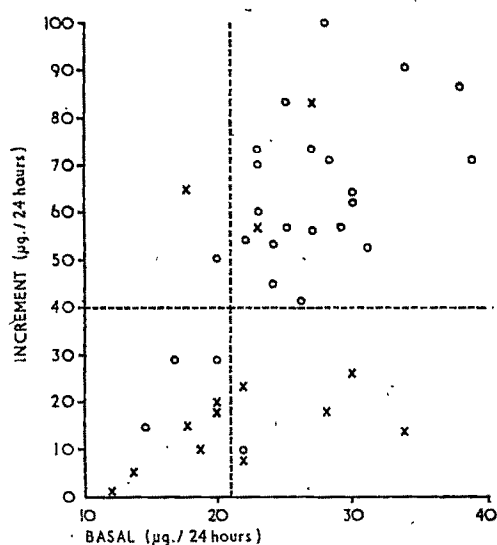
Ovulatory Response in Relation to Basal Oestrogen Excretion.

—The Chart relates basal oestrogen excretion for each patient to the increments of oestrogen excretion after clomiphene therapy and the presence or absence of an ovulatory response. Scrutiny suggests significant dividing lines between basal oestrogen excretions above or below 21 $\mu\text{g.}/24$ hours, and between increments of oestrogen excretion above and below 40 $\mu\text{g.}/24$ hours. Patients with basal excretions below 21 $\mu\text{g.}/24$ hours generally have increments of excretion below 40 $\mu\text{g.}/24$ hours and lack of ovulatory response. Patients with basal oestrogen excretions above 21 $\mu\text{g.}/24$ hours generally have increments of excretion above 40 $\mu\text{g.}/24$ hours and an ovulatory response. Several patients show high increments of excretion without ovulation, though usually with menstruation. Others show ovulation with low increments of excretion; examination of basal temperature charts showed that this was invariably caused by failure to collect specimens for assay during the progestational phase, a defect in our experimental design. The data are set out in Table II. The tendency for ovulatory response to be related to higher basal oestrogen excretion is clear, and the figures approach significance at the 5% level ($\chi^2=3.582$ by Yates's method; Maxwell, 1961).

Ovulatory Response in Relation to Ovarian Size.—Table III shows ovulatory response in patients with normal and polycystic ovaries. It is clear that patients with polycystic ovaries

TABLE II.—Relation of Ovulatory Response to Basal Oestrogen Excretion

Oestrogen Excretion	Patients	
	Ovulated	Total
< 21 $\mu\text{g.}/24$ hours	4	11
> 21 "	21	28



Relation of basal oestrogen excretion to increment of oestrogen excretion and ovulatory response after clomiphene therapy. O=Patients with ovulatory response. X=Those showing lack of response.

TABLE III.—Relation of Ovulatory Response to Ovarian Size

Ovarian Size	Patients	
	Ovulated	Total
Normal	14	27
Polycystic	21	24

fare better than those with normal ovaries. The difference is very significant at the 1% level ($\chi^2=7.498$).

Ovulatory Response in Relation to Duration of Cycles and Ovarian Size.—The data relating ovulatory response to duration of cycles have been broken down into groups with normal and polycystic ovaries in Table IV. The same tendency for patients with cycles of less than six months' duration to fare better than those with longer cycles is shown in both groups, though this is much more pronounced in patients with normal-sized ovaries than in those with polycystic ovaries. Patients with polycystic ovaries noticeably predominated in the group with cycles of less than six months' duration, and those with normal-sized ovaries noticeably predominated in the group with longer cycles; this is very significant at the 1% level ($\chi^2=10.283$).

TABLE IV.—Comparison of Ovulatory Responses in Relation to Duration of Cycles Between Patients with Normal and Polycystic Ovaries

Cycles	Ovaries			
	Normal		Polycystic	
	Ovulated	Total	Ovulated	Total
> 6 months	8	20	5	7
< 6 "	6	7	16	17

Conception.—Nine out of the 41 patients complaining of infertility conceived. Five have successfully gone to term and three were still pregnant at the time of writing. Pregnancy in the ninth ended in abortion. One of the patients subsequently going to term had an abortion after an earlier course of clomiphene.

Table V shows the incidence of conception in patients with normal and polycystic ovaries. Clearly, patients with normal ovaries fared better than those with polycystic ovaries. The figures approach significance at the 5% level ($\chi^2=3.197$ by Yates's method; Maxwell, 1961).

TABLE V.—Relation of Conception to Ovarian Size

Ovarian Size	Patients	
	Conceived	Total
Normal	6	16
Polycystic	2	21

Discussion

Our classification of response to clomiphene based upon basal temperature charts and the occurrence or otherwise of menstruation complement the findings of Bell and Loraine (1966), based on steroid excretion studies. These workers found three types of response: (1) no change in oestrogen nor in pregnanediol excretion; (2) a rise in oestrogen but none in pregnanediol excretion; and (3) a rise in both oestrogen and pregnanediol excretion similar to that found in the normal menstrual cycle.

Our finding that patients with basal oestrogen excretion levels exceeding 21 $\mu\text{g.}/24$ hours respond better than those with lower excretion levels is very similar to findings reported by Bell and Loraine (1966) and Townsend *et al.* (1966), bearing in mind the nonspecific background fluorescence of 10 $\mu\text{g.}/24$ hours found in our method.

Our group of patients with menstrual cycles of less than six months' duration contain a marked preponderance with polycystic ovaries, while the group with cycles of more than six months' duration contain a marked preponderance of normal-sized ovaries. The explanation in the present state of knowledge can only be conjectural. If one postulates an underlying disturbance of hypothalamic centres governing gonadotrophin production, the milder forms of the disorder may have some

residual follicle stimulating hormone secretion leading to the production of polycystic ovaries (Ferriman, 1960); all follicle stimulating hormone secretion may have disappeared in the more severely affected patients. The development of sensitive and precise radio-immunological assays for gonadotrophins may shed some light on the problem before long.

The incidence of conception in our series (9 out of 41) is higher than we would have anticipated from our previous experiences in the field. This has been the experience of many other workers (Greenblatt, 1966). It is not possible to make a precise statistical assessment of the comparative value of this drug in the absence of control data. The provision of such data would be of great interest.

It is odd that while patients with polycystic ovaries show a better ovulatory response to clomiphene than those with normal-sized ovaries their conception rate should be lower. Perhaps the thickened capsules of the polycystic ovaries interfere with the release of ova, or the increased production of androgen by these ovaries impairs nidation.

Summary

The ovulatory response to clomiphene is significantly better in patients with menstrual cycles of less than six months' duration compared with those whose cycles exceed this figure, and

in patients with polycystic ovaries compared with those whose ovaries are of normal size. It is better in patients with basal oestrogen excretions exceeding 21 $\mu\text{g.}/24$ hours than in those whose excretion levels fall below this figure (obtained by a method having a nonspecific background fluorescence of 10 $\mu\text{g.}/24$ hours), though the difference does not quite reach formal significance.

Patients with normal-sized ovaries conceive more readily than those with polycystic ovaries. The difference does not quite reach formal significance.

We wish to thank Dr. D. Mansell-Jones and Dr. J. P. Birkett, of Merrell-National, for supplies of Clomid and for a generous grant towards expenses; Dr. W. G. Dangerfield for laboratory facilities; Mrs. F. Norris for statistical analyses; and Miss S. Ferriman and Miss E. Whiteley for preparation of the diagram.

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Current Concepts in the Treatment of Anovulation

E. RABAU,* M.D.; D. M. SERR,* M.B.; S. MASHIACH,* M.D.; V. INSLER,* M.B., B.CH.
 M. SALOMY,* M.D.; B. LUNENFELD,† M.D.

Brit. med. J., 1967, 4, 446-449

When mechanical or anatomical lesions are excluded, disturbances of ovulation and corpus luteum function represent the main cause of infertility.

The factors which disturb the proper function of the reproductive system from within may stem from any of the participating cells or populations of cells in the central nervous system, the pituitary gland, the ovary, or perhaps even the uterus. These factors may involve faulty stimulation (abnormal magnitude, sequence of appearance, or time of action of stimuli) or faulty response of the target cells or organs. Each and every one of these factors, if sufficiently powerful, or when acting long enough, may lead to an imbalance of the hormonal feedback mechanism and consequently to impaired fertility. In the majority of cases some absolute or relative primary or secondary abnormality in the nature or magnitude of gonadotropic stimulus exists, regardless of the primary cause. A convenient simplification is to divide these patients into two groups: those with gonadotropic insufficiency due to primary failure in production of gonadotrophins, and those with abnormal gonadotropic stimulus due to disturbed release of gonadotropic hormones.

Preparations of human gonadotrophins and clomiphene citrate have proved to be of definite value in the treatment of these two groups of patients.

Recently gonadotropic extracts from human post-mortem pituitaries and human menopausal urine have been made available for clinical use. These preparations in conjunction with human chorionic gonadotrophins have proved capable of inducing ovulation. Numerous pregnancies have resulted from such treatment (Gemzell, 1966; Lunenfeld and Donini, 1966; Shearman, 1966; Rabau *et al.*, 1967). It was shown by Crooke *et al.* (1963) and Diczfalussy *et al.* (1964) that gonadotropic preparations derived either from human post-mortem pituitary glands or from postmenopausal urine, administered to the same patients, provoked a similar response as judged by steroid excretion patterns and by vaginal or endometrial morphology.

Another approach to the treatment of anovulation was made possible by the introduction of clomiphene citrate (MER-41). This synthetic non-steroid preparation is a derivative of chlorotrianisene (TACE) and possesses both oestrogenic and anti-oestrogenic properties (Greenblatt, 1966). The exact mechanism of action of clomiphene in inducing ovulation is as yet unclear. Since urinary excretion of gonadotrophins was reported to be increased during or immediately after administration of clomiphene (Dickey *et al.*, 1965), it has been suggested that the drug acts either directly or indirectly on

* Department of Obstetrics and Gynaecology, Tel-Hashomer Government Hospital and Tel Aviv University Medical School, Tel Aviv, Israel.

† Institute of Endocrinology, Tel-Hashomer Government Hospital and Tel Aviv University Medical School, Tel Aviv, Israel.

the release of gonadotropins. There is, however, no general agreement whether clomiphene causes the release of follicle-stimulating hormone (F.S.H.) (Kistner, 1966), luteinizing hormone (L.H.) (Igarashi *et al.*, 1967), or both (Dickey *et al.*, 1965). Whatever the exact nature of its action, clomiphene citrate has been shown capable of inducing ovulation in certain types of anovulatory patients (Johnson *et al.*, 1965; Greenblatt, 1966; Kistner, 1966; Serr *et al.*, 1966; Shearman, 1966).

Principles and Results of Treatment

Human gonadotropins or clomiphene citrate were administered to 235 patients through 761 courses of treatment. The patients were divided into two main groups according to the level of gonadotropins and to the endogenous oestrogen activity as judged by urinary oestrogen, vaginal smears, cervical mucus, and/or occurrence of withdrawal bleeding following administration of medroxyprogesterone acetate (MAP).[‡] The two main groups were subsequently subdivided according to the clinical signs, such as amenorrhoea and other ovulatory disturbances as outlined in Table I. Patients who had low

TABLE I.—Number of Cases and Treatment Courses in Various Groups of Patients With Ovulatory Failure

	No. of Cases	No. of Treatment Courses
Group I (low gonadotropins, no evidence of endogenous oestrogen activity):		
Primary amenorrhoea	27	52
Secondary	65	127
Post-partum amenorrhoea (Chiari-Frommel syndrome)	7	9
Sheehan's syndrome	1	1
Group II (gonadotropins in normal range, evidence of endogenous oestrogen activity):		
Secondary amenorrhoea	18	53
Follicular phase disturbances (oligomenorrhoea)	34	105
Polycystic ovary syndrome (histologically proved)	6	29
Anovulation with fairly regular cycles	31	83
Group III (corpus luteum insufficiency)	46	302
Total	235	761

urinary gonadotropins and no detectable oestrogenic activity were treated by human gonadotropins; those with urinary gonadotropins within the normal range and evidence of endogenous oestrogen activity (MAP-positive) were given either gonadotropic preparations or clomiphene citrate; cases diagnosed as corpus luteum insufficiency were treated with clomiphene only, and formed a separate group (group III).

Dosage, Treatment Schedules, and Results of Gonadotropic Treatment

Human menopausal gonadotropin (H.M.G.)[§] having both follicle-stimulating and luteinizing activities was used. Each ampoule of the preparation contains approximately 75 i.u. of F.S.H. and 75 i.u. of L.H. Each treatment course was scheduled according to the patient's individual response. Treatment was started with H.M.G. (Pergonal) at a dose varying from 1 to 4 ampoules per day. Follicle maturation and oestrogen secretion were evaluated from urinary oestrogen levels, crystallization of cervical mucus (ferning pattern), the appearance of external cervical os, vaginal smears, and ovarian size. Treatment was continued until oestrogen secretion, as evidenced by the response of these target organs, was somewhat greater than during the peak of a normal preovulatory phase.

[‡] Progestational agent with no intrinsic oestrogenic activity.

[§] Supplied as Pergonal by Istituto Farmacologico "Sersono," Rome, Italy, and later by Ikapharm, Ramat-Gan, Israel.

Administration of human chorionic gonadotropin (H.C.G.)^{||} was then started. Pergonal was usually continued during the first two days of H.C.G. administration, which was given in a dose of 5,000–10,000 i.u. daily for three to four days. The patients were instructed to have intercourse on each of these days.

Diagnosis of ovulation was regarded as proved only if pregnancy ensued. The occurrence of ovulation and the presence of a functioning corpus luteum were, however, presumed on the basis of the following criteria: basal body temperature shift, progestational changes in vaginal smears, disappearance of previously strong positive ferning pattern, urinary pregnanediol excretion of at least 2 mg./24 hours, secretory changes in the endometrium, and menstrual bleeding appearing 13±2 days after the presumed day of ovulation.

Table II shows the results of sequential H.M.G.-H.C.G. therapy. Most of the patients responded to treatment with doses varying up to 50 ampoules of Pergonal and 25,000 i.u. of H.C.G. Only in a few cases were higher doses needed to produce the desired effect. Statistical evaluation showed a significant correlation between the nature of the hormonal disturbance and the quantity of H.M.G. required for ovulatory response. Patients with amenorrhoea needed significantly more Pergonal than those with follicular phase disturbances (oligomenorrhoea) and anovulation ($P<0.001$). Whether these differences in response were caused by differences in ovarian sensitivity to gonadotropins or were related to the effect of the patient's endogenous feedback mechanism is as yet unknown.

TABLE II.—Results of Sequential H.M.G.-H.C.G. Treatment in 134 Patients (1961–6)

	No. of Cases	No. of Courses	Courses per Patient	Presumed Ovulation		Pregnancy		
				No.	% of Courses	No.	% of Patients	% of Courses
Group I								
Primary amenorrhoea ..	27	52	1.9	43	82.6	17	62.9	32.7
Secondary ..	65	127	1.9	114	89.7	41	63.0	32.3
Post-partum amenorrhoea (Chiari-Frommel syndrome) ..	7	9	1.3	9	100.0	6	85.7	66.6
Sheehan's syndrome ..	1	1		1		1		
Subtotal (group I) ..	100	189	1.9	167	88.3	65	65.0	34.4
Group II								
Secondary amenorrhoea ..	7	16	2.3	16	100.0	5	71.4	31.3
Follicular phase disturbances (oligomenorrhoea) ..	11	17	1.5	15	88.2	7	63.6	41.1
Anovulation with fairly regular cycles ..	16	34	2.1	26	76.5	3	18.8	9.0
Subtotal (group II) ..	34	67	1.9	57	85.0	15	44.1	22.4
Total	134	256	1.9	224	87.5	80	60.0	31.3

The overall abortion rate after treatment with H.M.G. and H.C.G. was 24%. Mild adverse reactions were noted in 4.2% and severe reactions (hyperstimulation syndrome) in 2.8% of patients. A detailed description of adverse reactions was reported elsewhere (Mozes *et al.*, 1965; Rabau *et al.*, 1967).

Dosage, Treatment Schedules, and Results of Clomiphene Treatment

One hundred and one patients were treated through 505 courses (Table III). The criteria of positive response were identical with those employed in gonadotropic treatment. As to the dosage schedules, numerous authors (Naville *et al.*, 1964; Dickey *et al.*, 1965; Kistner, 1965; Pildes, 1965; Serr *et al.*, 1966; Shearman, 1966) pointed out that lower dosage and shorter treatment resulted in a decrease of more serious side-effects related to ovarian overstimulation, while the overall pregnancy rate remained unaffected.

^{||} Supplied as Chorigon by Ikapharm, Ramat-Gan, Israel.

We generally start with a dose of 50 mg. of clomiphene daily for seven consecutive days. Only those patients who do not respond to this dosage (with either rise in basal body temperature or increase in urinary pregnanediol) are given 75 mg. daily for seven days. Those who still do not respond are then given a trial course of 100 mg. daily for the same length of time. If two trials with this latter regimen are ineffective the patient is classified as unsuitable for clomiphene therapy and is scheduled for treatment with human gonadotropins. Gonadotropic treatment after failure to respond to clomiphene has been used so far in five patients. Two of them conceived.

TABLE III.—Results of Clomiphene Treatment in 101 Patients

	No. of Cases	No. of Courses	Courses per Patient	Presumed Ovulation		Pregnancy		
				No.	% of Courses	No.	% of Patients	% of Courses
Group II:								
Secondary amenorrhoea	11	37	3.4	16	43.2	4	36.3	10.8
Follicular phase disturbances (oligomenorrhoea)	23	88	3.8	63	71.6	13	56.5	15.7
Polycystic ovary syndrome*	6	29	4.8	25	86.2	2	33.3	7.0
Anovulation with fairly regular cycles	15	49	3.3	36	73.4	8	53.3	16.3
Subtotal (group II)	55	203	3.7	140	68.9	27	49.0	13.3
Group III: Corpus luteum insufficiency (or anovulation with luteinization of follicles)	46	302	6.6	176	58.2	7	15.2	2.3
Total	101	505	5.0	316	62.6	34	33.6	6.7

* Proved by histology.

The overall abortion rate in patients treated with clomiphene was 20.6%. No serious adverse reactions were noted.

Discussion

Disturbance of ovulation is one of the main causes of sterility. The use of sequential H.M.G.-H.C.G. therapy and of clomiphene enabled induction of ovulation in a considerable number of anovulatory patients. A prerequisite condition for successful induction of ovulation is the presence of ovaries capable of response to stimulation. Therefore patients with ovarian agenesis or dysgenesis or with menopausal-like ovaries are unsuitable for this treatment. Since the action of clomiphene is mediated through the pituitary, in patients treated with this agent the presence of a pituitary gland capable of synthesizing gonadotropins is essential. We have divided patients with anovulation into two groups: those with primary failure in production of gonadotropins, and those with abnormal gonadotropic stimulus due to disturbed release of gonadotropic hormones. The latter condition may be caused either by a defect in the pituitary-hypothalamic complex or by abnormal ovarian feedback mechanism. Patients in group I present with primary or secondary amenorrhoea, low or undetectable gonadotropins, and absence of endogenous oestrogen production. Patients in group II have gonadotropins in the normal range (sometimes low), secondary amenorrhoea, oligomenorrhoea or anovulatory cycles, and evidence of endogenous oestrogen production. In group I cases substitution therapy by H.M.G. and H.C.G. is needed. Patients in group II may be treated with human gonadotropins or with clomiphene with a very similar success rate.

Since pregnancy is the main goal of treatment and the only unequivocal sign of ovulation, the results of treatment with human gonadotropins or with clomiphene should be analysed in relation to the pregnancy rate. Such an analysis shows that in our material sequential H.M.G.-H.C.G. therapy gave the

best results in patients of group I, and the pregnancy rate obtained in group II was somewhat lower (65% and 44.1% respectively). The mean percentage of treatment courses resulting in pregnancy was significantly higher in group I (34.4) than in group II (22.4). The lower pregnancy rate in this latter group was due mainly to the poor results obtained in patients with anovulation associated with fairly regular menstrual cycles. However, it should be pointed out that these patients responded well to clomiphene treatment—53.3% of pregnancies. It might be speculated that in these cases the patient's feedback mechanism interferes unfavourably with gonadotropic treatment. Clomiphene, allowing a more flexible interplay between gonadotropic release and ovarian feedback, provides better results.

The overall results of clomiphene treatment in group II were similar to those obtained by gonadotropic therapy, 49.0% and 44.1% pregnancies respectively. It should be noted, however, that clomiphene required more treatment courses than sequential H.M.G.-H.C.G. administration. The mean number of courses per patient was 3.7 in clomiphene treatment and 1.9 in gonadotropic therapy. The percentage of treatment cycles resulting in pregnancy was 13.3 and 22.4 in clomiphene and gonadotropic therapy respectively. This may be due to the simpler but more rigid dosage scheme used in clomiphene treatment as compared with the flexible, individually adjusted treatment schedule of gonadotropic therapy.

Our results with clomiphene treatment show a pregnancy rate higher than that reported by other authors (Bishop, 1965; Johnson *et al.*, 1965; Beck *et al.*, 1966; Greenblatt *et al.*, 1966). This is probably due to preselection of patients.

In group III (corpus luteum insufficiency) clomiphene gave rather poor results. Pregnancy was achieved in only 15.2% of patients and in 2.3% of treatment courses. Sequential H.M.G.-H.C.G. given to a few patients produced even poorer results. Patients in this group differ from those in groups I and II because they show indirect signs of ovulation such as a rise in basal body temperature, disappearance of previously positive ferning pattern, progestational effect in vaginal smears, and some degree of secretory changes in the endometrium. Urinary pregnanediol excretion is above 1 mg./24 hours but rarely reaches normal values.

Oestrogen deficiency found in some of these patients during the follicular phase suggests that at least a part of this group represent anovulation with luteinization of unruptured follicles, rather than ovulatory cycles with insufficient corpus luteum function. It might be speculated that in these patients the disease is due to faulty response of the ovaries to gonadotropic stimulation. Detailed investigations of this group of patients are in progress.

On the basis of presented data it may be concluded that treatment with human gonadotropins and with clomiphene citrate is highly effective in sterility due to anovulation. When the patients are carefully selected for suitable treatment an overall pregnancy rate of 57% may be expected.

Summary

A series of 235 patients with infertility due to disturbances of ovulation were treated with human gonadotropins or with clomiphene citrate. The patients were divided into two main groups according to the level of urinary gonadotropins to the endogenous oestrogen activity. Patients with corpus luteum insufficiency formed a separate group. Group I (low urinary gonadotropins, no evidence of endogenous oestrogen activity) comprised 100 patients with primary, secondary, or postpartum amenorrhoea. Group II (gonadotropins in normal range, evidence of endogenous oestrogen activity) included 89 patients with secondary amenorrhoea, oligomenorrhoea, or anovulatory cycles. Forty-six patients with corpus luteum insufficiency formed group III.

‡ Generously supplied as Clomid by Wm. Merrell Co., U.S.A., and later as Ikaclomin by Ikapharm, Israel.

Patients of group I were given sequential H.M.G.-H.C.G. therapy, those of group II received either gonadotropins (34 cases) or clomiphene (55 cases), and those of group III were treated with clomiphene only.*

Gonadotropic therapy gave better results in patients of group I than in those of group II (65% and 44.1% of pregnancies respectively). In group II patients gonadotropins and clomiphene gave similar results (49% and 44.1% pregnancies respectively). The results in group III were poor (15.2% of pregnancies).

When patients are carefully selected for suitable therapy, sequential H.M.G.-H.C.G. or clomiphene therapy provides an overall pregnancy rate of approximately 57%.

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Three Swedish Families with Porphyrria Variegata*

B. HAMNSTRÖM, M.D.; B. HAEGER-ARONSEN, M.D.; J. WALDENSTRÖM, M.D., F.R.C.P.; B. HYSING, M.D.
J. MOLANDER, M.D.

Brit. med. J., 1967, 4, 449-453

The interest in porphyrins and porphyria diseases has increased considerably during the last decades. This fact is probably partly due to the great progress made in porphyrin chemistry during that time.

In Sweden porphyria acuta intermittens (PAI) is predominant among the diseases with disturbances in the porphyrin metabolism. One of us (Waldenström) has studied this disease and its spread in our country during the last 35 years. About 600 cases are now known, half of them still living. Careful genetic studies have revealed a non-sex-linked inheritance of Mendelian dominant type. Clinically the classical symptoms are, first, severe abdominal pain which may lead to operations with fatal outcome; psychiatric symptoms, varying from short periods of confusion to severe psychosis, where sedating drugs aggravate the state; and neurological manifestations such as coma or epileptic fits, and above all pareses, including respiratory paralysis, which has often been the cause of death. We do not know of any clear-cut PAI patient with light-sensitivity. Chemically the typical findings in PAI are increased urinary excretion of porphyrin precursors—that is, porphobilinogen (PBG) and δ -aminolaevulinic acid (ALA). The disease has therefore been designated as pyrrholia or pyrrholoporphyrria. The latent cases were found by analysis of PBG in the urine (Waldenström, 1937). The faecal excretion of porphyrins is only slightly increased or not at all increased (Haeger-Aronsen, 1962). The absence of preformed porphyrins inside the body has been regarded as the explanation of the lack of light-sensitivity.

Among the white population in South Africa a great number of patients have been shown to have a special type of porphyria (Dean, 1953; Dean and Barnes, 1955, 1958; Eales, 1956, 1960). Clinically, all the symptoms typical of PAI may be present, often with light-sensitivity. In many cases only the skin is affected. As in PAI, the inheritance is dominant, non-sex-linked. Because of the varying symptoms the disease was given the name porphyria variegata (PV) by Dean and Barnes (1959). The best way to find the latent cases of this disease is to analyse the faecal excretion of porphyrins, which is almost always markedly increased. It has been claimed that only during the acute stage is the PBG and ALA excretion in the urine pathologically increased. At first the difference between PAI and PV regarding cutaneous symptoms was supposed to be due to the higher intensity of sunlight in Africa. However, the different biochemical characteristics mentioned above and the appearance of PAI in South Africa with signs and symptoms quite typical and without genetical connexion with PV (Dean, 1963) supported the earlier opinion of Waldenström that PAI and PV were two different gene defects. Dean and Barnes (1959) confirmed this statement once and for all.

Earlier, 13 Swedish cases from four different families with porphyria variegata or protocoproporphyrria were reported (Waldenström and Haeger-Aronsen, 1963). We suspected that these cases, of which five were latent, represented PV, since one from each family suffered from light-sensitivity and several cases had considerably higher faecal excretion of porphyrins than is usually seen in PAI. The only case which fulfilled all the criteria so completely that the diagnosis PV could be made with certainty was that of a Danish woman (Case 3).

* From the Departments of Medicine in Karlstad, Malmö, and Ängelholm, Sweden.

Material and Results

Our material consists of 24 cases occurring in three families (Figs. 1-3). Two of the families (A and B) were descended from Småland, in the southern part of Sweden. Genetical studies tracing the ancestors back to the middle of the nineteenth century failed to reveal any blood relationship between these two families or with any families having acute porphyria intermittens. The third family (C) is of particular interest because of its origin from the Skellefteå area, on the Gulf of Bothnia, where most PAI patients live. Some of the ancestors have been traced back to the end of the eighteenth century, but no relationship to the PAI families has been found. The so-called church books have, however, been partly destroyed by fire, and so the genetical studies have not been completed.

Case Reports

Family A. Case III:3.

House painter, born in 1937. During 1952 to 1955 he indulged heavily in alcohol, but since then has always been sober. He married in 1958. From that time he began to feel more nervous than previously, probably partly because of domestic problems. In 1960 he took eight tablets of Diminal (butenemal + allypropymal), possibly with suicidal intention. He had to stay in hospital for one day, and was then discharged in good shape. In 1960-3 he consulted several doctors because of his nervousness and was prescribed sedatives in the form of meprobamate, with barbiturates and especially Mebumal (pentobarbitone B.P.), of which he took 0.10-0.15 g. almost every evening during long periods. In September 1961 he had acute pains in his arms and particularly in the thumbs. The pain was deeply located, totally independent of effort, and of a

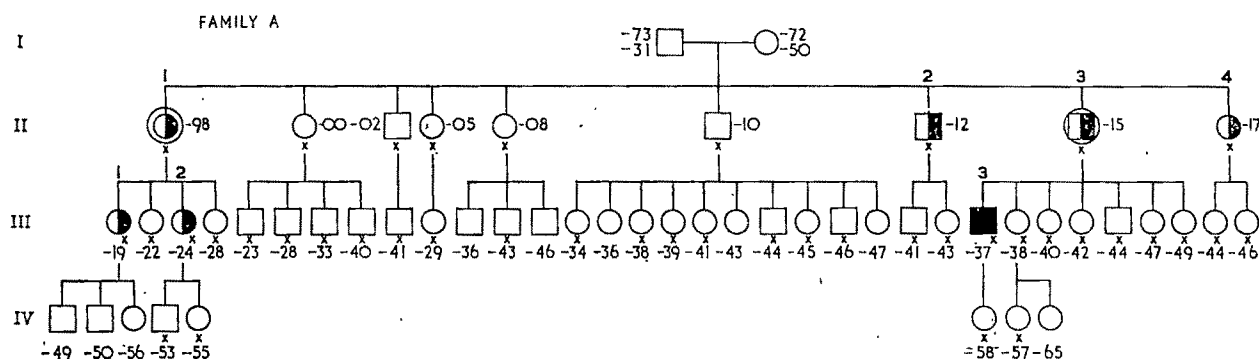


FIG. 1.—Family A, with porphyria variegata. Squares represent males and circles females; solid symbols, manifest cases; semisolid symbols, latent cases; hollow symbols, unaffected members. x below symbol indicates that the member has been examined. Circle around symbol means carrier of the porphyria trait.

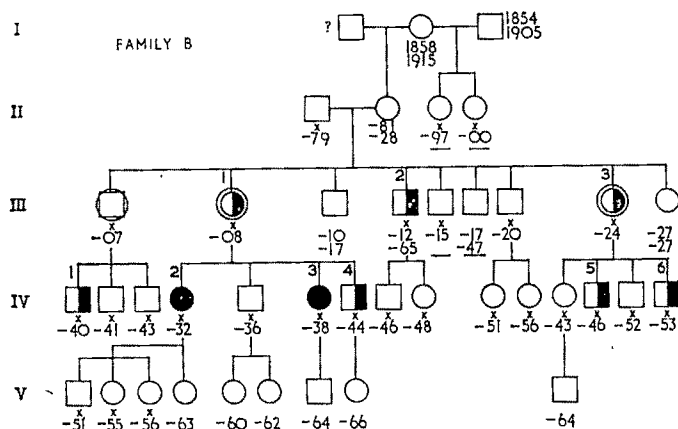


FIG. 2.—Family B, with porphyria variegata.

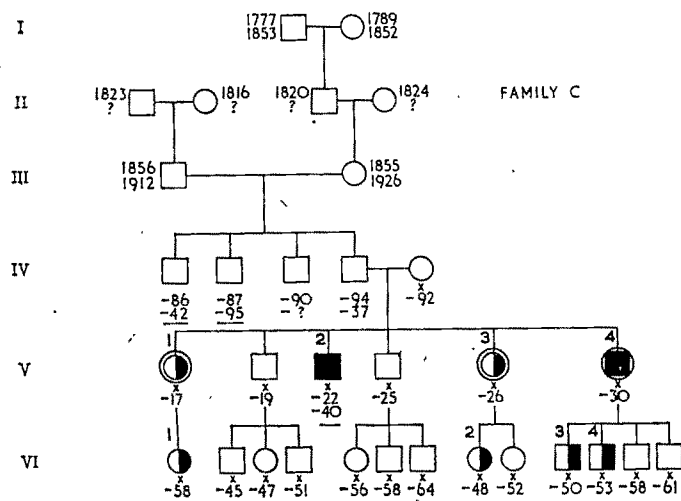


FIG. 3.—Family C, with porphyria variegata.

continuous, very unpleasant character. The muscles were not tender. The pains disappeared spontaneously but sometimes returned later. In the summer of 1962 the patient noticed sensitivity to light for the first time. Because of his profession his hands had often to be in the sunshine during the summer, and blisters developed on the backs of them. The blisters ulcerated, and not until the autumn did they heal, with scars and pigmentation (Fig. 4). The skin was also rather sensitive to mechanical trauma. In the summer of 1963 the skin symptoms returned and were located in his face.

For many years the patient had had epigastric discomfort resembling acid gastritis (some of his brothers and sisters had the same symptoms without being carriers of the PV gene). In the autumn of 1962, when there was a sharp marital conflict, he had particu-

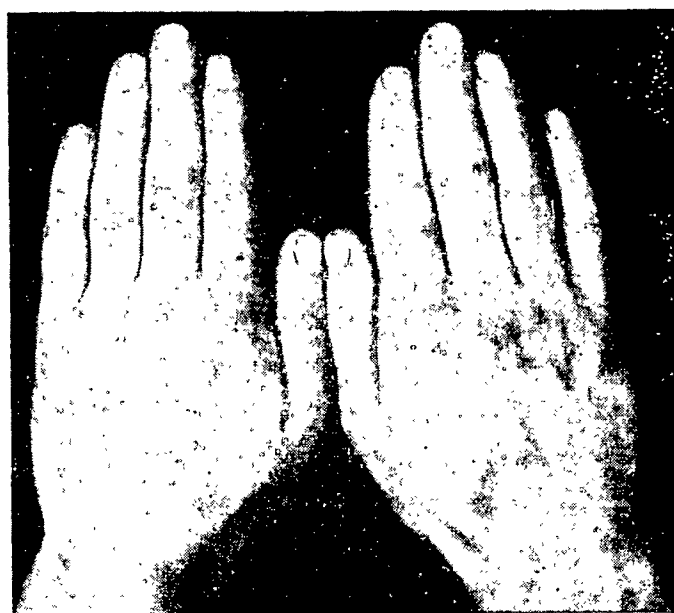


FIG. 4.—Hands of Case A, III:3.

larly severe abdominal pains, which led to increased drug consumption. He at last called in a doctor, and went to the hospital surgical ward with the diagnosis of *ulcus penetrans* (?). He could not distinguish between the gastralgia and these new pains—no doubt explained by his porphyria—in any other way than that the latter were more severe and much more continuous. At the hospital, where he was admitted on 3 December 1962, the pains disappeared after a few days; and a confusion state with hallucinations developed. Later the patient remembered that he thought the hospital was on fire, which he could see and smell. The psychotic symptoms were so severe and he was so agitated that on 10 December he was sent to a mental hospital; there he soon improved.

During the first few days in the hospital he was given barbiturates, but from 8 December only chlorpromazine was prescribed.

The colour of his urine was always normal. The diagnosis porphyria variegata (see Table) was suspected by one of us (Hamnström) and fully confirmed by the laboratory data.

Urinary Excretion of δ -aminolaevulinic Acid (ALA), Porphobilinogen (PBG), Uroporphyrin (UP), and Coproporphyrin (CP) and of Faecal CP and Protoporphyrin (PP) in 24 Patients from 3 Families with Porphyria Variegata

Family	Case	Urine				Faeces	
		ALA (mg./ 100 ml.)	PBG (mg./ 100 ml.)	UP (μ g./ 100 ml.)	CP (μ g./ 100 ml.)	CP (μ g./g.) (Dry Weight)	PP (μ g./g.) (Dry Weight)
A	II:1 L*	0.19	0.09	3	40	42	53
	II:2 L	0.27	0.10	3	4	14	56
	II:3 L	2.49	0.59	75	91	100	310
	II:4 L	0.93	0.35	16	4	17	50
	III:1 L	0.25	0.23	31	19	44	105
	III:2 L	0.35	0.19	1	4	149	333
	III:3 M†	2.66	3.21	438	281	176	393
B	III:1 L	0.46	0.16	13	6	42	110
	III:2 L	—	0.82	—	—	—	—
	III:3 L	0.22	0.18	3	7	7	66
	IV:1 L	0.39	0.09	0	3	134	261
	IV:2 M	0.94	0.82	72	128	176	342
	IV:3 M	3.44	3.61	130	1,022	213	626
	IV:4 L	0.34	0.03	6	2	32	60
	IV:5 L	0.27	0.19	1	0	42	63
	IV:6 L	0.48	0.16	5	0	17	48
C	V:1 L	0.17	0.08	20	3	86	34
	V:2 M	—	—	+++	—	—	—
	V:3 L	0.15	0.03	8	20	401	106
	V:4 M	0.68	0.09	14	3	2,381	378
	VI:1 L	0.47	0.13	7	3	85	16
	VI:2 L	2.00	0.08	0	1	11	51
	VI:3 L	0.04	0.06	5	2	307	89
	VI:4 L	0.19	0.06	27	46	151	77
Normal upper limits ($m+2$ S.D.)		0.60	0.20	11	15	6	39

* L = latent. † M = manifest.

The patient left the hospital in a good condition. During the late spring of 1963 he began to work outdoors again, but his skin condition was aggravated, and he had very severe abdominal pains. He knew the risks of barbiturates, and has denied having taken such medicine after 1962. Since that time he could not take alcohol either, because it caused abdominal pains.

In July 1963 he again developed confusion. He was sent to hospital, where he spent nine days without receiving any barbiturates and was discharged in a good condition. Since then he has not had any abdominal or psychiatric crises, nor has he shown any neurological symptoms. His physical status was always mainly normal. His blood pressure, for example, was almost normal, and he had had no tachycardia, not even in the acute stage of the disease. Routine blood analyses showed nothing abnormal. In the acute stage, however, an increased activity of serum alanine aminotransferase and serum aspartate aminotransferase to a maximum of 204 units and 142 units respectively was registered. Later the transaminases became normal.

Analysis of urine and faeces from 41 of the proband's relatives was performed. It was then found that the patient's father (Case II:3), two of the father's sisters (Cases II:1 and II:4), one of the father's brothers (Case II:2), and two cousins (Cases III:1 and III:2) were also carriers of the porphyria variegata trait (see Table). As they had never had any symptoms typical of porphyria variegata they were considered to be latent cases. The grandmother who died in 1950 was said to have had a vesicular dermatitis occasionally on the back of her hands. Maybe she also was a carrier of the gene.

Family B. Case IV: 2.

Housewife, born in 1932. Up to 1960 she had always been in good health. She had had three pregnancies during 1951–6 without any complications. Since 1960 she had been nervous and irritable periodically. In November 1962 she started to use barbiturates during these occasions. In early December of the same year she was taken ill with abdominal pains, restlessness, and insomnia. She increased her barbiturate consumption but became rapidly worse, with pains and numbness in her extremities. She also felt sick and began to vomit. On 20 December she was admitted to the obstetrical and gynaecological department of Ångelholm. There she was found to be in the sixth week of gestation, and was dehydrated and mentally confused. After some days' treatment with chlorpromazine, water, and electrolytes she rapidly improved, but was mentally exalted and unstable during her stay at the hospital. At her own request she left the hospital on 24 December, and while at home continued to take barbiturates. Because of ill-health she was readmitted after 24 hours at home. It was noticed that her urine was dark brown. As acute porphyria intermittens was suspected, a PBG analysis was made on her urine. Since the excretion of this metabolite was markedly increased the suspected diagnosis was regarded as confirmed.

On admission she was mentally lucid, but she complained of double vision and severe pains in her extremities and abdomen. Her reactions bore witness to her agony and she could not lie still. Neurological examination revealed normal conditions. The electrocardiogram showed sinus tachycardia but was otherwise normal. Her blood pressure was 160/100 mm. Hg. Routine blood analyses were mainly normal with the exception of a moderate hypochromia (Hb 11.2 g./100 ml., R.B.C. 4.1 mill./cu. mm.) and a slightly increased serum alanine aminotransferase (56 units). For analyses of porphyrins and their precursors in urine and faeces see Table.

She was treated with adrenocorticotrophic hormone, chlorpromazine, and morphine. During this treatment she rapidly felt better. On 9 January 1963 she had fully recovered and left the hospital. It was then discussed whether she would be allowed to continue her pregnancy, but as the patient herself was very eager to do so and she had had three pregnancies without any complications, she was allowed to continue it.

She was well until the 32nd week (July 1963), when she had to be taken to hospital because of intense itching. She had scratches all over her body and symptoms which, according to the consultant dermatologist, seemed to be a dermatitis artefacta. She had no icterus. The scratches as well as the itching disappeared rapidly on symptomatic therapy. The analyses of ALA and PBG are given in the Table.

On 12 August 1963 the patient gave birth, without any complications, to a well-shaped girl, weighing 4,350 g. Since then she has felt well with the exception of some short periods with slight colicky pains.

On analysing the urine and faeces of 26 of the proband's relatives for porphyrins and their precursors, we found another eight cases with pathological excretion of porphobilinogen (see Table and Fig. 2). These cases were: the sister (Case IV:3), the mother (Case III:1), one uncle (Case III:2), one aunt (Case III:3), one brother (Case IV:4), and three cousins (Cases IV:1, IV:5, and IV:6). The latter seven were clinically free of symptoms and consequently were regarded as latent cases, while the sister had had some troubles of colicky type, until then unaccountable, and she was therefore regarded as a manifest case of acute intermittent porphyria. Case IV:1 is especially interesting, as his father, who must be a carrier of the PV trait, seems to have a normal porphyrin metabolism with a normal urinary and faecal excretion of porphyrins. This we have never found in carriers of the PAI trait (Waldenström and Haeger-Aronsen, 1964).

Family B. Case IV: 3.

This patient, born in 1938, was an unmarried practical nurse in a nursing-home. During childhood she had frequent bouts of unexplained colicky pain in the left side of her abdomen. She had no recollection of dark urine during these bouts. In November 1964 she was admitted to the gynaecological clinic because of pains in the lower abdomen. Abrasio mucosae uteri was performed. Three days later she experienced severe abdominal pains. A left-sided gonorrhoeic salpingitis was diagnosed and treatment with antibiotics was started.

In January 1963 the patient's ALA and PBG excretion had been checked when her sister's (Case IV:2) porphyria was discovered. The excretion was at that time abnormally high, and when rechecked during the current hospitalization the excretions were again found to be very high (see Table). The patient was therefore admitted to Malmö General Hospital. On admission she was nauseated and complaining of pains in her abdomen, the heart rate was 90–100 beats/min., and she vomited frequently. Because of her sister's diagnosis she was thought to suffer from the same condition. When, however, one of us (Waldenström) examined the patient the day after admission several blisters and scars on the back of the hands, the forehead, and the nose were discovered. It was then suspected that she suffered from PV rather than PAI. This was confirmed when the excretion of porphyrins in the stools was found to be raised to a level never seen in PAI (Haeger-Aronsen, 1962).

During the past few years the patient has had shorter periods of colicky pains and, especially during the summers, there have been several blisters on her hands. Her family think that she has become a little more nervous.

An appointment was made with the sister (Case IV:2), whom we had not seen earlier at Malmö. On physical examination she too was found to have blisters and scars on her hands and nose. She reported spontaneously that her skin had become more brittle during recent years, and she also was subsequently found to have high amounts of porphyrins in her stools.

Family C. Case V: 2.

This man, an unmarried machinist born in 1922, had been healthy up to the age of 18, when he was admitted to hospital because of aching pains in the lower quadrants of the abdomen, nausea, and vomiting. On admission the abdomen was soft and the urine was porter-coloured. Analysis of the urine by one of us (Waldenström) revealed large amounts of uroporphyrin. The diagnosis of acute intermittent porphyria was established—porphyria variegata being unknown at the time.

The patient's condition deteriorated rapidly, and he died in an aspiration pneumonia a few days after the diagnosis was established. At necropsy nothing remarkable was found.

Family C. Case V: 4.

A driving instructor, born in 1930, had good health up to 1962, when he experienced aching pains in the abdomen. As one brother (Case V:2) had died with porphyria he consulted a physician, who, however, did not discover anything remarkable. Routine laboratory tests and PBG in urine were all within normal limits. He was admitted to hospital for four days in October 1963 because of tonsillitis, and treated with penicillin. Dark urine was noted, but no analysis of porphyrins or their precursors was made. The patient had no gastrointestinal symptoms. In August 1966 he was seen by one of us (Haeger-Aronsen) because of backache and intermittent colicky cramps. Several partly pigmented pinhead-sized scars were noted on the back of the hands, particularly in the metacarpophalangeal areas (Fig. 5). The patient reported that during recent years the skin of his hands had become more frail and that he developed chaps and blisters after the slightest trauma. The presence of PV was suspected, and was confirmed by stool analysis, which revealed high excretion of porphyrins (see Table). The patient has never had any symptoms from the central nervous system.

Urine and stool analyses on mother, siblings, and their offspring have shown the mother to be negative, while two sisters (Cases V:1 and V:3), two sons (Cases VI:3 and VI:4), and two nieces (Cases VI:1 and VI:2) are latent. The patient's father died at the age of 42 from pulmonary tuberculosis. His hospital records (Piteå) stated that on three separate occasions his urine was darkish yellow. Porphyrin analysis was not performed.

Discussion

The discovery that the diagnosis porphyria variegata was the correct one in families where the existence of porphyria acuta intermittens earlier had been believed to be confirmed (families B and C) emphasizes the importance of adding faecal

analyses for porphyrins to the examination of urine for the presence of porphyrins and their precursors. Not until the level of faecal porphyrins has been established will it be possible to differentiate between porphyria acuta intermittens and porphyria variegata in the absence of skin symptoms.



FIG. 5.—Hand of Case C, V:4.

From a nosological point of view and also genetically it is of great interest to find out if the two porphyrias with acute abdominal symptoms, one with and one without cutaneous manifestations, are in any way related or are quite independent. We have previously tried in Sweden to discover if cutaneous porphyria might be present in any members of our (approximately) 125 thoroughly studied families with acute intermittent porphyria. So far we have not observed any such cases. It has also become clear that the limited number of cases with the various cutaneous porphyria types have no predilection for the north of Sweden, whereas this is the part of the country

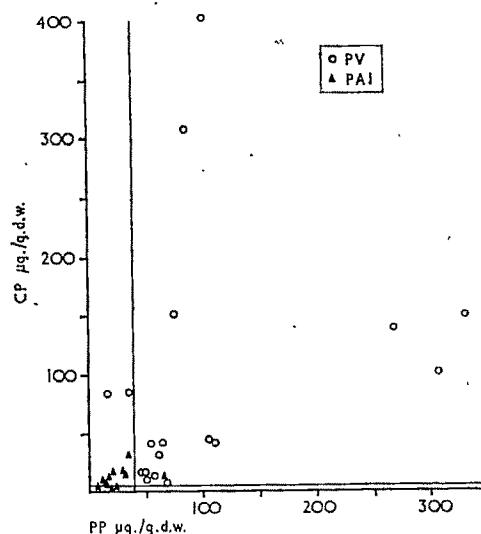


FIG. 6.—Faecal excretion of CP and PP in 18 patients with latent porphyria variegata (PV) and in 12 patients with latent porphyria acuta intermittens (PAI). Inserted vertical and horizontal lines indicate upper limit of normal range of excretion of PP and CP respectively.

where acute intermittent porphyria is very common. A third approach to this problem would be if we could state that the increase in faecal porphyrins characteristic of South African porphyria could be found in members of families with what is believed to be acute intermittent (Swedish) porphyria. So far this has not been possible. Another problem that we have been trying to solve is the following. Could it be that the large number of persons with latent porphyria in Sweden belonging both to PAI and to PV families have about the same biochemical picture, or is there a sharp demarcation line between these groups? We have therefore plotted the data for faecal porphyrins from 18 latent members of our three variegata families in Sweden, together with the data from some persons with latent PAI. This has also been done with urinary ALA and PBG values (Figs. 6 and 7). The graphs clearly show that

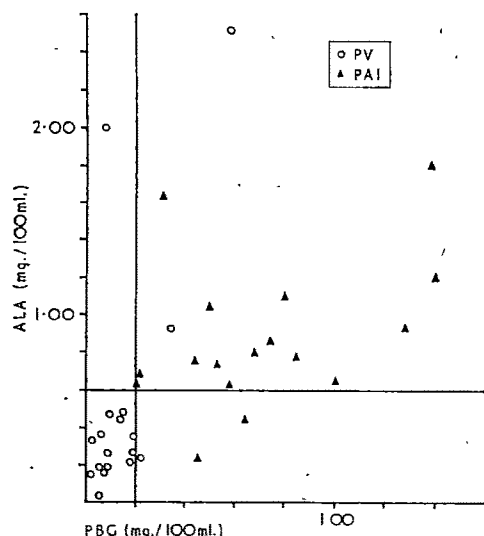


FIG. 7.—Urinary excretion of ALA and PBG in 18 patients with latent PV and in 17 patients with latent PAI. Inserted vertical and horizontal lines indicate upper limit of normal range of excretion of PBG and ALA respectively.

the two diseases have different excretory patterns: PV with relatively high faecal porphyrins but mostly normal urinary ALA and PBG, PAI with near normal faecal porphyrins but high ALA and PBG in the urine.

Two different interpretations of the findings regarding these disease pictures have been given. One interpretation, represented among others by Dean, Barnes, and the Malmö group, is that they are fundamentally different. The other, with Watson (1960) as the chief advocate, is that they are "mixed" and that some members for some reason or other also develop skin sensitivity. The most elegant way to prove that the diseases are different would be if they could be shown to be linked and not linked to some well-defined heritable condition. Such studies on our very extensive material are now in progress.

Summary

The three first families with porphyria variegata from Sweden are described. Two of them are descended from Småland, in southern Sweden. In spite of tracing the families back to the beginning and middle of the nineteenth century no relationship has been found with any family in which acute porphyria intermittens has occurred. In all, 24 cases of porphyria variegata are reported—5 manifest and 19 latent.

Supported by a grant to J. Waldenström and B. Haeger-Aronsen from the Swedish Medical Research Council.

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Double-blind Experiments on the Effect of a Peanut Extract on the Bleeding Incidence in 92 Haemophiliacs*

M. VERSTRAETE,† M.D.; C. A. J. RUYS,‡ M.D.

Brit. med. J., 1967, 4, 453–456

It is the fate of patients afflicted with a life-long disease to be subjected to therapeutic trials with new drugs or substances, of which the possible impact on the underlying diseases is not always apparent. A classical example is haemophilia; a long list of drugs has stirred a fleeting hope in patients affected with this bleeding disorder when the new therapy coincides with one of their cyclic symptomless periods.

The fortuitous observation by a haemophilic patient that while consuming daily roasted peanuts the tenderness of an acute knee haemarthrosis seemed to subside more rapidly has

focused attention to a possible beneficial factor in peanuts for the treatment of haemophilia (Boudreaux *et al.*, 1960). Largely because of untimely and uncontrolled rumours in the lay press, many haemophiliacs started experimenting on their own with any available source of peanuts—for example, commercial peanut butter, roasted and raw peanuts, or peanut flour.

The discovery of antifibrinolytic properties in peanuts, together with a possibly increased fibrinolytic potential in haemophiliacs (van Creveld *et al.*, 1961), were thought to offer a reasonable basis for further investigation; also because in isolated studies a beneficial effect of peanuts or peanut extracts on the bleeding incidence of haemophilic patients continued to be reported (Brüster, 1961; Bisordi, 1964). Unfortunately these investigations were conducted in a limited number of patients and with a variety of peanut preparations (raw or roasted peanuts, peanut butter, peanut flour, or screw-pressed extracted peanut meal) or peanut extracts (crude peanut oil, hexane-extracted roasted peanuts, or 95% ethanol extract of peanut flour).

* Study organized with the kind co-operation of Belgian and Dutch groups interested in the treatment of haemophilia. Belgium: Louvain (M. Verstraete, J. Vermeylen, and H. Van Isterbeek). Netherlands: Amsterdam (S. van Creveld, I. A. Mochtar, and J. Jonker), Leiden (E. A. Loeliger, A. Hensen, N. Fekkes, and J. J. Velkamp), Breda (C. P. M. Strybos), The Hague (C. H. W. Leeksa), Zevenaar (F. B. M. Verhey).

† Associate Professor of Medicine, University of Louvain, Belgium.

‡ Investigator ACF Amsterdam, Netherlands.

From the Laboratory of Blood Coagulation and Proteolysis, Department of Medicine, University of Louvain, Belgium.

As no double-blind trial on a large group of haemophiliacs had apparently been instituted, it was decided to organize a joint study in Belgium and in the Netherlands, making use of a uniform protocol and a single batch of a given peanut preparation.

Design of the Double-blind Study

Selection of Patients

Only seriously affected haemophiliacs (type A or B) were admitted to this study. In addition to clinical judgement, it was considered that a coagulation time of whole blood over 45 minutes, as assessed with a standardized thromboelastographic method, was a satisfactory criterion, as it would be observed only in haemophiliacs with a very low level of factor VIII or IX. Indeed, it was found that an *r*-value of 45 minutes or more corresponds to 3% factor VIII activity or less.

The different patients were paired according to haemophilia type, age, and social class, so that two groups of patients were obtained in each centre. One group received the placebo product first during 12 weeks, followed by the experimental product during the next 12 weeks (P_1 , E_2); in the second group the order was reversed (E_1 , P_2). The pairing of the patients was made by a person who did not know the treatment group. The purpose of pairing patients according to the criteria given was to take into account the effects of other influences and to avoid a bias due to decreased or increased attention of the patient in his symptoms and the diary kept during the course of the trial.

Evaluation of the Incidence of Bleeding

All patients participating in the collaborative study were requested to visit their physician before and after every sixth week of the trial. At the first visit a questionnaire was explained to the patient which he had to fill in daily (diary). The first list was centred on five frequent bleeding manifestations in haemophilia (ecchymoses, haematomata, haemarthroses, haematuria, and epistaxis); 12 subsidiary questions were aimed to give a rough estimation of duration and importance of a bleeding episode. The patient was also requested to mention each time he sought medical help, was unable to attend class or work, or had to be transfused or admitted to hospital because of bleeding.

The haemophiliacs accepted in this collaborative study were not allowed to take synthetic fibrinolytic inhibitors during the course of the trial—for example, aminocaproic acid or tranexamic acid. If a haemophilic patient had to be admitted to hospital because of bleeding and needed blood transfusion, he interrupted the intake of the experimental product until discharge; during the hospital stay the diary was not filled in. Any other drug—for example, antibiotics, laxatives, expectorants—administered at home had to be recorded daily on the information sheet. The patient was also asked to report any intercurrent disease—for example, common cold, bronchitis.

Haemophiliacs were recommended to refrain from drugs containing salicylates at any time, and particularly during this trial.

At each six-weekly visit the material under trial for the following period was handed to the patient. The physician also inquired about any possible side-effects and the subjective opinion of the patient on the value of the therapy.

Though a new supply of substance was provided every sixth week, it was arranged that placebo or peanut extract was given without interruption for 12 weeks. This rather long period was thought to be essential because peanut extract could require some time before exerting its alleged action on bleeding, which, if present, could last a few weeks after withdrawal of the drug.

At the onset 107 haemophiliacs were included in the trial. In the final study of the results 15 patients had to be excluded for a variety of reasons, such as lack of sustained co-operation, repeated administration of blood or plasma transfusions during the three-month course of the trial, or intervening illness treated with a variety of other drugs.

The final evaluation includes 67 Belgian and 25 Dutch haemophiliacs, four of them being cases of haemophilia B or Christmas disease. The distribution according to age groups was as follows: between 1 and 3 years old, 6 (5 haemophilia A and 1 haemophilia B); over 3 to 14 years, 38 (37 haemophilia A and 1 haemophilia B); and over 14 years, 48 (46 haemophilia A and 2 haemophilia B).

Preparation and Dosage of the Peanut Extract

The peanuts used are of South African origin (common Natal 70/80 hand-picked selected). The peanut extract was prepared and kindly made available free of charge by a pharmaceutical company.¹ One single large batch of experimental product and placebo was used in this trial. Raw peanuts still containing their skin are ground and extracted with hexane until freed of the oily material (Astrup *et al.*, 1962). An alkaline aqueous extract is prepared (pH 6.5), and after centrifugation treated four times with acetone (pH kept at 5.5) and the dry water residue used. Three grammes of raw peanuts yield about 100 mg. of the final powder.

The placebo powder used had the same appearance, smell, and taste as the experimental product.

The daily administered dose of this powder varied according to the age of the patient, but was always given thrice daily (between 1 and 3 years 100 mg. three times; between 3 and 14 years 300 mg. three times; and over 14 years 600 mg. three times). A daily dose of 1,800 mg. of experimental product is the equivalent of about 54 g. of raw pindas.

Results of the Statistical Analysis

Three criteria were used in the final statistical evaluation: the frequency of ecchymoses or of all other bleeding episodes excluding ecchymoses, (epistaxis, haemarthrosis, haematuria, haematoma in muscles, bleeding in mouth and throat) and the duration of absence from school or work because of haemorrhagic incidents. From statistical analysis it appeared that no significant difference in the results for the three criteria mentioned were obtained between the 67 Belgian and 25 Dutch patients. Furthermore, the overall difference in incidence between those who took placebo first and treatment first are not significant. Subsidiary analysis by ages did not reveal a significant difference between the six classes of age groups (1–5 years, 6–10 years, 11–15 years, 16–20 years, 21–30 years, 31 years and over). Therefore as regards nationality, age, class, and trial order the material can be regarded as homogeneous and used as a single group in the final comparison between the effects of the experimental substance and the placebo.

In the left-hand columns of the three sections of the Table are given the differences in incidence for a given criterion between the experimental and placebo period ($E-P$) for the group of 92 haemophiliacs. Negative values of $E-P$ mean a greater bleeding incidence in the placebo periods, positive values of $E-P$ correspond to a greater bleeding incidence in the active treatment period for a given patient. For the three selected criteria the mean of the differences between the treatment periods were close to zero and excludes therefore a significant difference.

¹ N.V. Amsterdamse Chininefabriek, Amsterdam.

Incidence of Ecchymoses, other Bleeding Manifestations and Duration in Days of Absence from School or Work in 92 Haemophilic Patients during Treatment with the Experimental Products (E) or Placebo (P)

Difference in Incidence of Ecchymoses During the E minus P Period				Difference in Incidence of Bleeding, Excluding Ecchymoses During the E minus P Period				Difference in Duration of Absence (in Days) from School or Work During the E minus P Period			
	Total (f)	Scores (V)	fV		Total (f)	Scores (V)	fV		Total (f)	Scores (V)	fV
18 and over	4	+4	16	11 and over	2	+4	4	39 and over	2	+4	8
13 to 17	2	+3	6	8 to 10	1	+3	3	28 to 38	1	+3	3
8 to 12	5	+2	10	5 to 7	3	+2	20	17 to 27	3	+2	6
3 to 7	14	+1	14	2 to 4	15	+1	15	6 to 16	15	+1	15
-2 to +2	37	0	0	-1 to 1	38	0	0	-5 to 5	38	0	0
-3 to -7	18	-1	-18	-2 to 4	11	-1	-16	-6 to -16	11	-1	-11
-8 to -12	4	-2	-8	-5 to -7	3	-2	-16	-17 to -27	3	-2	-6
-13 to -17	2	-3	-6	-8 to -10	2	-3	-12	-28 to -38	2	-3	-6
-18 and over	2	-4	-8	-11 and over	2	-4	-4	-39 and over	2	-3	-8
Total	88		6 $t=0.35$		77		-6 $t=-0.37$		77		1 $t\approx 0$

Discussion

The initial hypothesis that a genetic block of the metabolic synthesis of factor VIII could have been partially overcome by a factor present in peanuts could not be maintained, as the activity of the coagulation factors VIII and IX was found to be uninfluenced by the consumption of peanuts (Schmutzler, 1961; van Creveld and Mochtar, 1961; Brakman *et al.*, 1962; Verstraete *et al.*, 1962).

Flavanones extracted from peanut skins have a favourable effect on capillary resistance and on the bleeding times of rats (Verstraete *et al.*, 1962). Cepelák (1965) extracted from peanut skins a potent antifibrinolytic substance which promoted haemostasis in haemophilia A and B patients as in other haemorrhagic states. Vasoconstricting compounds were also found in an ethanol extract of defatted peanuts with which a favourable clinical effect was reported (Boudreaux *et al.*, 1960). The same investigators showed that a component of peanuts is being adsorbed into platelets resulting, after viscous metamorphosis, in a potent vasoactive activity which differs from serotonin and cannot be inhibited by atropine. Van Creveld *et al.* (1965), however, obtained a haemostatic effect with a peanut preparation exhibiting antifibrinolytic but no vasoconstrictor activity. More recently it was suggested that the peanut factor might enhance the platelet-plug-stabilization process, and that vasoconstriction was merely incidental to the phenomenon of platelet-plug-induced haemostasis (Frampton *et al.*, 1966).

Astrup *et al.* (1961) found that peanuts and their extracts, with hexane, saline, barbital buffer, or 2 M potassium thiocyanate, exert a powerful protease-inhibiting effect. These results were later confirmed (Schmutzler, 1961; van Creveld and Mochtar, 1961; Verstraete *et al.*, 1962). The antiprotease activity is directed rather against the activation of plasminogen than against formed plasmin. The observation that haemophilic patients may have an increased fibrinolytic activity, as suggested by a short euglobulin lysis time (van Creveld *et al.*, 1961), fits well with the hypothesis of Astrup *et al.* (1961) that an increased fibrinolytic activity which causes no harm in a normal individual could produce bleeding in a patient with an impaired haemostatic balance.

It has further been demonstrated that naturally occurring protease inhibitors, which are proteins or peptides, can pass the intestinal wall and enter the blood stream. After oral adsorption of roasted peanuts a decrease in fibrinolytic activity of euglobulin precipitate (Astrup *et al.*, 1961; van Creveld and Mochtar, 1961; Moers and den Otlander, 1961; Brakman *et al.*, 1962) and an increased inhibitory activity against streptokinase activated human blood (Nilsson, 1960) have been ascribed to the passage of the protease inhibitor through the membranes of the intestinal villi.

In consequence a critical clinical trial with a peanut extract was thought necessary. Our double-blind trial in 92 haemophiliacs did not reveal a statistical difference in the bleeding frequency between the two periods of 12 weeks. These negative

results cannot reasonably be ascribed to an improper selection of the peanut extract used; the hexane extract was prepared from raw peanuts, as it was shown that defatted unroasted peanuts have a twentyfold antifibrinolytic activity compared with roasted peanuts. Moreover, the same type of preparation was reported to be active—that is, induces a decrease of the fibrinolytic activity in the peripheral blood (van Creveld and Mochtar, 1961) and an apparent diminished bleeding incidence in haemophiliacs (Brakman *et al.*, 1962; van Creveld *et al.*, 1965). In the experiments of van Creveld and Mochtar (1961) even the same source of material (Unilever-A.C.F.) but at a lower dose (1.3 times less compared with present trial) was used.

Though it is beyond doubt that peanut extracts, when administered orally, exert an antifibrinolytic effect in the blood, the point is not proved that this inhibitory action is relevant for the prevention of bleeding in haemophiliacs. Some but not all haemophiliacs have a decreased euglobulin lysis time, and a fixed relation between this fibrinolytic activity and the occurrence of bleeding episodes has never been demonstrated (Schmutzler, 1961). Moreover, it was recently shown that peanut extracts almost devoid of antiprotease activity still maintain a haemostatic function probably related to choline or choline derivatives (Frampton *et al.*, 1966; Jackson *et al.*, 1966; Boudreaux, 1967). The choline content of the extract used in this trial was less than 0.22% (Boudreaux, 1967). The hypothesis that the haemostatic effect of ethanol extracts of defatted peanuts were related to their vasoconstricting properties (Boudreaux *et al.*, 1960; Frampton *et al.*, 1966) could not be studied in this trial.

Only patients with severe haemophilia were on purpose selected for this study; it was thought that the clinical evaluation of any drug in haemophilia can hardly be made in mild cases, because such patients have haemorrhagic incidents only after significant haemostatic challenge; the severe haemophiliacs, on the other hand, have incidents of spontaneous haemorrhage.

Most of our patients claimed that their bleeding was less frequent, and that periods of relapse were milder and of shorter duration during the trial; however, these subjective observations were made also during the placebo period, while the patient received the trial substance. Many patients complained on termination of the six months' trial that the bleeding symptoms became worse. One possible explanation is that hope and better medical attention of the haemophilic patients induced by the six-weekly visits to their physicians could be responsible for this bias.

Our results are not in keeping with the experiments of Brüster (1961, 1962), who observed after the oral intake of 15 g. of the hexane extract of peanuts a decrease in the coagulation time, an improvement in the results with the thromboplastin generation test and prothrombin consumption, and a definite haemostatic effect in five haemophiliacs A and seven haemophiliacs B.

With the peanut preparation evaluated in the present double-blind trial on 92 haemophiliacs no favourable effect on bleeding could be observed. Based on these findings we would propose to refrain from recommending peanuts or their extracts as a haemostatic agent to haemophilic patients until definite proof of the beneficial effect of a given peanut preparation to the control of haemophilic bleeding is presented.

Summary

The haemostatic value of an aqueous extract of raw ground and hexane-defatted peanut kernels was evaluated in 92 severely affected haemophilic patients during a six-months double-blind trial. With the criteria selected, no statistical proved benefit on the bleeding incidence could be demonstrated during the "active" treatment.

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Effect of Vagotomy on Gastric Acid Secretion Stimulated by Pentagastrin and Histamine

R. A. PAYNE,* M.S., F.R.C.S.; ALAN G. COX,† M.D., F.R.C.S.ED.; JOHN SPENCER,‡ M.B., B.S., F.R.C.S.
 F. C. Y. CHENG,§ M.B., B.S., F.R.C.S., F.R.C.S.ED.

Brit. med. J., 1967, 4, 456-457

The study of human gastric acid secretion has been hindered by lack of a readily available agent which has the properties of gastrin and which can be administered to man with safety. Hog antral mucosa has provided a source of gastrin for animal experimentation, but until isolated in a pure form by Gregory and Tracy (1964) gastrin has not been available for use in man. The production of pure gastrin on a commercial scale has not proved practicable. However, since the introduction of a synthetic substance known as pentagastrin (Peptavlon, I.C.I.) the physiological properties of gastrin can be studied. This is a pentapeptide with a terminal tetrapeptide which appears to be the physiologically active constituent of gastrin (Tracy and Gregory, 1964).

The present investigation was undertaken to compare the effect of vagotomy (with pyloroplasty) on the maximal gastric responses to stimulation by histamine and by pentagastrin. Histamine has been widely used to study acid secretion, but it may now be superseded by pentagastrin. It is therefore important to determine if the results of investigations with pentagastrin can be compared with those of previous work with histamine.

Method of Study

Fifteen patients with uncomplicated chronic duodenal ulcer were studied before and after total vagotomy with pyloroplasty. Before operation the maximal acid responses to histamine and to pentagastrin were measured on two separate days. Seven to 10 days after operation an insulin test was performed to confirm the completeness of vagotomy, and the two tests with

histamine and pentagastrin were then repeated on successive days.

All secretory tests were carried out in the morning after an overnight fast. Before operation a 16 French gauge nasogastric tube was passed into the most dependent part of the stomach under x-ray control. In the postoperative tests use was made of a double-lumen feeding gastrostomy tube for collection of the gastric secretions. The tube was placed at operation with one limb in the dependent part of the stomach and the other in the duodenum (Burns and Menzies, 1966). In all tests gastric juice was aspirated continuously by an electric pump at a subatmospheric pressure of 5 cm. Hg, and the patency of the tube was checked at frequent intervals throughout each test. The aspirations were collected in 15-minute samples and their total acid content in mEq was measured by titration with 0.1N NaOH to the phenol red end-point (pH 6.8-8.4).

In each test two 15-minute specimens of basal secretion were collected after aspiration of the fasting juice. The tests then continued as follows:

Maximal Histamine Response.—Histamine acid phosphate was infused intravenously at a rate of 40 µg./kg./hour (Lawrie *et al.*, 1964) for 120 minutes. The maximal response was taken as the sum of the four consecutive samples giving the highest total.

Maximal Pentagastrin Response.—Pentagastrin was infused intravenously at a rate of 6 µg./kg./hour for 90 minutes, which is sufficient to give a steady level of secretion (Multicentre Pilot Study, 1967). The maximal response was calculated as for the histamine test.

Insulin Test.—Soluble insulin, 0.25 unit/mg., was injected in a single intravenous dose and completeness of vagotomy was accepted if the concentration of acid in the next two hours failed to rise by more than 20 mEq/litre above the basal concentration.

Results

Table I shows the maximal response to histamine and pentagastrin before and after vagotomy in each patient. All 15 patients showed a substantially reduced response to both

* Consultant Surgeon, North Middlesex Hospital, London N.18; Honorary Lecturer in Surgery, Royal Postgraduate Medical School, London W.12.

† Lecturer in Surgery, Royal Postgraduate Medical School; Consultant Surgeon, Hammersmith Hospital, London W.12.

‡ Tutor in Surgery, Royal Postgraduate Medical School; Senior Registrar, Hammersmith Hospital, London W.12.

§ Honorary Registrar, Hammersmith Hospital; Lecturer in Surgery, University of Hong Kong.

agents after vagotomy. The reduction in the response due to vagotomy is usually expressed as a percentage of the preoperative value, and the result of this calculation is shown for each patient in Table II. The mean reduction in the histamine response (66.4%) does not differ significantly from the mean reduction in the pentagastrin response (61.5%). The correlation between the two reductions is shown in the Chart and is statistically significant ($P < 0.001$).

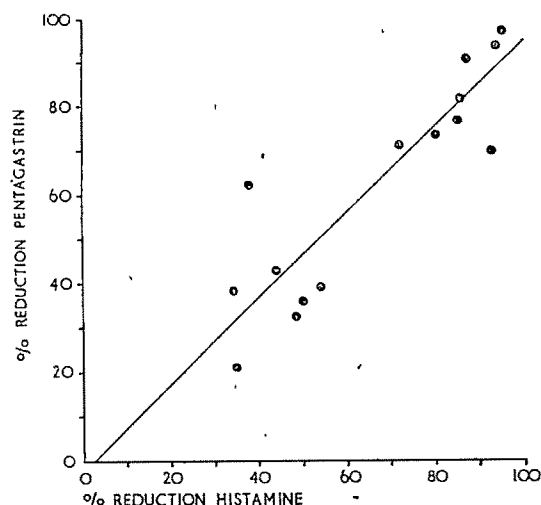
Some of our results with pentagastrin formed part of an investigation into the effects of vagotomy on gastric acid secretion elicited by pentagastrin (Multicentre Study, 1967).

TABLE I.—Maximal One-hour Gastric Acid Secretion in Response to Intravenous Histamine and Intravenous Pentagastrin Before and After Total Vagotomy

Case No.	Maximal Gastric Acid Secretion (mEq/hour)			
	Before Vagotomy		After Vagotomy	
	Histamine	Pentagastrin	Histamine	Pentagastrin
1	49.3	46.3	13.8	13.0
2	25.4	41.5	3.8	9.5
3	38.3	27.8	19.4	18.5
4	36.7	32.0	1.9	0.5
5	34.9	34.6	4.6	3.2
6	28.1	28.1	16.1	18.4
7	13.7	23.1	8.8	18.4
8	26.6	35.2	12.9	21.3
9	59.2	51.8	36.7	19.8
10	46.5	47.2	26.1	26.9
11	41.8	63.7	27.0	39.1
12	40.3	40.1	7.9	10.6
13	43.9	48.9	6.2	8.0
14	19.2	25.3	1.3	8.0
15	29.0	35.9	1.7	1.6
Mean	35.5	38.8	12.6	14.4
S.D.	12.1	11.3	10.7	10.3

TABLE II.—Percentage Reduction in Maximal Gastric Acid Secretion After Vagotomy in Response to Intravenous Histamine and Intravenous Pentagastrin

Case No.	% Reduction in Maximal Acid Secretion after Vagotomy	
	Histamine Stimulation	Pentagastrin Stimulation
1	72	72
2	85	77
3	49	32
4	95	98
5	87	91
6	50	35
7	36	20
8	52	39
9	38	62
10	44	43
11	35	38
12	80	74
13	86	83
14	93	69
15	94	96
Mean	66.4	61.9
S.D.	23.4	25.5



Correlation of percentage reduction after vagotomy of Pentagastrin- and histamine-stimulated maximal gastric acid secretion. The correlation coefficient is $+0.968$ ($P < 0.001$). The equation for the regression line is $y = 0.968x \pm 2.37$.

Discussion

This investigation shows that vagotomy reduces the maximal gastric acid secretory response to pentagastrin and to histamine by similar proportions. A similar finding has been reported by Jepson and Johnston (1967) in a study of the effects of vagotomy on Histalog- (ametazone hydrochloride) and pentagastrin-stimulated acid secretion. Their observations contrast with the results of a previous study from this centre (Barabas *et al.*, 1966) in which a hog antral mucosal extract of gastrin (Leo) was used instead of pentagastrin. In that study the reduction in acid secretion after vagotomy was 60% with histamine and only 33% with the mucosal extract. A similar observation has been made by Weir *et al.* (1966). Bank *et al.* (1967), in a study of patients after vagotomy, state that the pentagastrin response is greater than the histamine response. The implication that the pentagastrin response is reduced less than the histamine response was not substantiated, since no tests with pentagastrin were carried out before vagotomy. In a Multicentre Study (1967) of the effects of vagotomy on the maximal acid secretory response to pentagastrin a mean reduction of 62% was found after vagotomy, but measurements of histamine-stimulated acid secretion were not made.

Comparison of the results of our earlier study (Barabas *et al.*, 1966) and the present one suggests a difference between the properties of the synthetic pentapeptide and the mucosal extract. This is supported by the work of Neely (1967), who made a direct comparison of the effect of these two agents on alimentary motility and found a difference in the response of the small intestine. Our present results with pentagastrin conform more closely with the observation of Welbourn and Burns (1964) that vagotomy in man reduced by 67% the acid output to endogenous gastrin after perfusion of the stomach with a meal extract.

Unlike histamine, pentagastrin has minimal side-effects and seems likely to supersede it in the measurement of gastric acid secretion. Our present study allows the practical conclusion that the results with pentagastrin are closely comparable to those following histamine stimulation both before and after vagotomy.

Summary

Maximal gastric acid secretion in response to intravenous infusions of pentagastrin (Peptavlon) and histamine has been measured before and after complete surgical vagotomy in 15 patients with chronic duodenal ulcer. After vagotomy the response to both stimulants was reduced by similar proportions.

We wish to express our appreciation to the following: Professor R. B. Welbourn for advice and encouragement; Staff Nurses Alexander, Sherman, and Pope and Mrs. Vedast for help with the tests; the N.E. Metropolitan Regional Hospital Board for a research grant (R. A. P.); and I.C.I. for supplies of Peptavlon and the salary of a technician (A. G. C.).

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Blood Groups and Enzymes of Human Red Cells after Five Years' Storage in Liquid Nitrogen

R. G. HUNTSMAN,* M.D., M.R.C.P., M.C.PATH.; B. A. L. HURN,† M.D., M.C.PATH.
ELIZABETH W. IKIN,‡ PH.D.; H. LEHMANN,§ M.D., SC.D., F.R.C.P., F.R.I.C., F.C.PATH.
J. LIDDELL,|| M.D., M.C.PATH.

Brit. med. J., 1967, 4, 458-460.

Laboratories interested in blood group serology need to preserve a reference panel of red cells of known antigenic structure. For the sake of continuous availability, especially of the rarer types, it is often desirable that the cells should be stored for long periods of time at sub-zero temperatures, a state which can be achieved without gross lysis only by the use of special techniques. For some years past we have been evaluating the quality of preservation of human red cells stored in liquid nitrogen (-196°C) after rapid freezing of droplets of a whole-blood/sucrose mixture; the present paper records the behaviour of a panel of such cells, selected on account of their diverse grouping properties, and tested after storage for five years.

The methods employed were as previously reported (Huntsman, *et al.*, 1962).

Results

Recovery of Intact Cells.—The average recovery in seven samples was 89.4% (range 87-94%); changes in the average recovery over the five-year period are shown in Table I.

Antigen Strength.—The blood groups of the panel of cells are listed in Table II, and the titration scores of these cells after varying periods of storage are shown in Table III. The results on fresh samples from four of the original donors, tested in parallel with the five-year stored samples, are also included in Table III.

TABLE I—Average Recovery of Intact Cells When Thawed After Storage for Various Periods of Time

Storage Recovery	1 hour 91.3*	1 month 92.5%*	1 year 94.1%	2 years 92.8%	3 years 91.8%	5 years 89.4%
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* Thawed in isotonic saline. Remaining specimens thawed in 1% saline.

TABLE II.—Blood Groups of the Seven Chosen Blood Samples

Specimen	ABO	Rh	MN	S	P ₁	Lu ^a	K	Le ^a	Le ^b	Fy ^a
1	O	(cDE/cde) R ₁ r	MN	—	+++	—	—	—	+	—
2	O	(CDe/cde) R ₁ r	M	+	—	—	—	—	+	+
3	A ₁	(CDe/cde) R ₁ r	N	—	—	+	—	—	+	+
4	O	(cDE/cde) R ₁ r	M	+	+++	—	—	+	—	—
5	O	(C ^w De/cde) R ₁ r	M	+	+++	—	+	+	—	+
6	O	(cD ^a E/cde) R ₁ r	MN	+	+	—	—	—	+	+
7	O	(cde/cde) rr	N	—	—	—	—	—	+	—

Enzymes.—Table IV compares the activities of aldolase, aspartate aminotransferase (glutamic oxalacetic transaminase), glucose 6-phosphate dehydrogenase, and 6-phosphogluconate dehydrogenase in four of the five-year stored samples with those found in fresh cells taken from the same donors.

* Consultant Haematologist, Lambeth and St. Thomas's Hospitals, London S.E.1.

† Clinical Pathologist, Wellcome Research Laboratories, Beckenham, Kent.

‡ Senior Scientific Officer, Medical Research Council Blood Group Reference Laboratory, London N.W.3.

§ Professor of Clinical Biochemistry, University of Cambridge.

|| Chemical Pathologist, Guy's Hospital, London S.E.1.

Discussion

Strumia *et al.* (1960) reported a 90% recovery of red cells after storage for two years at -93°C . and Doebbler *et al.* (1965) found no significant change in red cell recovery rates after two and a half years at -170°C . The recovery of a high proportion of intact cells after five years' storage at -196°C . (Table I) confirms that this technique is capable of preserving red cells intact for long periods. The increase in recovery at one year was due to the use of 1% (rather than isotonic) saline for thawing; thereafter the proportion of cells recovered intact appears to drop by approximately 1% per annum.

Earlier work had suggested that the antigenic strength of frozen red cells would show little deterioration during storage. The panel of cells reported in this paper retained their antigenic strength after three years in liquid nitrogen (Huntsman *et al.*, 1964). Strumia *et al.* (1962) showed that a small panel of cells grouped satisfactorily after five months at -93°C . One specimen after three years' storage was equivalent to fresh cells. Bronson and McGinniss (1962) reported good preservation of antigenic properties after the storage of two samples for six months in liquid nitrogen. Gibbs *et al.* (1962) showed that the antigens of the ABO systems were preserved after two and a half years in liquid nitrogen.

As previously observed (Huntsman *et al.*, 1964) saline suspensions of thawed cells showed progressive lysis during further storage over a period of hours or days at 4°C ., but this feature was no more pronounced in the five-year specimens than in those frozen for a shorter period. All cell samples after repeated washing in isotonic saline showed no further haemolysis before grouping tests, some of which were carried out as long as 48 hours after thawing.

The quality of the antigen strength of red cells after five years of frozen storage is reflected by the titration scores shown in Table III, and, with few exceptions of doubtful significance, the results are similar to those obtained with the original fresh material. After this period of trial it is fair to say that cells stored by the method described compare favourably with cells frozen in high concentrations of glycerol and stored under the best conditions at -80°C . or below. Storage of glycerolized cells at -20°C . gives inferior results, and indeed few of the cells would be expected to survive for five years under such conditions.

In order to detect enzyme deterioration in the stored red cells we have previously relied on assays repeated sequentially over a number of years. As a result of such tests it appeared that the concentrations of two of the four enzymes (aldolase and aspartate aminotransferase) had fallen during storage for two years. However, it is difficult to stabilize enzyme assay systems so as to yield strictly comparable results over long periods of time, and adequate preparations for quality control of these assay procedures do not exist. The possibility was therefore considered that the observations might be due to technical variation rather than to changes in the stored enzymes (Huntsman *et al.*, 1965). Samples after five years' storage were com-

pared with freshly drawn specimens from the original donors, related samples being assayed simultaneously in each case. During the period of storage whenever specimens were temporarily removed from the liquid nitrogen refrigerator care was taken that the frozen blood remained at liquid nitrogen temperature. This was achieved by ensuring that the boxes containing the blood were filled with liquid nitrogen the moment they were removed from the refrigerator. The results of these tests are given in Table IV. The present evidence,

though inconclusive, suggests a reasonable degree of stability of these four enzymes during storage at -196°C .

Summary

Tests after five years' storage of human blood in liquid nitrogen (-196°C) after rapid freezing shows the method to be very suitable for preservation of cells for blood group

TABLE III.—Titration Scores of Blood Group Antigens Before and Immediately After Freezing and After Storage for Various Periods. Control Values Expressed in Parentheses

Antigen Tested and Control ()	Specimen 1					
	H (O)	D (R ₂ r)	E (R ₂ r)	M (MN)	N (MN)	P ₁ (P ₁ + +)
Before freezing ..	26 (31)	75 (82)	57 (57)	57 (57)	31 (33)	24 (34)
After " ..	24 (31)	70 (82)	57 (57)	57 (57)	29 (33)	19 (34)
1 year ..	26 (32)	84 (84)	60 (62)	55 (52)	21 (23)	16 (27)
2 years ..	32 (34)	82 (84)	57 (60)	58 (55)	26 (26)	14 (22)
5 " ..	31 (32)	67 (82)	52 (60)	50 (52)	26 (33)	11 (22)
Fresh* ..	34	82	55	58	34	14

Antigen Tested and Control ()	Specimen 2				
	H (O)	C (R ₁ r)	D (R ₁ r)	M (MM)	Fy ^a ▲ (Fy(a +))
Before freezing ..	31 (31)	40 (40)	74 (75)	67 (67)	72 (74)
After " ..	26 (31)	40 (40)	69 (75)	64 (67)	72 (74)
1 year ..	29 (32)	42 (52)	74 (75)	57 (57)	56 (56)
2 years ..	34 (34)	55 (55)	80 (80)	58 (57)	61 (59)
5 " ..	31 (32)	27 (37)	65 (75)	54 (58)	71 (76)
Fresh* ..	33	37	77	58	76

Antigen Tested and Control ()	Specimen 3					
	A (A)	C (R ₁ r)	D (R ₁ r)	N (NN)	Lu ^a (Lu (a +))	Fy ^a ▲ (Fy(a +))
Before freezing ..	61 (61)	44 (47)	75 (75)	35 (35)	27 (38)	69 (71)
After " ..	49 (61)	42 (47)	74 (75)	35 (35)	22 (38)	66 (71)
1 year ..	54 (58)	44 (52)	74 (75)	31 (31)	27 (30)	64 (56)
2 years ..	51 (56)	45 (55)	74 (80)	33 (33)	26 (24)	59 (59)
5 " ..	51 (75)	27 (37)	75 (75)	34 (40)	20 (27)	71 (76)

Antigen Tested and Control ()	Specimen 4				
	H (O)	D (R ₂ r)	E (R ₂ r)	M (MM)	P ₁ (P ₁ + +)
Before freezing ..	26 (31)	74 (72)	56 (52)	57 (57)	29 (22)
After " ..	24 (31)	72 (72)	56 (52)	55 (57)	21 (22)
1 year ..	24 (32)	82 (84)	56 (62)	57 (57)	26 (27)
2 years ..	28 (34)	82 (84)	57 (60)	57 (57)	22 (22)
5 " ..	26 (32)	75 (82)	52 (60)	52 (58)	16 (22)
Fresh* ..	32	82	57	60	24

Antigen Tested and Control ()	Specimen 5							
	H (O)	C (R ₁ r)	C ^w (R ₁ r)	D (R ₁ r)	M (MM)	P ₁ (P ₁ + +)	Kell ▲ (K +)	Fy ^a ▲ (Fy(a +))
Before freezing ..	31 (31)	40 (45)	75 (75)	77 (84)	58 (60)	31 (21)	61 (64)	66 (66)
After " ..	31 (31)	35 (45)	72 (75)	77 (84)	57 (60)	31 (21)	61 (64)	63 (66)
1 year ..	31 (32)	35 (52)	77 (77)	74 (75)	53 (57)	27 (27)	62 (60)	60 (56)
2 years ..	32 (34)	35 (35)	77 (75)	78 (80)	57 (57)	24 (22)	66 (66)	61 (59)
5 " ..	34 (32)	20 (37)	63 (75)	65 (75)	54 (58)	24 (22)	81 (76)	71 (76)

Antigen Tested and Control ()	Specimen 6							
	H (O)	D (R ₂ r)	D ■ (R ₂ r)	E (R ₂ r)	M (MN)	N (MN)	P ₁ (P ₁ +)	Fy ^a ▲ (Fy(a +))
Before freezing ..	26 (31)	17 (17)	52 (46)	57 (57)	57 (57)	21 (28)	14 (11)	66 (66)
After " ..	24 (31)	14 (17)	47 (46)	52 (57)	50 (57)	19 (28)	8 (11)	63 (66)
1 year ..	21 (32)	4 (9)	50 (45)	57 (62)	55 (52)	23 (23)	4 (11)	59 (56)
2 years ..	24 (34)	12 (35 +)	49 (66 +)	60 (60)	55 (55)	24 (26)	4 (11)	61 (59)
5 " ..	26 (32)	8 (0 +)	66 (66 +)	57 (60)	52 (52)	26 (33)	4 (4)	71 (76)

Antigen Tested and Control ()	Specimen 7		
	H (O)	c (rr)	N (NN)
Before freezing ..	29 (32)	76 (77)	33 (36)
1 year ..	31 (32)	62 (65)	31 (31)
2 years ..	26 (34)	75 (75)	33 (33)
5 " ..	31 (32)	57 (67)	26 (40)
Fresh* ..	32	67	33

All tests saline titrations except ▲ = Antiglobulin (Coombs) test and ■ = antiglobulin test
* Fresh blood taken from original donors tested in parallel with five-year stored sample.

Complete Anti-D. Different control (cells from different donor) = +

TABLE IV.—Comparison of the Enzyme Content of Red Cells Stored for Five Years with those of Fresh Cells from the same Donors

Specimen	Aldolase*		Aspartate Aminotransferase*		Glucose 6-Phosphate Dehydrogenase†		6-Phosphogluconate Dehydrogenase†	
	Fresh	Stored	Fresh	Stored	Fresh	Stored	Fresh	Stored
1	1.2	1.1 (92%)	0.5	0.6 (120%)	3.3	2.3 (70%)	4.1	2.3 (56%)
2	1.1	0.9 (82%)	0.5	0.5 (100%)	3.7	3.5 (95%)	4.5	2.5 (56%)
4	1.4	0.8 (57%)	0.7	0.6 (86%)	4.5	1.7 (38%)	4.2	2.1 (50%)
7	1.3	1.5 (115%)	0.6	0.7 (117%)	4.5	5.6 (125%)	4.5	3.9 (85%)

* International units per g. Hb at 37°C . † International units per g. Hb at 25°C .

reference work. It is probably the method of choice for rare blood samples.

Intraerythrocytic enzymes appear to be reasonably stable under the conditions of storage.

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Haemorrhagic Necrosis of the Intestine

J. S. MCKINNELL,* M.B., CH.B., D.PATH., F.C.PATH.; M. S. KEARNEY,† M.B., CH.B.

Brit. med. J., 1967, 4, 460-463

The fact that necrosis of the bowel can occur in the absence of demonstrable occlusion of the mesenteric vessels has long been recognized. Kleckner, Bagen, and Baggenstoss (1953) recognized that enterocolitis occurred in heart disease, but Wilson and Qualheim (1954) seem to have been the first to define a specific syndrome occurring mainly in elderly subjects suffering from heart disease and characterized by patchy haemorrhagic necrosis of the intestinal mucosa unrelated to the distribution of the mesenteric arteries. These authors observed eight cases of acute haemorrhagic enterocolitis in one and a half years and discovered 12 similar cases in a survey of the hospital necropsy records between 1947 and 1953. Subsequently a number of American authors have described further cases of the same type: Ming and Levitan (1960) encountered 11 in three years among 698 necropsies; Glotzer and Shaw (1959) collected nine in a period of 10 years; Grosh, Mann, and O'Donnell (1965) described 10 cases seen in three years; in a study of hospital records over a 12-year period Berger and Byrne (1961) found 23 cases of massive bowel infarction in the absence of mesenteric artery or vein occlusion, though at necropsy the majority showed infarction in the distribution of the superior mesenteric artery and only a minority showed involvement of multiple segments at random sites; Fogarty and Fletcher (1966) studied 18 patients during five years; Drucker, Davis, Holden, and Reagan (1964) observed seven patients within two years. The last-mentioned authors discuss the pathogenesis. In a report from Australia, McGovern and Goulston (1965) recorded 33 cases in a 14-year period.

No series of exactly comparable cases seems to have been reported from this country. During the five months July to November 1964 we encountered 13 cases among fewer than 200 necropsies. Previous to this period such cases were very rare in the experience of one of us (J. S. McK.), and subsequently in the same hospital there have been only two similar cases among over 1,000 necropsies. The only unusual feature of the five months in question was that they were unusually dry; the rainfall in these five months totalled 3.5 in. (8.9 cm.), as compared with an average of 7 in. (17.8 cm.) for the same five months in the years 1947 to 1961. No other late summer and autumn since 1947 had been so dry.

Reports of two representative cases are given.

Case 1

The patient, a man aged 85, was admitted to hospital with a history of abdominal pain for some days, becoming more severe in the previous 24 hours.

* Consultant Pathologist, Selly Oak Hospital, Birmingham 29.
† Surgeon Lieutenant, R.N.; Late Registrar in Pathology, Selly Oak Hospital, Birmingham 29.

On examination the transverse colon was distended and showed visible peristalsis. He was dehydrated. The rectum contained hard faeces. Levels of serum electrolytes were: sodium 134 mEq/l., potassium 3.5 mEq/l., chloride 86 mEq/l., and bicarbonate 29 mEq/l. The blood urea was 76 mg./100 ml. A provisional diagnosis of carcinoma of the colon was made. One litre of dextrose saline and one litre of Dacron solution were infused in 12 hours, but the patient collapsed unexpectedly and died 48 hours after admission.

At necropsy the heart was of normal size. The myocardium was flabby. The valves were normal. The coronary arteries were moderately dilated and there was diffuse thickening of their walls, but there were no atheromatous plaques and no restriction of their lumina. The lungs were oedematous and congested. The liver was rather small and its surface was mottled, due to irregular patches of congestion. The gastric mucosa and the mucosa of the whole length of the small intestine were acutely congested, and gas bubbles were observed under the mucosa of the duodenum. There were small haemorrhages in the mesentery of the jejunum. The mucosa of the caecum was severely haemorrhagic and much thickened. In the transverse colon there were two segments in which the mucosa was greenish and the wall of the bowel thinned owing to dilatation. The mucosa of the pelvic colon was thickened and haemorrhagic, like that of the caecum. The aorta was well preserved for the age of the subject, and the superior and inferior mesenteric arteries and veins were patent. The kidneys showed some loss of cortical substance with coarse granularity of the subcapsular surface, suggestive of scarring due to senile arteriosclerosis. There was moderate dilatation of both renal pelves, the bladder was moderately dilated and trabeculated, and the prostate was enlarged.

On histological examination the more severely affected areas of the small intestine, the caecum, and the pelvic colon all showed essentially similar changes, consisting of haemorrhage into the mucosa and severe congestion of the submucosa with thrombosis



Fig. 1.—Case 1. Superficial necrosis of the mucosa with haemorrhage in the deeper zone. Severe congestion of the vessels of the submucosa with some oedema.

of a few small veins (see Fig. 1). Inflammatory cellular exudate was slight and diffuse in all coats. Large numbers of thick Gram-positive rods were present on the surface of the haemorrhagic mucosa. There were also large numbers of organisms in the mucosa and submucosa, and to a lesser extent in the other coats, but these were mainly Gram-negative rods. In the transverse colon affected areas showed thinning and necrosis of the mucosa with thinning of the wall of the colon, presumably due to dilatation of its lumen. Here organisms were less numerous, there being a few Gram-negative rods in the mucosa and submucosa. Culture of the small intestine revealed *Clostridium welchii* and *Escherichia coli*.

Case 4

This man, aged 75, had been treated by his family doctor for several years for congestive heart failure. He had been well maintained on diuretics and digoxin. On the day of admission he became jaundiced and complained of vague abdominal pain.

On examination he was obviously very ill, jaundiced, dyspnoeic, and cyanosed, with gross ankle oedema. He was pulseless and the heart sounds were inaudible. Shortly afterwards he had a massive rectal haemorrhage of fresh blood and died 33 hours after admission.

At necropsy there were bilateral pleural adhesions, and the lungs were oedematous and congested. Both ventricles of the heart were hypertrophied and dilated, and there was some dilatation of the atria. The myocardium was soft and flabby. The valves were normal and the coronary arteries showed only minimal atheroma. The heart weighed 505 g. There were several small acute ulcers of the gastric mucosa and petechial haemorrhages in patches at the cardiac end. From the duodenum to the rectum there was intense congestion, most severe in the duodenum, terminal ileum, and colon. The mucosa of the terminal ileum was haemorrhagic and thickened, with small irregular ulcers between thickened mucosal folds. The caecum was less severely congested and haemorrhagic, but there were a few ragged erosions and rounded ulcers 2 to 6 mm. in diameter. The mucosa of the anterior wall of the ascending colon was ulcerated in a strip 2 cm. wide. The distal half of the transverse colon and the descending colon showed the most severe changes. The mucosa was almost black, due to massive haemorrhage, and much thickened; areas up to 1.5 cm. in diameter were denuded of mucosa. There was no pseudomembrane. There were some calcified mesenteric lymph nodes. The mesenteric arteries and veins were patent and the aorta was only moderately atheromatous. Liver and kidneys showed cloudy swelling but were otherwise normal. The other organs showed nothing remarkable.

Histological examination showed much mucosal haemorrhage and a variable amount of necrosis and ulceration in the affected zones at all levels in the intestine. There was submucosal oedema and congestion with "thrombi" consisting mainly of aggregated red cells in small veins. Many Gram-negative rods and a few Gram-positive rods were found in the mucosa.

Clinical Picture

Table I summarizes the clinical features. Of the 13 patients, 12 were 64 years of age or older; the exception was a 45-year-old mentally subnormal woman who refused food and required tube-feeding. There were seven women and six men. Abdominal pain was a feature in seven cases. Vomiting was recorded in six patients and haematemesis in one of these. Diarrhoea occurred in four, and rectal bleeding in six. There was no abdominal pain in five cases. Terminal collapse was observed in 10 cases and severe peripheral cyanosis was recorded in three.

In 10 cases congestive cardiac failure had been present at some time, but only six of these were in failure at the time of admission to hospital. In two cases there was a recent myocardial infarct. In three cases there was no evidence of any heart disease. In two cases there was thrombocytopenia; one of these was uraemic owing to urinary tract infection. One case was on anticoagulant therapy with phenindione. In all cases the blood urea was above normal, but in the only three in which it was estimated on more than one occasion there was evidence of a steep rise between the onset of abdominal symptoms and death. In three cases significant nitrogen reten-

TABLE I.—Summary of Clinical Features

Case No.	Date of Death	Age	Sex	Symptoms	Abdominal Pain	Distension	Vomiting	Diarrhoea	Haematemesis	Rectal Bleeding	Cyanosis	Collapse	Heart Failure on Admission	Failure in Past	Type of Heart Disease	Blood Urea (mg./100 ml.)		Other Features
																1st	2nd	
1	4/7/64	85	M	4 days	+	+	+	++	+	+	+	+	+	—	None	78	171*	On phenindione.
2	24/7/64	68	M	8 days	+	+	—	+	—	+	+	+	+	—	Myocardial fibrosis.	84	171*	Prothrombin index 2.5
3	21/7/64	45	F	2 weeks	?	—	—	—	—	—	—	—	—	—	Recent infarct	64	450	Mentally subnormal. Refused food or drink
4	22/7/64	75	M	2 days	Discomfort	—	—	—	—	+	+	+	+	—	Hypertensive	—	146*	Jaundice
5	23/7/64	69	M	1 day	—	—	—	—	—	+	+	+	+	—	Myocardial fibrosis	—	78	Caustic prostatic
6	10/8/64	82	M	Weakness 4 days	—	—	—	—	—	—	+	+	+	—	Myocardial fibrosis	36	195*	Recent prostatectomy.
7	5/9/64	76	F	3 days	+	—	+	—	—	—	+	+	—	+	Coronary atheroma	—	92*	Urinary infection
8	16/9/64	67	F	2 weeks	Slight	—	+	+	—	+	+	+	—	—	Unknown cause	—	136*	Purpura on arms and legs
9	24/9/64	80	F	Several weeks	+	+	+	—	+	—	—	—	—	—	Adherent pulmonary fibrosis	—	59*	Chronic bronchitis and emphysema
10	1/10/64	79	M	1 day	—	—	+	—	—	—	+	+	+	—	Recent myocardial infarct.	—	—	Recent operation: strangulated omentum in femoral hernia
11	17/10/64	69	F	Several days	+	+	—	—	—	+	+	+	+	—	Fibrosis	91	—	Megaloblastic anaemia. Hb 2.4 g./100 ml. Platelets 15,000
12	26/10/64	77	F	Weakness, 10 weeks	—	+	—	—	—	+	+	+	+	—	Myocardial fibrosis.	209	—	Purpura. Platelets 25,000. Digoxin overdose. Jaundice.
13	20/11/64	64	F	3 weeks	+	—	+	+	—	+	+	+	—	+	Coronary atheroma	119	366	Urinary tract infection

* Post-mortem value

tion could have been the result of primary renal disease, there being evidence of pyelonephritis in two and carcinoma of the prostate in one. In three cases plasma potassium was low or rather low—3.5, 4, and 4.1 mEq/l.—while in one case it was raised to 5.6 mEq/l.

Table II summarizes the treatment which 10 of these patients had received before the terminal illness. Case 1 had no previous significant illness, and in Cases 7 and 10 our information is incomplete. One patient was known to have taken an overdose of digitalis in the period immediately before the onset of abdominal symptoms. The antibiotics had been given at varying intervals before the final catastrophe and do not seem to have played a significant part.

TABLE II.—Summary of Drugs Which Had Been Administered Before the Onset of Symptoms

Case	Digitalis	Thiazide Diuretics	Antibacterial Therapy	Other Drugs
1	—	—	—	—
2	+	—	—	—
3	—	—	Sulphonamides Penicillin. Tetracycline	Phenindione. Cholel Ephedrine. Aminophylline
4	+	+	Penicillin. Tetracycline	Oestrogens. Paracetamol. Stromba
5	—	—	Streptomycin	Paracetamol. Peritrate
6	—	—	Penicillin	—
7	+	?	—	—
8	+	+	—	—
9	+	+	—	—
10	?	?	—	—
11	+	—	Erythromycin	Barbiturates Ferrous sulphate
12	—	+	—	Mersalyl. Quinidine
13	+	+	—	—

Pathology

A characteristic feature was the patchy distribution of the changes, which consisted mainly of congestion of the mucosa, varying in degree from slight to very severe, accompanied by intramucosal haemorrhage which rendered the bowel wall thick and turgid, the mucosal surface being dark brown and slightly rough to the touch in those areas. In a few, as in Case 1, there were areas in which the wall of the colon was thinned, the mucosal surface being greenish and smooth; this phenomenon seemed to be secondary to dilatation of the colon proximal to haemorrhagic necrosis of the mucosa of the distal colon. In some cases the wall of the small intestine was diffusely plum-coloured and there was a little blood-stained fluid in the peritoneal cavity. In some such areas there were bubbles of gas in the submucosa. Fig. 2 gives a diagrammatic representation of the extent of involvement in the individual cases.

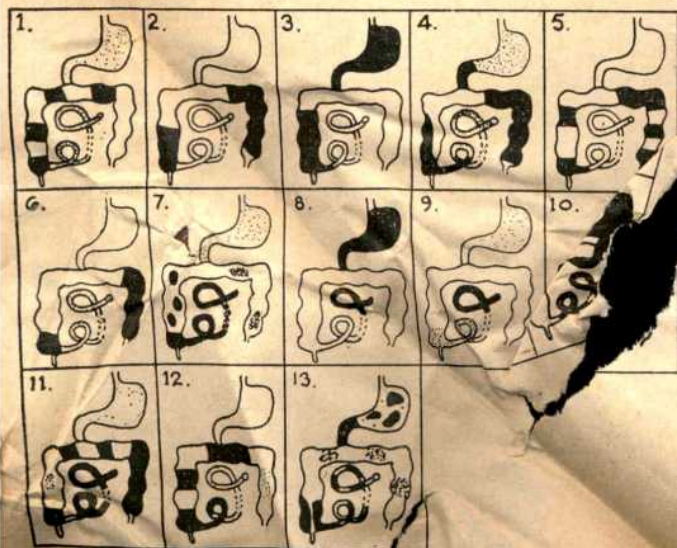


FIG. 2.—The solid black areas indicate haemorrhagic necrosis of the mucosa. The stippled areas indicate severe congestion with petechial haemorrhages.

Microscopically the characteristic features were haemorrhage into the mucosa with superficial necrosis. In the submucosa the veins were congested, some giving an impression of thrombosis, probably due to aggregation of red cells rather than to actual clotting, there being no obvious fibrin or platelet thrombi. In some cases there was oedema of the submucosa. Cellular inflammatory exudate was mainly slight, except in the few cases where there were areas of ulceration. The muscular and serosal coats were not greatly affected in most cases. In the dilated colon, where the mucosa was green and smooth, macroscopic examination showed necrosis of the thinned mucosa with almost no reaction.

Bacteriological Examination

Culture of the affected intestine, the small intestine being sampled when it was involved, gave in all cases a growth of *Cl. welchii*. All strains were tested for heat resistance, with negative results. This observation is of doubtful value, however, as the test was performed on cultures of the organism in Robertson's meat medium and not on the tissue itself: in these circumstances the spores may have germinated before being subjected to heat. The three strains which were tested were shown by toxin analysis to be of type A. Of the eight cases in which the other organisms present were identified, *E. coli* was recognized in five, *Streptococcus faecalis* in six, a *Klebsiella* in two, and *Pseudomonas pyocyanea* and *Sarcina* in one each. In three cases intestinal viruses were looked for, with negative results.

Discussion

Haemorrhagic necrosis of the bowel mucosa of patchy distribution occurring in elderly cardiac invalids has its own characteristics, but it shares some features with other types of acute non-occlusive intestinal necrosis. Among others, Dawson-Edwards and Morrissey (1955) and Kay, Richards, and Watson (1958) described cases of acute necrotizing colitis characterized by disseminated areas of congestion, necrosis, and ulceration of the mucosa. Not all of these cases could properly be described as "pseudomembranous" colitis, but they lacked the massive haemorrhage seen in the present series. These cases were predominantly postoperative and usually followed partial gastrectomy, though two cases of the series of Kay *et al.* were preceded by myocardial infarction. Undue operative shock was not a feature of either series and antibiotic administration was not thought to be an important factor. *Cl. welchii* was isolated in eight of the 14 cases described by Kay *et al.*, while in the other cases bacteriological examination was incomplete or omitted. Staphylococci were isolated in four cases. It is of interest that Howie, Duncan, and Mackie (1953) have demonstrated growth of *Cl. welchii* in the stomach after partial gastrectomy.

A number of types of necrotizing intestinal lesions have been described in which the causative agent seems to have been *Cl. welchii*. Cases of enteritis necroticans (*Darmbrand*) thought to have been due to ingestion of *Cl. welchii* from tinned meats were seen in Northern Germany in the summer of 1946 and again in 1947 (Jeckeln, 1947, 1948). The jejunum was most severely involved, but the ileum and the colon were occasionally affected. The disease was most severe in elderly patients and in young children, but occurred at all ages. Malnutrition may well have been a contributing factor. In those who survived the acute stage there was a tendency to perforation and stricture formation. A similar condition has been described in Papuan natives, caused by the consumption of poorly preserved pork in large quantities at times of festival (Murrell and Roth, 1963). Heat-resistant strains of *Cl. welchii* were incriminated in these outbreaks. The German strain is said to have been of type F (Zeissler and Rassfeld-Sternberg, 1949), while that from Papua was probably of type C.

Gas gangrene of the intestine has been described as a complication of leukaemia (Amromin and Solomon, 1962) and is not rare after haemorrhage from a peptic ulcer. Killingback and Lloyd Williams (1961) described six cases of necrotizing colitis of acute onset in previously well elderly subjects. Histological examination suggested the possibility of a clostridial cause. Resection of the affected colon was life-saving in three cases. Tate, Thompson, and Willis (1965) isolated a heat-resistant strain of *Cl. welchii* type A from a similar case.

The fact that we were able to grow *Cl. welchii* from all our cases may have been significant. Though *Cl. welchii* is a common inhabitant of the colon it can in our experience be isolated from the bowel in only about 70% of necropsies. The significance of heat resistance as a characteristic of food-poisoning strains of *Cl. welchii* has probably been exaggerated in the past, and there is some evidence to suggest that non-heat-resistant strains may also be capable of producing food poisoning (Taylor and Coetzee, 1966). The same consideration may well apply to the production of necrotizing enterocolitis in susceptible subjects, but even if *Cl. welchii* is a factor in precipitating this condition there are obviously important predisposing causes.

Among others, Marston (1962, 1964) stressed the role of ischaemia in the production of necrosis of the intestine. He also drew attention to the condition of haemorrhagic necrosis of the intestine occurring in dogs subjected to hypovolaemic shock. While we agree that anoxia is an important factor, the mesenteric arteries in our cases were not affected by atheroma to any significant degree, except in one case in which the inferior mesenteric artery was completely occluded and a plaque of atheroma was present in the main trunk of the superior mesenteric; and there was nothing in the histological sections to suggest anatomical occlusion of the small arteries, though in some cases apparent thickening of the walls of the small arteries relative to the area of the cross-section of their lumina suggested the possibility of spasm. Except for the two cases of myocardial infarction there was no reason to suspect shock as a primary factor. However, Corday, Irving, Gold, Bernstein, and Skelton (1962) have pointed out that mesenteric arteriolar spasm may result from cardiac arrhythmias and congestive heart failure as well as from hypotension and from the administration of vasopressor drugs.

Dehydration from diuretic therapy may aggravate both the arteriospasm and the congestion, favouring aggregation of red cells in the submucosal venules. Dehydration was perhaps a major factor in the youngest patient, who had been refusing food and drink. Prolonged treatment of congestive cardiac failure with thiazide diuretics tends to deplete the cells of potassium, even though serum potassium may remain normal. Though the effect of electrolyte imbalance on the intestine is complex, loss of cellular potassium tends to lower intestinal motility and may well favour proliferation of organisms in the small bowel.

The role of digitalis has been emphasized by Gazes, Holmes, Moseley, and Pratt-Thomas (1961); all their 10 patients seen in a period of 10 years had received large doses of digitalis and several were suffering from digitalis toxicity. They reviewed the evidence in the literature that digitalis causes pooling of blood in splanchnic vessels, possibly by causing spasm of hepatic veins or of portal venules. They also pointed out that a maintenance dose of digitalis may become toxic when potassium is lost from the body.

Treatment

The treatment of haemorrhagic enterocolitis is unsatisfactory. Laparotomy may have to be performed to rule out mesenteric vascular occlusion or necrotizing colitis, but resection of bowel should be avoided if possible. The administration of dextran of low molecular weights may improve the circulation in the intestinal wall, not so much by expanding the plasma volume

as by favouring the disaggregation of red cells. Potassium depletion should be corrected. Vasopressors, especially angiotensin amide, should be avoided as being likely to increase vascular spasm. Judicious dosage of metaraminol or nor-adrenaline acid tartrate (levarterenol) may be less objectionable in the presence of septic shock (Smulyan, Cuddy, and Eich, 1964), but present opinion on the treatment of shock favours drugs which increase peripheral blood flow (*Brit. med. J.*, 1966). For this purpose either the alpha-adrenergic antagonist phenoxybenzamine or the quicker-acting beta-adrenergic receptor stimulator isoprenaline (du Toit, du Plessis, Dommissie, Rorke, Theron, and de Villiers, 1966) or orciprenaline, which is recommended by Shanks, Brick, Hutchison, and Roddie (1967) as being more easily obtainable, may be given. When using any of these drugs appropriate infusions should be administered to expand the blood volume to match the increased vascular bed. If we are correct in thinking that splanchnic vasoconstriction is an important cause of haemorrhagic enterocolitis this treatment should be instituted at the earliest possible moment, preferably before the development of the terminal collapse.

It would seem reasonable to administer anti-gas-gangrene serum and massive doses of antibiotics directed both against *Cl. welchii* and against the secondary invaders which may colonize the haemorrhagic and necrotic mucosa.

Summary

The clinical and pathological features of 13 cases of acute haemorrhagic enterocolitis which were seen in one hospital during an unusually dry spell in the summer and autumn of 1964 are described. It is suggested that, while the basic cause is probably reduction of the blood flow through the wall of the intestine, this is usually due to functional factors associated with heart failure and its treatment and not to anatomical lesions in the splanchnic blood vessels. It is also suggested that usually harmless organisms ingested in unusually large numbers owing to climatic conditions, and possibly proliferating in the intestinal contents owing to stasis, may have precipitated this haemorrhagic necrosis of the mucosa.

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Preliminary Communications

Prevention of Delayed Traumatic Facial Palsy

Brit. med. J., 1967, 4, 464-465

Taverner *et al.* (1966) showed that treatment with intramuscular A.C.T.H. gel increased the recovery rate from Bell's palsy and reduced the incidence of denervation. They claimed that even better results would be obtained if all patients were treated within 24 hours of the onset of paralysis. It is possible that the mechanism of delayed traumatic facial weakness is similar to that of Bell's palsy and that in both conditions there is an inflammatory reaction in or around, or a swelling of the facial nerve in its canal, and that this leads to ischaemia and in some cases to denervation. If this is so, and if one could identify those patients particularly liable to develop this complication of head injury, it might be expected that prophylactic treatment with A.C.T.H. would be effective.

The results we have obtained so far are sufficiently suggestive of a protective value of A.C.T.H. against late traumatic facial weakness that we feel justified in publishing this preliminary communication—particularly since, with Taverner *et al.*, we have found the treatment itself to be harmless, provided a correct dosage is observed.

SELECTION OF PATIENTS

In cases of head injury, damage to the facial nerve in its canal is nearly always associated with a fractured petrous bone, though it may sometimes be difficult, even with specially projected views, to demonstrate radiologically the fracture and its precise relation to the facial canal. A common clinical sign of this type of fracture is bleeding from the ear on the same side. In a series of 2,712 consecutive and unselected cases of head injury admitted to the Radcliffe Infirmary, Oxford, some degree of facial nerve involvement was detected in approximately 50% of patients showing unequivocal radiological evidence of a fractured petrous bone whether or not this was accompanied by a bleeding ear (Potter, 1964).

Two varieties of facial weakness are usually recognized: *immediate*, where the nerve has been directly concussed, contused, or lacerated at the moment of injury; and *delayed*, where the weakness results from some reaction occurring after an interval, usually during the first week or occasionally even later. In addition, a third, or *mixed*, group of cases can be recognized, where there has been an immediate weakness, which may then either recover and be followed by delayed weakness or progress later to a more severe weakness or complete paralysis (Potter, 1964). It is not our policy to operate on patients in the first group, and the present paper is concerned with *delayed facial weakness only*. The prognosis in this variety is normally good, but denervation and perverted reinnervation may occur and result in some permanent disfigurement. Prevention of the complication should therefore be attempted if a simple and safe method is available, and this appears to be provided by A.C.T.H.

In choosing patients for prophylactic treatment we felt it desirable that criteria should be used which could be readily recognized in casualty departments without the need to employ sophisticated techniques of investigation. It was also necessary that we should be able to discover, from an untreated control

group, the expected incidence of facial weakness in the series to be treated.

During the past year we therefore selected all patients who had a bleeding ear and who were shown also to have radiological evidence of a petrous temporal fracture on the same side. Those with blood behind an intact drum were not included. In an earlier series of 5,000 consecutive and unselected cases of head injury admitted to this unit between 5 January 1962 and 9 May 1965 we found that there had been 70 patients with the same combination of a fractured petrous bone and a bleeding ear and that 27 of these had shown some degree of delayed facial weakness—an expected incidence for this complication, therefore, of 38.5%.

RESULTS

In the past year there have been 16 patients showing the combination of a fractured petrous bone and bleeding ear, and all have received prophylactic A.C.T.H. soon after the injury. Without treatment we should have expected six of these patients to develop some delayed facial weakness; but only two did so. One developed rapidly a complete facial palsy on the second day after injury; denervation ensued despite treatment, and there has been no recovery during the month following the injury. In the second case there was only slight and transient facial weakness lasting for some 10 hours on the second day after injury. The ages of the 16 patients ranged from 2 to 77.

We have the impression—but it is no more than a clinical impression—that these patients receiving A.C.T.H. have recovered unusually smoothly from the other effects of their head injuries.

METHOD

Corticotrophin (A.C.T.H.) gelatin injection B.P. was given daily by intramuscular injection for eight days. Since, in the great majority of cases, delayed traumatic facial weakness appears during the week following injury (Turner, 1944; Potter, 1964) and because our object was prophylaxis, we did not feel it necessary to employ the full 10-day therapeutic course adopted by Taverner *et al.* for patients with Bell's palsy, except in the case of a single patient who developed the complete paralysis between the second and third doses.

The first injection was given within a few hours of the injury. The dosage was as follows: 80 units daily for three days, 60 units on the fourth day, 40 units on the fifth day, 20 units on the sixth day, and 10 units on both the seventh and eighth days. For children the dosage was reduced according to weight and age, but this reduction was apparently insufficient in a 3½-year-old who showed marked oedema of the lower abdominal wall and genitalia for five days at the end of his course of treatment.

Though one might suspect that the plasma cortisol level is relevant to this problem, we know of no certain evidence yet that this is so, and Taverner (1954) had already found cortisone ineffective in the treatment of Bell's palsy. Nevertheless, after the first dose we gave the A.C.T.H. in the afternoons, because it is known that the plasma cortisol is normally at a relatively low level at that time—as also is the level of A.C.T.H. (Ney *et al.*, 1963). (If, indeed, a high plasma cortisol level contributes to the protection of a patient from delayed traumatic facial weakness we would expect this complication to occur less often in the more severely injured patients. This possibility is at present under investigation.)

SUMMARY

Sixteen patients were given prophylactic A.C.T.H. after they had sustained head injuries. Each had shown radiological evidence of a fractured petrous bone and had had bleeding from the ipsilateral ear.

The expected incidence in an untreated group of the same size would have been six patients showing delayed facial weakness.

Only two patients developed delayed facial weakness. In both this occurred on the second day. In one it was mild and lasted only 10 hours; in the other it was complete and denervation occurred despite treatment.

It seems that A.C.T.H. offers some protection against this complication of head injury.

We are grateful to Dr. T. D. A. Hockaday and Mr. George Higgins for their expert help and advice.

M. BRIGGS, M.B., B.S.

Registrar.

JOHN M. POTTER, M.A., D.M., F.R.C.S.

Consultant Neurosurgeon.

Department of Neurological Surgery and the Accident Service,
Radcliffe Infirmary, Oxford

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Medical Memoranda**Sarcoid Myopathy**

Brit. med. J., 1967, 4, 465-466

Only 12 cases (Hinterbuchner and Hinterbuchner, 1964) have been found in the literature where sarcoidosis presented as a pure myopathy with no evidence of other systemic involvement. I present another case which has responded dramatically to corticosteroid therapy.

CASE HISTORY

A 55-year-old Englishwoman presented in March 1966 with a three-week history of calf stiffness alleviated by exercise. She had no other symptoms, was on no drugs, and had no relevant family or social history.

In April she was admitted to hospital, and examination showed severe weakness in her legs, more so on the left, with slight thigh wasting. Weakness was also present in the elbows and wrists, but without wasting. The muscles were non-tender and felt normal. Her gait was stiff and wide-based, and she tired easily. No other significant abnormality was found and no definitive diagnosis made. Physiotherapy produced some improvement, and she was discharged after one month. By August wasting and weakness had developed in all proximal limb muscles. Walking was difficult without support, resulting in several falls.

She was readmitted to hospital in January 1967 with severe weakness in her hands, hardly able to walk even with support, and unable to sit up unaided or do her hair. She had an occasional dry cough but no other complaints. Examination showed obvious muscle wasting of all the limbs, whose tone was slightly reduced. The muscles felt rubbery but were not tender, fasciculating, or showing involuntary movements. Movement was full, but with severe generalized weakness, including the sternomastoids and face. The other systems showed no abnormality.

Investigations.—A skeletogram showed mild osteoporosis; W.B.C. 3,900-7,000/cu. mm. (monocytes 8.5-12.5%); serum proteins 6.5-7.2 mg./100 ml. (albumin 3.0-4.4 mg., globulin 2.8-3.5 mg.); normal electrophoresis; latex fixation test weakly positive (Putkonen *et al.*, 1965); urine creatine 460 mg./24 hours (normal 0-50 mg.). Muscle biopsy showed no necrosis or acid-fast bacilli but the characteristics of sarcoidosis—a granulomatous process with small foci of epithelioid cells surrounded by small mononucleated cells and some multinucleated giant cells.

The following investigations showed no abnormality. Blood: haemoglobin, platelets, P.C.V., M.C.H.C., film, L.E. cells, E.S.R., urea, electrolytes, cholesterol, alkaline phosphatase, calcium, phosphorus, liver function, antistreptolysin titre, aldolase, lactic acid

dehydrogenase, creatine, creatine phosphokinase, creatinine, lead, culture. Urine: routine analysis, bile derivatives, porphobilinogen, uroporphyrins, Bence Jones protein, calcium, creatinine, renal steroid leucocyte excretion, intravenous pyelogram. Throat swab, culture for tubercle, 1:10 tuberculin test, Wassermann reaction, V.D.R.L., cerebrospinal fluid, electrocardiogram, Kveim test, radioactive iodine uptake.

Treatment was begun in February with prednisone, 15 mg. daily, reducing to 10 mg. daily in June, the only available therapy of value (Crompton and MacDermot, 1961; Silverstein *et al.*, 1965). After three weeks she could sit up unaided, and by April felt much improved and could walk 30 yards (27 metres) with support. Power had improved considerably in her legs and was normal in her arms apart from slight weakness in her right fingers. In June she was walking up to 100 yards (90 metres) with slight support.

Though remissions occur in the sarcoid process, I thought that, since the condition had progressed inexorably for 15 months, corticosteroid therapy had caused rapid improvement.

COMMENT

The skin lesions of sarcoidosis were first described by Boeck (1899), and literature has amassed covering involvement of nearly all the tissues in the process (Maycock *et al.*, 1963). The diagnosis of sarcoidosis should always be confirmed by histology (Maycock *et al.*, 1963), usually accompanied by an intermittent monocytosis, eosinophilia, leucopenia, raised serum calcium and globulin, and occasionally a raised alkaline phosphatase. A positive Kveim reaction occurs in 60% of patients, with false-negative results in long-standing or inactive disease (Siltzbach, 1964) and during corticosteroid therapy.

The outcome of sarcoidosis is usually spontaneous remission, but irreversible lung or myocardial fibrosis may cause death. Treatment with A.C.T.H. or corticosteroids may produce remission (Silverstein *et al.*, 1965), but 60% of patients do not respond (Crompton and MacDermot, 1961).

Since Sundelin's (1925) original report several cases of muscular involvement in generalized sarcoidosis have been described, taking several forms—asymptomatic microscopic granulomata, palpable nodules, or myopathic. A purely myopathic presentation is very rare, only 12 cases have been found in the literature (McConkey, 1958; Hinterbuchner and Hinterbuchner, 1964). Muscle biopsy shows characteristic sarcoid histology—interstitial infiltration with giant cells, epithelioid cells, and lymphocytes, with tissue replacement by a pallisade-like and reticular collagen fibre network, leading to fibrosis. Occasionally widespread muscle fibre degeneration

occurs with floccular necrosis and macrophagia or epithelioid tubercles and intramysial multinucleated giant cells (Coërs, 1967).

I am grateful to Dr. T. Grahame-Wilson for allowing me to study this case, and to Professor W. Blackwood, Dr. G. M. Churcher, Dr. H. Greenbergh, and Miss J. K. Bowman for their help and advice.

P. S. TALBOT, M.B., B.S.

Department of Medical and Surgical Neurology,
Plymouth General Hospitals.

Transfusion Malaria in a Man with Christmas Disease

Brit. med. J., 1967, 4, 466

Malaria as a complication of blood transfusion has been reported in the United Kingdom only four times (Thomas *et al.*, 1936; Nabarro and Edward, 1939; Rogers, 1947; Grant *et al.*, 1960), though it is a relatively common occurrence in countries where malaria has until recently been endemic. The rarity of this complication in England can make diagnosis difficult, as is illustrated in the following case.

CASE REPORT

An Englishman aged 33 who had never travelled abroad had been admitted to hospital many times since childhood for haemarthroses and haematuria, secondary to Factor IX deficiency. He was first admitted to the Churchill Hospital on 14 April 1966 for the treatment of a haematoma in the arm caused by an intramuscular injection.

Examination showed a pale, anxious man with a large tense haematoma of the deltoid muscle. His haemoglobin was only 47% (6.9 g./100 ml.), though he had been given 3 pints (1.7 litres) of blood during the previous week. Investigation revealed chronic renal disease with raised blood urea and proteinuria; an intravenous pyelogram later showed small contracted kidneys. Coagulation studies showed Factor IX deficiency.

The deltoid haematoma was treated during the next two weeks by the infusion of three doses of Factor IX concentrate (equivalent to 1.5–3 litres of fresh plasma), three doses of plasma (dose volume 800 ml.), and packed cells from 4 pints (2.3 litres) of blood. The latter was given on 14 and 15 April. Three more doses of plasma were given later for the treatment of haemarthroses.

He was discharged home on 4 June, only to be readmitted on 17 June with a haemarthrosis of the knee of five days' duration. This was treated by immobilization without intravenous therapy.

On 29 June he developed an unexplained irregular fever and at the same time became hypotensive and developed pancytopenia and splenomegaly.

Investigations from 30 June to 5 August.—The following tests gave normal results: blood, urine, stool, and throat-swab cultures; chest x-ray examination; salmonella and brucella agglutinations; L.E. cell preparations; one search for malaria parasites; a sternal marrow puncture; and cultures of marrow and urine for tuberculosis. During July his anaemia was aggravated by recurrent haematemesis associated with rigors. Thrombocytopenia probably contributed to the gastrointestinal bleeding (platelets 45,000–120,000 cu. mm.). He was transfused with fresh packed cells from 10 pints (5.7 litres) of blood during this time. Meanwhile he developed boils on his buttocks and his blood urea rose from 100 to 186 mg./100 ml. After four weeks of irregular fever the temperature chart began to show a regular periodicity with two clear days between each attack. The character of the fever became strongly suggestive of quartan malaria, and on 5 August parasites of *Plasmodium malariae* were found in the peripheral blood. A review of blood films showed that parasites first appeared in small numbers

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in a blood film on 5 July, while six previous films between 3 April and 1 June failed to show parasites.

Chloroquine 500 mg. followed by 250 mg. daily for three days and primaquine 15 mg. base daily for 14 days were given. During the writing of this paper I have been informed that malaria transmitted by blood transfusion does not give rise to exoerythrocytic forms of the parasite. Treatment with primaquine was therefore unnecessary (P. G. Shute, 1967).

Blood counts returned to normal, the boils healed, and the blood urea fell to its former level. During the next three weeks five doses of plasma (dose volume 800 ml.) were administered for haemarthroses, which developed during mobilization, and the patient was discharged home on 10 September.

COMMENT

Investigation of the blood donors in this case revealed one Englishman who had suffered malaria in 1946 while serving with the Army in the Far East. He had been in good health since that time. During prolonged searches of his blood films one young malaria parasite was found. This donor had given 34 pints (19.3 litres) of blood in the past and an attempt was made to discover whether previous recipients of his blood had contracted malaria. A temperature chart suggestive of quartan malaria was found in the records of one recipient 39 days after transfusion. This could not be confirmed on the only available blood film.

In a series of 36 cases of transfusion malaria studied by Lepeš (1965) in Yugoslavia the incubation period varied between 5 and 70 days, the infected blood having been stored 1 to 10 days. The incubation period in the present case was 74 days, the blood having been stored 10 days.

Transfusion malaria should thus be remembered when a patient develops a pyrexia of unknown origin as late as 10 weeks after receiving blood, for in spite of the precautions taken by the National Blood Transfusion Service the occasional donor may be a chronic malaria carrier.

I would like to thank Professor R. G. Macfarlane for encouraging me to publish this case; Professor P. B. Beeson for helping to make the diagnosis; Dr. Jean Grant, who investigated the blood donors; Dr. F. G. Bolton, Mr. P. G. Shute, and Dr. F. E. Lipscomb, who spent much time studying blood films from the patient and donors; and Dr. W. d'A. Maycock for his helpful advice.

ANGELA E. VARTAN,* M.B., B.S.,
Registrar, M.R.C. Blood Coagulation Research Unit,
Churchill Hospital, Oxford.

* Present address: Department of Pathology, Stoke Mandeville Hospital, Aylesbury, Bucks.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Postgastrectomy Problems—II

J. ALEXANDER WILLIAMS,* CH.M., F.R.C.S.

(Last week Mr. Williams considered the cause and management of some symptoms arising after partial gastrectomy. The article continues with an account of other common complaints.)

Loss of Weight

Many patients lose weight or fail to gain weight after gastrectomy. Those who are undernourished at the time of the operation seem to be at the greatest risk.

Some degree of malabsorption of food is common after gastrectomy. It is only a malabsorption of fats that is important. Carbohydrate digestion and absorption as judged by xylose and glucose absorption tests are almost always normal. Although intestinal intubation studies have suggested that protein digestion is impaired by gastrectomy, it is unknown for protein deficiency to occur as the result of gastrectomy provided that oral intake is normal and there is no excess loss. Malabsorption of fat is the easiest form of malabsorption to detect, as the residuum is passed relatively unaltered and can be measured in the faeces. The normal person on an average intake excretes in the faeces no more than five grammes of fat per day. After partial gastrectomy the average daily output of fat in the faeces is from seven grammes (with a Billroth I anastomosis) to ten grammes (with a Billroth II anastomosis).

It is the diminished intake that is the most important cause of weight loss after gastrectomy. The causes of the diminished intake are: lack of appetite, early satiation after a small quantity of food, and fear of provoking postcibal symptoms. The analysis of these three factors is the initial step in the evaluation and treatment of weight loss.

Appetite.—This is determined by a number of apparently unrelated factors, including low blood sugar, empty stomach, and feeling of mental and physical wellbeing. The patient may have a poor appetite because he takes too much tobacco or alcohol or because he is deficient in minerals or vitamins. Iron deficiency is particularly likely to impair the appetite, so to a lesser extent do deficiencies of vitamin B₁₂ and folic acid. In the correct evaluation of the postgastrectomy patient all these factors must be assessed. Treatment may not be easy, particularly of those patients who poison themselves with nicotine or alcohol. For those who suffer from, but do not deserve, a poor appetite even after the correction of deficiencies some form of gastric stimulation before meals may be advised. The French gastroenterologist will advocate a glass of wine, the American chilled orange juice, while the British adviser may prefer sherry.

Early satiation will depend on the size of the gastric remnant, its speed of emptying, and its ability to distend. The more radical the gastric resection, the greater the likelihood of loss of weight. This is a generalization that needs qualifica-

tion and it is unwise to suggest treating weight loss due to a feeling of fullness after meals by reoperation to increase the size of the gastric remnant.

The ability of the gastric remnant to dilate without symptoms may be related to the health of the gastric mucosa. There is a good correlation between the presence on biopsy of atrophic or inflammatory gastritis and the symptom of fullness after meals. General nutritional measures to improve appetite may also increase the capacity to take food. Nevertheless, the simplest way to overcome early satiation is to take small, frequent meals. This is the oldest and simplest of the pieces of advice offered to patients after gastrectomy, but it is still the best.

Fear of Discomfort.—Some of the most severe malnutrition after gastrectomy occurs in patients in whom oesophagitis and regurgitation were provoked by taking food. The patients sought relief from these distressing symptoms in the only way they found effective—by starvation. Treatment is that of the responsible symptom.

Severe malabsorption is relatively uncommon after gastrectomy and always suggests additional disease. This may be pancreatic insufficiency, jejunoileic fistula, regional enteritis, gluten enteropathy, or the intestinal blind loop syndrome.

Diarrhoea

Increased frequency of bowel action is common after gastrectomy, and to many patients cured of both dyspepsia and constipation this is an added bonus of the operation. Many patients complaining of loss of weight, faintness, or vomiting also complain of diarrhoea, though the diarrhoea is not usually disabling.

Some of the important causes of increased frequency and fluid consistency of stool after gastric resection are: increased small bowel transit time resulting from the loss of the gastric emptying regulation once the antrum and pylorus are removed; the osmotic cathartic effect of large quantities of hypertonic foodstuff arriving in the jejunum and attracting fluid into the lumen; the production of large bowel irritants within the gut. Probably the most important factor in this mechanism is the breakdown of bile salts by bacteria. In addition to depriving the digestive tract of an effective emulsifying agent, this breakdown of bile salts liberates powerful colonic irritants which cause diarrhoea. The impaired enzymatic digestion of foods provides more fuel for fermentation and bacterial breakdown in the gut.

As all these factors are present to some extent in all patients after gastrectomy, it is not surprising that mild upsets of bowel habit are common. The practical policy of management is to treat all with simple empirical methods and to reserve sophisticated investigations for those with severe and unremitting symptoms.

* Consultant Surgeon, United Birmingham Hospitals, External Scientific Staff, Medical Research Council.

Diet.—The oldest gimmick known to gastroenterologists is to inquire if any particular food causes diarrhoea and advise its avoidance. Milk and milk products are the commonest provoking agents. The avoidance of all milk products for a trial of two weeks and then observation of the provocative effect of a glass of raw milk should indicate those patients who are sensitive to milk.

Absorbents.—The safest medicaments are the methylcellulose group of water-absorbing compounds. If they produce symptomatic control they can be used indefinitely.

Sedatives.—Sedatives of the codeine or diphenoxylate type can be used and many patients are so controlled permanently. Because of the dangers of habituation they should be used with caution.

Antibiotics.—A short course of broad spectrum antibiotics will often control an attack of diarrhoea. The agents effective against the gram-negative organisms are the most useful, presumably because they abolish or alter the flora of the upper gastrointestinal tract, and in particular control those organisms that cause breakdown of bile salts.

Neomycin, which is not normally significantly absorbed from the alimentary tract, is the safest for prolonged administration, though even this drug may cause mucosal damage. Combinations of tetracycline and nystatin may also be used. Prolonged therapy rarely produces prolonged relief, but intermittent antibiotic therapy may help to control symptoms.

The investigation and treatment of severe or intractable diarrhoea is best accomplished in a specialized gastroenterological unit. Gastrojejunal fistulae may be due to recurrent ulceration. This is investigated by barium enema and barium meal examinations as well as acid secretion studies to evaluate the cause of the ulceration.

Pancreatic insufficiency is investigated by pancreatic function studies with duodenal intubation and hormonal stimulation of the pancreas.

Gluten enteropathy may be demonstrated by peroral jejunal biopsy. The intestinal blind loop syndrome is studied by intestinal aspiration and culture and vitamin B₁₂ absorption tests.

Faintness

The feeling of faintness after meals is the predominant symptom of the so-called "dumping syndrome." The faintness occurs within thirty minutes of taking food and is usually accompanied by one or more of the following symptoms: flushing, sweating, palpitation, anorexia, nausea, and sometimes colic and diarrhoea. This combination of symptoms may occur after any gastric resection, even after pyloroplasty, but is usually worse if there is a small gastric remnant that empties rapidly. After partial gastrectomy almost all patients experience some of these symptoms at some time in the early months after operation, but in most the symptoms are transient. Prolonged complaint of annoying or disabling symptoms occur in less than 5% of most reported series.

The term "dumping" was first used by Mix,³ in 1922, who believed that the symptoms were produced by food being dumped straight into the small bowel. The physiological implications of this syndrome are so fascinating that an increasing amount of research has been devoted to its study. This work has all confirmed Mix's original concept, but it is only in the last five or six years that there has been much significant advance.

There are three essential features of the phenomenon of dumping. The small bowel cannot handle the glucose load of a meal "dumped" into it straight through the stomach. This results in the osmotic retention of large volumes of fluid in the gut with a consequent fall in blood volume, usually greater than 10%.

Symptoms are produced by distension of the small bowel and may occur even if the blood volume is maintained at normal levels by rapid transfusion. The humoral role of serotonin has been postulated but its aetiological significance is not proved.

These symptoms tend to occur in patients who can be shown preoperatively to have a predilection to dumping. These same patients have a more than average incidence of allergic diseases such as hay-fever or asthma. They are also said to have a less than normal mental and emotional stability.

Certain additional observations about these patients help us to keep this problem in perspective. Patients with dumping often develop these symptoms after several symptom-free years. The symptoms are not always constant and they may have weeks or even months of freedom at a time. Dumping is rarely seen in a patient who is otherwise fit and mentally stable.

It will be seen from these observations that any purely mechanistic theory of aetiology cannot be the whole explanation, and a purely mechanistic approach is unlikely to succeed.

Special investigations in these patients are of little practical value in determining the type of treatment and should be employed only if their purpose is to advance knowledge. There is no practical value in determining whether a patient has hyper- or hypoglycaemia during an attack, nor what type of glucose tolerance curve they have, nor yet whether the barium meal empties rapidly from the stomach. Exactly comparable results to these tests would be obtained from many asymptomatic postgastrectomy patients.

Treatment is, once more, empirical on a progressive scale, the first treatment for the least severe and earliest cases.

Reassurance.—Most patients who, soon after operation, experience faintness after meals require nothing more than an explanation and reassurance. They may be reassured that their symptoms are likely to become less and will probably disappear in the coming months.

Correction of Deficiencies.—It is essential in the management of any postgastrectomy problem to consider the possible role of mineral and vitamin deficiencies. Iron deficiency is the commonest abnormality found after gastrectomy and may predispose to "dumping" symptoms. Vitamin B₁₂ and folic acid deficiencies should also be sought and corrected.

Diet.—In addition to reassurance and iron therapy, simple dietary measures may be advised. These are sufficient to control most mild symptoms. Rather than eating, as many do, one main meal each day, the patient should be advised to take three small meals, and, unless obesity is a problem, to take a small snack between each meal. Large carbohydrate meals should be avoided and the caloric intake should be made up with proteins and fats. Restriction of fluid intake at mealtimes also helps to delay emptying of the gastric remnant and relieves symptoms.

Advice to lie down or rest after a meal may be useful in the immediate postoperative period, but is impracticable once the patient returns to work.

Drug Therapy.—The appreciation of the aetiological role of impaired intestinal handling of glucose and the observation⁴ that in patients with "dumping" insulin given before meals prevents symptoms have led to a most significant new therapeutic approach with oral hypoglycaemic drugs. Tolbutamide 500 mg. before each main meal will often control symptoms, and should be a first line of treatment in the patient with severe symptoms. Some success has been claimed with anti-serotonin drugs, and Sullivan⁵ advocated 4 mg. of cyproheptadine before meals in addition to or instead of tolbutamide.

Operative Treatment.—The principle behind attempted surgical treatment of patients with "dumping" is the attempt to delay the rate of emptying of the gastric remnant by narrowing the stoma, rerouting the food through the duodenum (by conversion to gastroduodenostomy), or the creation of an

artificial "sphincter" by placing a reversed jejunal loop between stomach and duodenum. There is, however, rarely if ever any need to operate on patients with "dumping."

Conclusions

The patient who complains of pain, nausea, vomiting, weight loss, diarrhoea, or faintness after partial gastrectomy presents a problem that is rarely easy to evaluate. All symptoms tend to be buried beneath a mound of ineffective antacids.

The essential principle of the approach to the problem is to take a careful history from the patient with no preconceived ideas or with no empty mental pigeonholes labelled "——— syndrome" waiting to receive the problem as soon as the patient admits to the first classical symptom. Then evaluate the symptoms, looking for objective evidence of organic disease. The symptoms of pain and vomiting always require a comprehensive series of investigations, whereas loss of weight, diarrhoea, or faintness are best managed initially by simple empirical methods.

In some patients with recurrent dyspepsia after gastrectomy no definite diagnosis will be made or no permanent cure found. Some of these will be psychologically unstable and others will appear to become so as their symptoms remain undiagnosed and unrelieved. This residual group of unhappy complaining patients taxes the sympathy and resources of anyone who has to deal with many postgastrectomy patients. From several years' experience of reviewing many and reoperating on some of these unfortunate patients, I believe that they frequently need sympathy and continued interest but only rarely benefit from reoperation.

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Corticosteroids in Pregnancy

Q.—What are the particular hazards in pregnancy and childbirth in primiparae who have been taking corticosteroids continuously for some years for intractable asthma? What may be done to minimize the hazards, and should the baby be given corticosteroids after birth?

A.—The dangers of long-term corticosteroid therapy are due mainly to adrenal suppression, but since pregnancy itself stimulates the adrenals to double the normal secretion of cortisol this effect is minimized.¹ There is usually no need to increase the dose of steroid during pregnancy, but the possibility of steroid deficiency arising during any acute illness remains.

Labour is regarded as any major surgical operation would be, and hydrocortisone is given parenterally throughout this period of stress. Postpartum haemorrhage may produce a more dramatic collapse than in the normal patient, and must be treated with intravenous hydrocortisone as well as blood volume replacement.

Though corticosteroids do cross the placenta, they do not usually produce any noticeable effect on the baby. There is no

reason to give steroids to the baby unless signs of deficiency are manifest.

Patients receiving corticosteroids should be confined in hospital.

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Animal Hosts to Rabies

Q.—Do lemurs contract rabies, and are there any other of the rarer infections which they may convey to humans by biting?

A.—The host specificity of rabies virus is low and the range of susceptible species includes man, domesticated mammals, and many wild ones, including foxes, wolves, mongoose, skunks, rodents, and certain kinds of bat. Monkeys can be infected experimentally, and the first natural case was recently recorded¹ in a rhesus monkey (*Macaca mulatta*) which had been imported into Britain from India. Lemurs are primitive primates of the suborder Prosimii. Though I know of no report of rabies in these animals, the possibility cannot be ruled out in view of the wide host-range of the virus, and it should not be ignored because

of the extreme danger attending the bite of an infected animal.

Monkeys may also, while showing trivial or no mouth lesions, harbour herpes B virus (*Herpesvirus simiae*), which, if transmitted to man, causes a serious and usually fatal condition. B-virus infection has been detected in many Old World monkeys,² and, though lemurs have not been examined, the risk of infection should be considered after any bite inflicted by these animals.

Local sepsis or septicaemia resulting from infection by mouth flora are also possible, and it might be remembered that pulmonary tuberculosis, with the production of infective sputum, can occur in captive primates. Extreme caution should be the watchword where primates are being kept. Every effort should be made to avoid contact with the animals or material derived from them, in particular from the mouth, and bites should be regarded most seriously as matters for immediate and thorough surgical attention.

During 1966 only one licence was issued, under the Animals (Restriction of Importation) Act, 1964, for the importation of a lemur—a *Lemur catti* from a French zoo. On the other hand, licences covering more than 20,000 Old World monkeys, required mainly for scientific purposes, were granted.³

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Book Reviews

Mental Retardation

The Pathology of Mental Retardation. By L. Crome, M.C., M.R.C.P.(Ed.), M.C.(Path.), and J. Stern, Ph.D. (Pp. 406+viii; illustrated. 84s.) London: J. & A. Churchill. 1967.

In this book a vast amount of information is presented about the pathology of mental retardation and the subject is interpreted in the widest possible sense. The opening chapter is on the genetic causes of mental retardation, paying particular attention to the anomalies of sex chromosomes and including a brief account of the classification of human chromosomes, several karyograms, and the structure of the D.N.A. molecule. A chapter on disorders of gestation follows in which numerous factors are briefly reviewed, ranging from the teratogenic viruses to emotional stress, seasonal fluctuations, and geographical distribution. Here some disappointment may arise, for, although an enormous range of information is given, a brief mention only is made of congenital toxoplasmosis and no detailed account of the pathology of the central nervous system in this infection appears anywhere in the book. In the section on intrauterine infections there is an account of the different abnormalities which occur with maternal rubella and a commentary on advice given to pregnant women contracting rubella. In a brief mention of Coxsackie B virus infection, although a photomicrograph of encephalitis and myocarditis is produced,

no account is given of the pathology of Coxsackie encephalitis in infancy. The part played by birth injury is reviewed and so are the post-natal causes of mental retardation.

The morbid anatomy of mental retardation is detailed in two lengthy sections. In the first the lesions found in the brain in the non-classified forms of mental retardation (the great majority) are described. The descriptions and illustrations of such conditions as micrencephaly, the disorders of cellular migration, gliotic encephalopathy, and cerebral calcification are excellent and the chapter is made more valuable by the figures of the frequency of the occurrence of such lesions in Dr. Crome's personal cases. A short chapter on the non-specific biochemical abnormalities in the body fluids follows and then an account of the specifically recognizable syndromes associated with mental retardation such as Down's disease, the various forms of hydrocephalus, tuberous sclerosis, and the metabolic diseases. The last subject occupies most of the second part of the book and begins with a comprehensive table of the conditions in which mental retardation and metabolic disorder are associated. This summarizes 47 syndromes,

giving their main clinical features, the specific defect where this is known, the main abnormal substances present in the urine or blood or tissues, the mode of transmission, and the key references in the literature. This is followed by an account of the morbid anatomy and chemistry of these disorders. Finally a series of appendices is given. These include a screening procedure and the details of biochemical and histological techniques used in investigating mental retardation and data in table form ranging from organ weights in infancy to the lipid content of unfixed cerebral tissue. Illustrations are well produced and relevant, and the references numerous, of wide range, and admirably recent.

To the pathologist or clinician involved in the care or investigation of cases of mental retardation this book will be invaluable. Few recently published texts will give so much information for the money. The subject is difficult and complicated and it is hoped that the rapid advances of knowledge in the field and the demand for the book will justify further editions. Perhaps the authors would then consider reducing the scope of some of the earlier chapters particularly in which brief reference to so many topics is distracting and may discourage some readers from further careful perusal of a pioneering volume of great value and merit.

B. E. TOMLINSON.

Ancillary Staff in the U.S.A.

A Textbook for Medical Assistants. By M. Murray Lawton, M.D., and Donald F. Foy, B.S., M.S. (Pp. 465+xii; illustrated. 66s.) London: Henry Kimpton. 1967.

This book is by Americans for Americans, but is surprisingly applicable to general practice in the N.H.S. in England. Specialization in the United States is increasing and the general practitioner is a rapidly disappearing phenomenon. This, the authors believe, is unfortunate, and the general public as well as the medical profession are concerned about the drift away from general practice. The American Medical Association is at present studying proposals to elevate general practice to the status of other specialties and make it more attractive to young physicians. The passage of the Medicare Bill will accentuate the need for general practitioners as old people realize the extent of their coverage under the Medicare programme and fill doctors' surgeries with hitherto untreated complaints.

This is precisely the situation which British doctors have faced since 1948, recently accentuated by greater demands by more patients on fewer doctors. The solution to the dilemma lies in better organization of general practice, which implies increasing use of ancillary workers, whom the authors more aptly term medical assistants. These are

people trained to assist the doctor by relieving him of routine responsibilities of running his practice—a combination of secretary, receptionist, nurse, and laboratory assistant doing everything from testing urine to clearing up after patients who have vomited. Fewer than one in every three general practitioners in this country employ even a full-time receptionist, let alone a nurse, despite repayment of 70% of their salaries, and this is partly because doctors are uncertain about what to delegate to them or how to train them. Drs. Lawton and Foy provide information in this book on every conceivable aspect of paramedical work. It includes chapters on the development of scientific medicine, medical ethics and jurisprudence, the correct use of English, and common medical terminology. Its clinical chapters give detailed instructions about blood-pressure readings, routine urinalysis, hypodermic and intravenous injection techniques, and haemoglobin estimations, all illustrated by charts, diagrams, and photographs admirably designed for intelligent lay people.

With the fee-paying American patient in mind the book devotes space to the décor of the waiting-room, flower arrangements, the personal appearance of the staff (so-called beehive hairdos should be avoided), and even the selection of magazines for the waiting-room (biased religious and political publications have no place there), but most of what it says makes sense in the English surgery. It is particularly good on the appointments

system (recent surveys have shown that American patients leave their doctors not because of high fees or failure to cure but rather because of the length of time they are kept waiting) and its advice on first aid in every emergency from simple fainting to acute poisoning is sound.

The day of the single-handed, horse-and-buggy doctor with the battered black bag is over, but his successor has not yet learned how to use non-medical assistants. This is a textbook for him and them.

ANDREW SMITH.

Treating Arterial Disease

Peripheral Arterial Disease. Major Problems in Clinical Surgery. Vol. 4. By Wiley F. Barker, M.D. (Pp. 229+xiv; illustrated. £2 19s. 6d.) Philadelphia and London: W. B. Saunders. 1966.

This short book on peripheral vascular disease has been limited to the problems of arteriosclerosis. Since this forms far away the largest group of vascular disorders this orientation is very proper and the whole emphasis of the book is towards surgeons who will be dealing with these problems. It starts with a rather long chapter on the anatomy of arterial supply, all of which should surely be well known to those likely to use this

book. Then follows an excellent chapter on the physiology and applied physiology of arterial flow. The pathology of atherosclerosis is dealt with clearly, though a future edition might well allow a little larger cover of the aetiological and metabolic background to this disease.

Most of the book is devoted to the clinical examination, investigation, management, and results of treating peripheral arterial disease. It is outstandingly good and packs an enormous amount of useful practical information into a short space. Thus in clinical assessment the much poorer prognosis where tissue necrosis is present is emphasized. The scope of conservative measures and the role of sympathectomy are discussed. The confused position with regard to anticoagulants is clearly stated. When it comes to the technical considerations of direct arterial surgery the book is full of sound advice and any experienced surgeon will recognize the many home truths discussed. The ground covered is far wider than actual operative technique, and an enormous number of small but important side-effects such as hypotension after declamping an artery receive careful consideration.

The book ends, very properly, with a detailed analysis of the results of surgery, which reflects the honesty so apparent throughout the book. This little book will be outstandingly useful to anyone groping with the problems involved in treating peripheral arterial disease.

W. T. IRVINE.

Learning about Viruses

Basic Medical Virology. Edited by James E. Prier, Ph.D. (Pp. 715+ix; illustrated. £5 16s.) Edinburgh and London: E. & S. Livingstone. 1967.

There have been a number of textbooks on medical virology in the last few years, and, although this is a rapidly changing field, it becomes increasingly difficult to justify each new one. The editor of this one is patently aware that it is no longer possible to include all facets of virology in a single textbook, so this book is directed to the preclinical student. In addition to medical and veterinary students, however, there is much to be found to interest the graduate who selects virology as a special subject.

With Dr. Prier teaching in the department of microbiology in Philadelphia, it is perhaps understandable that no fewer than 11 of the 25 contributors are from the medical schools of Philadelphia and all but three contributors come from America. Each has been chosen for his specialist knowledge of the particular subject, and, since their only brief was to provide information for the student, there is a lack of uniformity in the presentation of the chapters. Classifying the viruses so that the chapters may be presented in some logical order is very difficult, but this problem has been solved by discussing them in groups formulated according to physical, chemical, and biological characteristics. There are exceptions to this rule, however, and viruses inadequately classified or those causing diseases of particular biological or economic significance are dealt with individually.

The basic sciences for the understanding of virus activity are well presented. The chapter on physical and chemical properties of viruses is easy to read. Although the presentation of the laboratory techniques for the cultivation of viruses is always very difficult, the student will certainly be better informed after reading this chapter. The pathology of viral infections, and especially the host-parasite relationship, are well explained, and the chapter on immunity deals with every aspect, citing nearly 300 references. The chapters dealing with particular groups of viruses are packed with data and references, and the only criticism to be made is that some tend to be short sentences joining together an oversized bibliography that is neither interesting nor easy to read. It is a pleasure to see the difficult subject of oncogenic viruses so well presented, since this will have particular interest for the student of virology today.

The diseases dealt with individually are rabies, rubella, infectious and serum hepatitis, lymphocytic choriomeningitis, hog cholera, and bovine virus diarrhoea. Although the selection of some diseases that have had separate treatment is obvious, the choice of others can only be on the grounds of inadequate classification. The last five chapters, dealing with all viruses of particular interest to an animal species, are most useful. Thus ovine, avian, feline, and canine, bovine, equine, and porcine viruses, as well as virus diseases of fish, are presented separately.

In a book of this kind there is bound to be some overlap of subject matter and differences in presentation. Nevertheless, the book is an up-to-date collection of facts and it

has a good index. The preclinical student of medicine will find it a very useful reference book, but it certainly goes beyond his needs in subject matter and price. Many research workers will wish to use it for reference purposes, and thus it should find a place in all good libraries.

FRANK T. PERKINS.

Anarchy

The Clerkenwell Riot. The Killing of Constable Culley. By Gavin Thurston. (Pp. 188+xv; illustrated. 28s.) London: George Allen & Unwin. 1967.

In an age when anarchistic forces of various kinds are working with considerable success in civilized societies it is of some interest to read a detailed account of the sort of situation that these forces ultimately produce.

In 1833 a policeman was murdered and some of his colleagues injured in a clash at a low-grade political meeting at Cold Bath Fields, off Grays Inn Road, London. At the coroner's inquest on the dead policeman the jurors made themselves national heroes by taking command of the inquiry, harrying police witnesses, and encouraging witnesses willing to recount tales of police brutality. Following their verdict of justifiable homicide the jury were feted and medals struck for them. Their popularity was, if anything, increased by the quashing of their verdict by the Court of King's Bench.

Throughout the account of this *cause célèbre* the frightening theme is the almost complete absence of any popular support for the forces of law and order, save from the remarkable men who were concerned with developing the new police force.

On another level, Dr. Thurston shows what an appalling spectacle can develop when a judicial inquiry gets out of hand. The weakness of the presiding coroner was itself an enemy of law and order. By his failure to control the pigheaded tradesmen defying authority in the limelight of the jury box more harm was done than by the forbidden meeting of workmen which sparked off all the fuss.

Dr. Thurston tells a gripping as well as a well-documented tale of an incident insignificant in itself in history, but interesting and important as a symptom of the *malaise* of a nation.

PETER BOWSHER.

Books Received

Review is not precluded by notice here of books recently received.

Baroreceptors and Hypertension. Proceedings of an International Symposium. Edited by P. Kezdi. (Pp. 460+xiv; illustrated. £5 5s.) Oxford: Pergamon. 1967.

Colostomy Care. By Betty Hughes and Edward Wilson. (Pp. 70; illustrated. \$A2.00.) Sydney, N.S.W.: Australasian Medical Publishing Co. 1967.

Emotional Stress. Proceedings of an International Symposium. Edited by Lennart Levi. (Pp. 280; illustrated. 99s.) London: Academic Press. 1967.

Medicine at the Paris Hospital. 1794-1848. By Erwin H. Ackerknecht, M.D. (Pp. 242+xiv; illustrated. 72s.) Baltimore: Johns Hopkins Press. London: Oxford University Press. 1967.

Signification du Tissu Lymphoïde des Muqueuses Digestives. By Paul Crabbé. (Pp. 248; illustrated. (No price given.) Brussels: Editions Arscia. 1967.

The Everyday Miracle. A Child is Born. By Axel Ingelman-Sundberg and Claes Wirsen. Photographs by Lennart Nilsson. (Pp. 156; illustrated. 42s.) London: Allen Lane The Penguin Press. 1967.

Circulation in the Extremities. By David I. Abramson, M.D. (Pp. 557+xvi; illustrated. £9.) New York and London: Academic Press. 1967.

Psychopharmacological Agents. Vol. 2. Edited by Maxwell Gordon. (Pp. 622+xviii; illustrated. £10.) New York and London: Academic Press. 1967.

Basic Anatomy. 2nd edition. By G. A. G. Mitchell and E. L. Patterson. (Pp. 623+viii; illustrated. £5 5s.) Edinburgh and London: E. & S. Livingstone. 1967.

Treatment of Common Acute Poisonings. By Henry Matthew, M.D., F.R.C.P.Ed., and Alexander A. H. Lawson, M.B., Ch.B., M.R.C.P.Ed. (Pp. 151+vii; illustrated. 16s.) Edinburgh and London: E. & S. Livingstone. 1967.

Men in Middle Life. Cross-Cultural Studies in Mental Health. By Kenneth Soddy with Mary C. Kidson. (Pp. 485+xii, 63s.) London: Tavistock. 1967.

Clinicopathological Conference

A Case of Cushing's Syndrome with Misleading Urinary Steroids

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL

Clinical History

Dr. C. L. COPE: The patient (Case No. 297379; P.M. No. 11154) we are considering today was a housewife aged 45 at the time of her death.

She was well until 1950, when she developed diabetes mellitus with thirst, polyuria, and loss of weight starting three months after the birth of her only child. She was started on insulin therapy at this time. In 1956 she was found to be hypertensive and in 1958 she was admitted to hospital because of tiredness. Her blood pressure was then 180/110 mm. Hg and at subsequent outpatient attendances the diastolic pressure varied between 120 and 150. By 1960 she was feeling more tired. She now had dyspnoea on exertion and intermittent swelling of her ankles. She had attacks of orthopnoea and she herself noted rounding and redness of her face, with growth of hair on both face and chin. She had also noticed that her abdomen had got larger but that her extremities were thinner. Her menses were regular. She reported easy bruising of her skin. Her diabetes was stabilized on a 1,800 calorie diet with 48 units soluble insulin and 24 units P.Z.I. each morning.

In 1961 she was admitted to a teaching hospital, where typical Cushingoid skin, facies, hirsuties, buffalo hump, and easy bruising were all noted. At that time she also had oedema of ankles and sacrum. Her blood pressure was 150/120 mm. Hg and there were bilateral basal crepitations in the chest. There was marked muscle weakness and muscle wasting. The clinical conclusion was "this should be Cushing's syndrome."

Accordingly, tests to confirm the clinical diagnosis were done. But the levels of urinary oxogenic steroids were 8.3 and 16 mg. and those of 17-oxogenic steroids were only 12.3 and 15 mg., analyses being done in two separate laboratories. A presacral air insufflation was not sufficiently clear for a useful opinion of adrenal size to be given, and the response to four days of corticotrophin was reported as being in the normal range, the level of 17-oxogenic steroids rising to 70 mg. on the fourth day.

She was discharged free of oedema on a regimen which included insulin, digitalis, guanethidine, reserpine, chlorothiazide, and potassium chloride. The diagnosis made was diabetes mellitus with essential hypertension.

By 1962-3 she had become irritable and restless and her memory was poor. Her menses were scanty and her exercise tolerance had become smaller still. By March 1964 her amenorrhoea was complete.

In October 1964 she was admitted to hospital elsewhere because of three to four months of attacks of nocturnal dyspnoea. She now had what was described as a typical Cushingoid appearance, though without striae. There was congestive cardiac failure and she had attacks of acute pulmonary oedema in which the blood pressure rose to 240/140 mm. Hg. The fundi showed pin-point haemorrhages but

no exudates or papilloedema. There was glycosuria but no albuminuria or ketonuria. The haemoglobin was 14.4 g./100 ml., with a W.B.C. 14,200, of which polymorphs were 89% and eosinophils 1%. The blood urea was 49 mg./100 ml. The urinary 17-oxosteroids were reported as 32 mg. but 17-oxogenic steroids as only 4.7 mg. She was treated with digoxin, mersalvi, cyclopentiazide, and methyl dopa, but made relatively little improvement.

Final Admission

She was transferred to Hammersmith Hospital on 10 December 1964. By now she had ceased to have attacks of pulmonary oedema, but her pulse was 140 and regular. The blood pressure was 150/114 mm. Hg and the jugular venous pressure was +1 cm.

There was now a heavy albuminuria and the blood urea was 60 mg./100 ml. The plasma sodium was 13, potassium 3.3, bicarbonate 34, and the chloride 88 mEq/l. The blood sugar varied between 200 and 320 mg./100 ml. The urinary calcium loss was 220 mg. daily.

X-ray studies showed an enlarged heart with several healed rib fractures in thin bones. The spine showed no evidence of vertebral collapse. The skull was thought to show osteoporosis; the sella turcica was not enlarged but did show asymmetry of its floor.

There was calcinosis in the pulp of several fingers and the thumbs. There was also extensive destruction of the articular surface of the distal interphalangeal joint of the right index finger.

Steroid studies left no doubt of the existence of a severe degree of Cushing's syndrome. The 17-oxosteroids were normal, as is commonly found (11.7 and 12.7 mg.), but the 17-oxogenic steroids were raised at 23 and 34 mg. The levels of plasma 11-hydroxycorticoids (cortisol) were 30.5 μ g. at 9 a.m. and 28.5 μ g. at midnight, a very high figure. The urine level of 11-hydroxycorticoids was 1,600 μ g. daily and the urine true cortisol was 580 μ g. a day, both values being about three times the upper limit of normal. The plasma levels of 11-O.H.C.S. after five days of suppression with 8 mg. of dexamethasone daily were not reduced, the morning value being 37 μ g. and the midnight 24 μ g. Suppression was therefore not observed. But the adrenals were shown to be corticotrophin dependent by a rise of 17-oxogenic steroid excretion to 93 and 118 mg. after metyrapone in a dose of 4.5 g. daily.

Management

Her glycosuria was fairly well controlled by soluble insulin and P.Z.I., but because of her borderline left ventricular failure she was not considered fit for major surgery or even for air

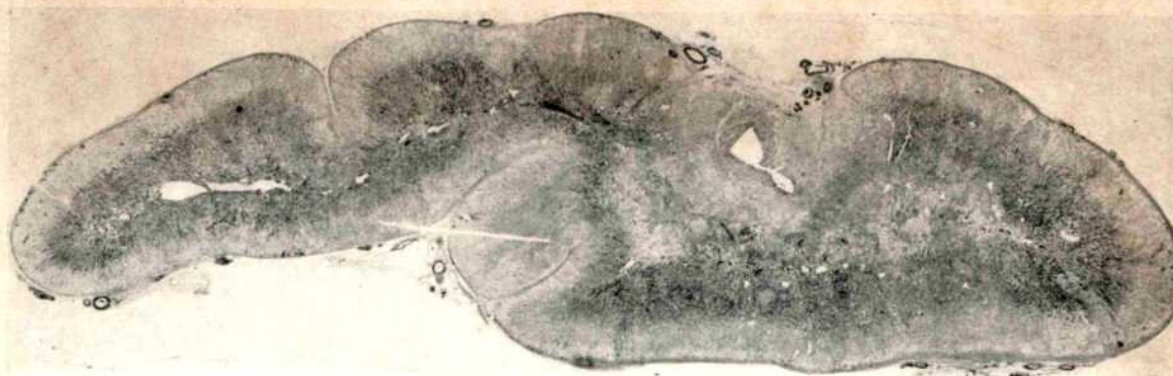


FIG. 1.—Hyperplastic adrenal cortex. (H. and E. $\times 5.4$.)

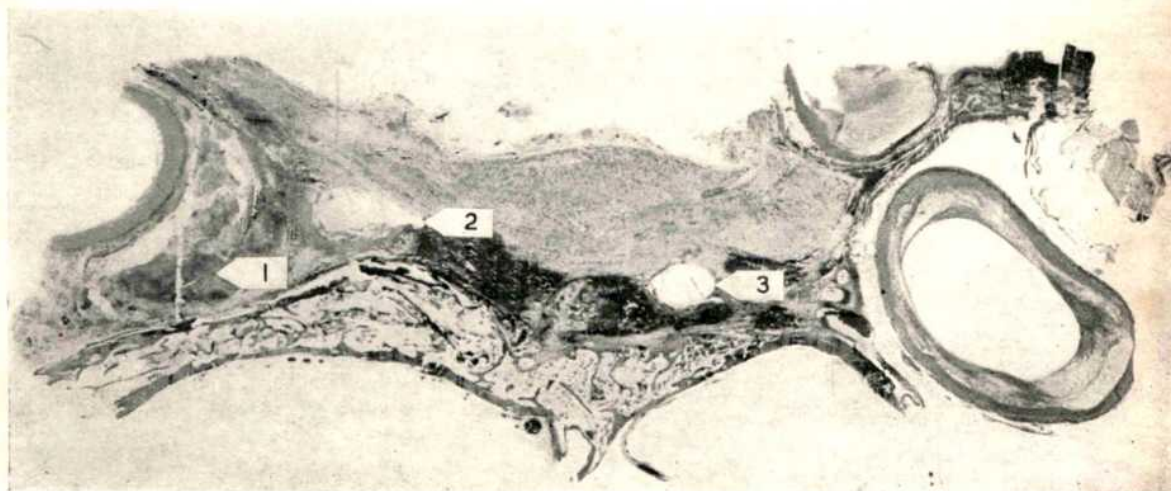


FIG. 2.—Coronal section of pituitary fossa. (Picro-Mallory. $\times 7$.) The carotid arteries are present at either side, the dark central mass is haemorrhagic and necrotic tissue. The holes (2 and 3) are the site of the yttrium seeds. The tumour (1) partly surrounds the right internal carotid artery.



FIG. 3.—Coronal section of pituitary fossa. (Picro-Mallory. $\times 60$.) The bony floor of the fossa is being eroded by an invasive pituitary tumour.

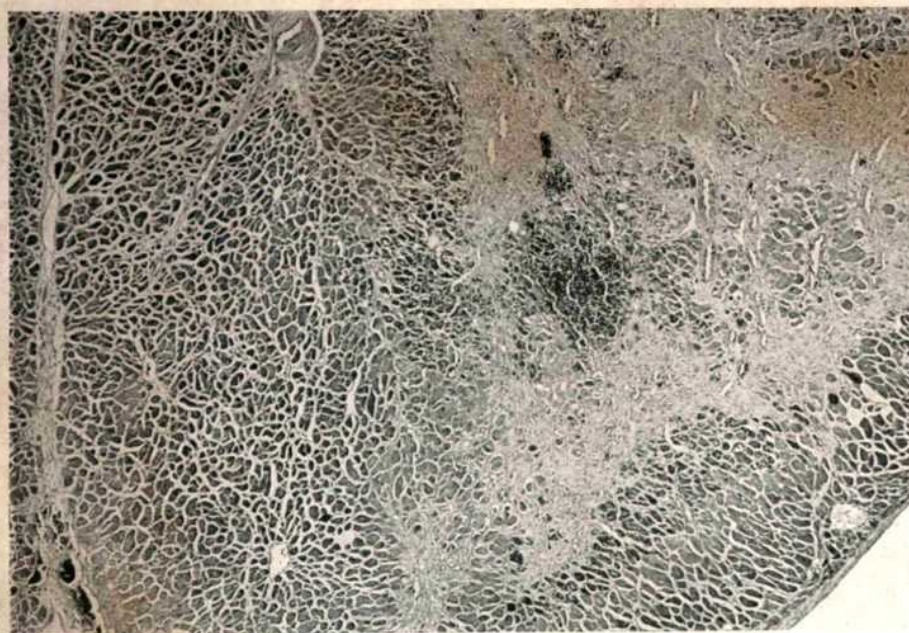


FIG. 4.—Focus of fibrosis in one papillary muscle. (H. and E. $\times 45$.)

FIG. 5.—Small artery, from myocardium adjacent to Fig. 4, showing a lumen almost completely obliterated by atherosclerosis. (H. and E. $\times 70$.)

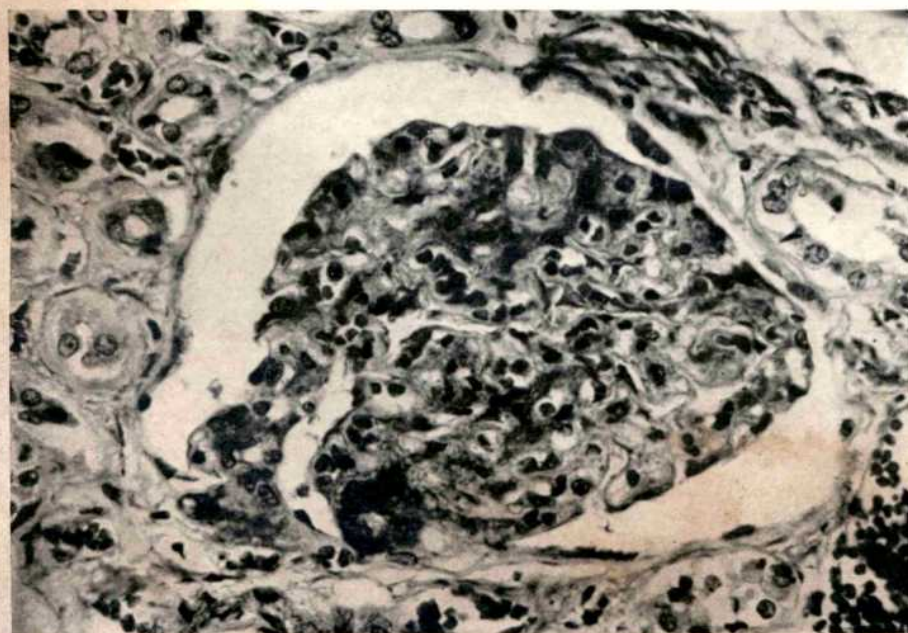


FIG. 6.—Renal glomerulus showing hyaline change in the afferent arteriole at the base of the tuft, and some diffuse stromal thickening. (Marsius Scarlet Blue. $\times 450$.)

insufflation. On 22 January a pituitary implant of yttrium-90 was inserted by Dr. M. Hartog.

On 25 January the plasma level of potassium was 2.5 mEq/l., although she was receiving 3 g. of potassium chloride four-hourly. The sodium was 141, bicarbonate 39, and chloride 74 mEq/l. The blood urea was 42 mg./100 ml. On 27 January she felt fairly well, her blood pressure was 150/90, but she had attacks of palpitation. The plasma potassium had fallen to 2.1 mEq/l., and intravenous potassium chloride in 5% dextrose was given at 20 mEq per hour until the plasma potassium was raised to normal.

The urinary 17-oxogenic steroids were still raised, figures of 38, 46, and 31 mg. being found.

On 28 January she suddenly collapsed at 7 a.m., an E.C.G. showing ventricular tachycardia. Therapy with procainamide, mephentermine, and cortisol resulted in restoration of sinus rhythm, but a tendency to ventricular ectopic beats persisted. She was soon restored to full consciousness and was well enough to start breakfast. At 9.30 a.m. she had a further sudden collapse, this time due to asystole. The electrical defibrillator was of no avail and she died.

Clinical Diagnoses

- (1) Left ventricular failure.
- (2) Hypertensive heart disease.
- (3) Cushing's syndrome, due to hyperplasia.
- (4) Diabetes mellitus.
- (5) Suspect Kimmelstiel-Wilson kidney.
- (6) Yttrium implant.

Post-mortem Findings

Dr. E. D. WILLIAMS: On examination this woman was rather short and showed the features of Cushing's syndrome described in the clinical presentation.

Both *adrenals* were enlarged (10 and 11 g.) with diffusely hyperplastic cortices (Fig. 1), in which microscopical study showed compact cells extending out to the zona glomerulosa. The *pituitary* was removed with the surrounding bone (Fig. 2), and sectioned after the centrally placed yttrium rods had been removed. The tissue around the rods was necrotic and haemorrhagic. On the left side the peripheral part of the anterior pituitary survived, though it was somewhat haemorrhagic. In this area numerous hyaline basophils (Crooke cells) could be identified. On the right side there was a tumour (Fig. 3), about 6 mm. in diameter, in the lateral part of the lobe, extending laterally into the cavernous sinus, with a tongue of tumour spreading above and below the carotid artery. Microscopically the tumour was a chromophobe adenoma, with a few cells containing basophil granules. Scattered cells in the tumour showed hyaline pale blue cytoplasm with the Crooke-Russell technique. The floor of the pituitary fossa showed only a single small area of invasion by the tumour. The dorsum sellae was intact, and there was no meningitis.

The *parathyroids* were slightly enlarged but showed the normal ratio of glandular cells to fat. The *thyroid* was normal. The *pancreatic islets* were enlarged but did not show any hyaline degeneration. The pancreas otherwise was very autolysed but did show very prominent centroacinar cells. Numerous hyaline arterioles were present.

The *heart* was moderately enlarged (480 g.), with marked left ventricular hypertrophy (2 cm. thickness). The valves were essentially normal. On microscopy there were small scattered areas of fibrosis throughout the myocardium, and a single small old infarct about 3 mm. in diameter in the left posterior papillary muscle (Fig. 4). This showed central scar-

ring, while some adjacent muscle bundles showed nuclear and cytoplasmic changes suggestive of recent extension of the old infarct. A small artery (Fig. 5) adjacent to this was virtually occluded by atheroma. The main coronary arteries showed non-occlusive atheromatous plaques. The aorta showed moderate atherosclerosis with calcification and ulceration in the lower abdominal aorta.

The *lungs* were oedematous but otherwise normal. On section a single asbestos body was an unexpected chance finding. In the alimentary tract the stomach showed recent mucosal haemorrhage; the large and small intestines were normal. The *liver* (1,775 g.) showed a large yellow clearly demarcated subcapsular area, a localized area of fatty change.

Both *kidneys* were of normal size and macroscopic appearance. Microscopically the glomeruli showed a mild diffuse stromal thickening (Fig. 6) but no nodular lesions of Kimmelstiel-Wilson type. The afferent glomerular arterioles showed a prominent hyaline change and a few proximal convoluted tubules showed coarse vacuolation attributable to hypokalaemia.

Several healed *rib* fractures were present. Sections of the vertebrae showed moderate osteoporosis. In the sections of one interphalangeal joint there was almost complete loss of the joint cartilage, with eburnation of the underlying bone. Considerable new bone formation was present.

In the *eye* sectioned there was hyalinization of some choroid vessels, and one retinal capillary showing aneurysmal dilatation.

Pathological Diagnosis

- (1) Chromophobe adenoma of pituitary.
- (2) Bilateral adrenal cortical hyperplasia.
- (3) Left ventricular hypertrophy with patchy fibrosis and a small infarct of one papillary muscle.
- (4) Mild diffuse diabetic glomerulosclerosis.

Discussion

Dr. COPE: I admit that I left out originally the diagnosis of diabetes mellitus. Whether we should call that part of the Cushing's syndrome or not I do not think we can answer here. We did not know enough about this patient before she came to us in her terminal illness. If successful treatment of the Cushing's syndrome had greatly relieved the diabetes we could have included it in the Cushing's syndrome. I think we might have made a case for her having separate diabetes mellitus, but I think it is largely speculative. She had a heavy albuminuria, and I would have expected that she would have shown some Kimmelstiel-Wilson changes. But the fact that she did not leaves the albuminuria unexplained unless we attribute it to the severe hypertension. To me the main interest of this patient by far is the events that happened in 1961, when an expert clinician and an endocrinologist came to the clinical conclusion that this should be Cushing's syndrome. But too much reliance was placed on laboratory diagnostic tests, which, even at that time, were known to be very fallible. The clinical impression was completely overruled and a final diagnosis of diabetes with independent essential hypertension was made. There is a very good object lesson here, I think. No one should interpret a diagnostic laboratory test to the point of taking action on it unless he knows how valid it is. Surely one of the functions of a clinician these days, an admittedly difficult one, is to seek evidence for the reliability or otherwise of the vast numbers of laboratory tests that are poured out every day. Urinary 17-oxogenic steroid assays are known to be fallible, and a whole series of them seem to have been misleading on this one single patient. In

such circumstances the physician should relinquish his clinical impression with reluctance.

However, there are other points about the case; there are indeed many. We were handicapped in many ways by the fact that she was so ill, and that we therefore did the minimum with her in the way of investigation. She was strongly suspected to have an adrenal hyperplasia, pituitary-dependent. The sella turcica was practically normal in x-ray, but there was asymmetry of the floor of the sella which was compatible with the development of tumour formation.

Dr. J. LAWS: No, I wouldn't agree there. The report said that there was asymmetry of the floor of the fossa and suggested tomography. This confirmed that the fossa was not enlarged.

Dr. COPE: Maybe that was the order of events. You were quite right to suggest that tomography of the floor may be helpful. Unfortunately we have not got those pictures, but one of the things to discuss is the extent to which x-ray tomography can give an indication of the degree of invasion. As I was looking at the films it struck me that she was a candidate for a meningitis in the near future. I have seen that happen before in a patient diagnosed as a diabetic. A pituitary tumour was found eroding into the sphenoidal sinus, producing a meningitis which complicated the whole clinical picture.

Another aspect of interest is the potassium troubles which she had towards the end. They were admittedly terminal, but we were very conscious of them. We were unable to keep her plasma level of potassium up and we didn't know why. It is possible that she had been severely potassium depleted before she came to us. The final circumstances of her cardiac breakdown are also worth discussion: ventricular tachycardia on the one hand—the type unfortunately unspecified—and the final asystole from which she never recovered.

Importance of Clinical Diagnosis

Professor Sir JOHN McMICHAEL: I think, as Dr. Cope has emphasized, this case is full of lessons. The important part of the diagnosis of Cushing's syndrome is really clinical. The laboratory tests, now of course more refined, could be misleading. I would like to get the record straight: it was reported in the other hospital in 1964 that she had no albuminuria. Did she develop it in the later stages?

Dr. COPE: She had it all the time she was with us from 10 December until her death on 28 January.

Professor McMICHAEL: I see. On those grounds—albuminuria in a diabetic—together with the evidence of aneurysms of the retina and hypertension, one must make the diagnosis of Kimmelstiel-Wilson syndrome; but, as has been shown by Dr. Williams, there were no characteristic glomerular lesions, though there was some thickening of the basement membrane.

Dr. WILLIAMS: There was a diffuse stromal lesion in the glomerulus, not truly a basement membrane thickening.

Professor McMICHAEL: So the glomeruli did show something which I presume could have antedated heavier deposition?

Dr. WILLIAMS: Yes, indeed this could have been responsible for the albuminuria. At the time it was detected, however, she was also a hypertensive in heart failure.

Unusual Infarction

Professor McMICHAEL: The other thing that is of great interest to me is that she had evidence of a small infarcted area in the capillary muscles of her heart without gross obstruction of the main coronary arteries on the surface of the heart. Now this is rather exceptional. Generally speaking, the basis of coronary disease is occlusion—and occlusive changes in the visible vessels on the surface. Very seldom do occlusive changes develop in the penetrating branches of the coronary artery. An

infarcted area is usually related to obstruction of the surface vessels. This is the first time I can recollect seeing an infarct due to occlusion of the penetrating branches of the coronary arteries running in towards the papillary muscles. That will no doubt call for comment from Professor Harrison.

Professor C. V. HARRISON: I'm casting my mind back to the various cases I have seen with very small vessels involved. They have all been in cases of polyarteritis nodosa. They have been still visible on the surface of the heart, so that they were not the ones that dip down into the muscle.

Dr. J. P. MOUNSEY: Can I make another point? We are told that the necropsy showed infarction of a papillary muscle. Functional mitral incompetence sometimes accompanies this anatomical lesion. Was there in life at any time a systolic murmur?

Dr. COPE: Not one of any significance. There may have been a slight one, but there was none recorded, and I have never heard one myself.

Professor McMICHAEL: There has to be considerable loss of function to the papillary muscle for that to occur. It may be ruptured or it may be unable to contract, so that the cusps may be blown out to give a systolic leak.

Dr. MOUNSEY: I wanted to know whether what we have been shown was purely of morbid anatomical interest or also of physiological and functional interest.

Dr. WILLIAMS: I should comment that it was only a small infarct, perhaps a third of the area of the papillary muscle in section. I wondered whether in the papillary muscle the blood supply was more tenuous, depending on a single artery rather than several anastomotic branches. This, therefore, may be a special case. I would like to stress that it was a small infarct; there were numerous smaller areas of fibrosis, which one could not dignify with the name of infarct, scattered over all the sections of the left ventricle.

Dr. COPE: If there was only such a very small infarct, why did she have hypertensive heart failure?

Professor McMICHAEL: Hypertension as such can cause overload failure.

Dr. COPE: I don't think that's an adequate explanation.

Professor HARRISON: May I throw a spanner in? We are fooling ourselves by equating the word fibrosis or necrosis and the word infarct. Now, may I refer you to the work of Mitchell and Schwartz,¹ of Oxford, who analysed these small lesions in the myocardium. They found that the big ones were constantly associated with disease of arteries. They found no association between small amounts of fibrosis and arterial disease. Dr. Williams said he is referring to a small point of fibrosis in a papillary muscle. To call this an infarct is, I think, misusing the English language.

Dr. WILLIAMS: It depends where you draw your size difference. I agree that most of the lesions were tiny and irrelevant. This was of the order of, say, two or three mm. across.

Professor HARRISON: Oh, this is in the non-significant group.

Professor McMICHAEL: You showed us an occluded vessel, so that I think that this very small infarct is an exception to the Mitchell rule.

Dr. J. P. SHILLINGFORD: I wonder if I may throw a few spanners, too? I believe that one finds in heart failure secondary to long-standing hypertension small areas of fibrosis throughout the myocardium.

Professor HARRISON: Yes.

Dr. SHILLINGFORD: Therefore it seems that in hypertensive heart failure there is some replacement of muscle fibres by fibrous tissue. Secondly, the heart lesions could possibly have been secondary to an embolus in a small artery.

Dr. WILLIAMS: There were two occluded arteries in separate sections; they may have been the same one. There were quite

a few small plaques of atheroma without significant occlusion in the major vessel. No other small artery, in the sections I have looked at, showed this change. I don't know where on earth this hypothetical embolus is coming from.

Dr. J. G. AZZOPARDI: I think it's fair to point out that ulcerating atheroma of the coronary arteries with peripheral embolization has rarely been described. It has more often been described in the abdominal aorta, where you get it embolizing to the spleen and the kidneys. There was very little atheroma in this case.

Dr. WILLIAMS: Just a few small plaques.

Urinary Steroid Tests

Dr. L. R. I. BAKER: Could I ask Dr. Cope what his experience is of urinary steroid tests in patients who may have defective renal function.

Dr. COPE: One cannot generalize about steroid tests. Most of the ordinary tests, if they are reliable, will remain reliable in the presence of quite a big drop in renal function; down to about 40% of the normal, perhaps. But with some of these tests—and the urinary cortisol is one of the sensitive ones—renal function can fall even further below normal. Even a blood urea raised above 100 mg. can still be compatible with a well-raised cortisol in the urine.

Dr. G. F. JOPLIN: May we take up one or two of the questions which Dr. Cope raised for discussion. I think the first point that he raised was the relationship between the diabetes and the Cushing's disease in this patient. Now we have it recorded here that the diabetes came on in 1950 and she was not hypertensive until 1956. This would be a very unusual order of events in the natural history of the evolution of Cushing's disease. For a start, only a small proportion of Cushing's cases develop diabetes even in the terminal phase of the disease. One would guess, therefore, that the odds are very much that the diabetes was unrelated to the Cushing's disease. There is another point here, which often puts off physicians from making the diagnosis of Cushing's disease, in that in 1960 the menses were recorded as regular. Now this is sometimes advanced as evidence against the diagnosis of Cushing's disease; but in our own series of about 50 patients with Cushing's disease about half of the women continued to menstruate after they'd clearly developed Cushing's disease. So continuation of menstruation by no means precludes the diagnosis.

On the question of the normal basal urinary steroids in the presence of Cushing's disease: in our own series we had three or four patients who had quite obvious Cushing's disease on clinical grounds, yet repeatedly normal urinary oxogenic steroids as recorded in our own laboratory; what showed these patients as being quite abnormal was the resistance to dexamethasone suppression. I would guess that if the dexamethasone suppression tests had been employed it's quite possible that a biochemical diagnosis might have been made.

A most important aspect of this case from the endocrine point of view is the pituitary tumour. Now review of the necropsy x-rays certainly would lead us to raise no questions of pituitary tumour here. This was a very, very normal pituitary fossa radiologically, and yet there was an unequivocal early tumour, which may have been invasive. This is of considerable importance in that it has been alleged that the reasonably high incidence of pituitary tumour following adrenalectomy for Cushing's disease is a consequence of the adrenalectomy. Our own series goes right against that view, in that a fifth of all the Cushing's cases had radiological evidence of pituitary tumours even before any treatment was done. Today's case is a very important bridge case, in that it shows quite clearly that tumour formation can occur in the absence of radiological abnormality. Could I finally ask Dr. Cope a question about the terminal illness? How many milliequivalents per day of potassium was this patient being given after implantation, and was she still getting this potent diuretic combination?

Dr. COPE: No, she was not having diuretics. She was getting potassium quite definitely, 3 g. potassium chloride four-hourly, that's six times a day, 18 g., and it was stepped up intravenously later. I can't help wondering whether the rapid swings in the potassium level didn't have an adverse effect on the myocardium, and I suspect, in fact, that metabolic myocardial trouble was vastly more important than any vascular. But that's an imponderable at the moment.

Dr. SHILLINGFORD: I should have thought that with the size of the area of ischaemia this is correct. Sudden death or sudden asystole, ventricular fibrillation, or ventricular tachycardia seldom occurs in hypertension without other cause. It is frequent in disturbances of potassium and other electrolytes, and with a potassium of 2.1 mEq one would perhaps expect some sort of arrhythmia in this condition, either ventricular tachycardia or ventricular fibrillation; I suspect at the end she developed ventricular fibrillation, then asystole.

Dr. JOPLIN: Was she receiving digitalis then?

Dr. COPE: No, she wasn't.

Dr. O. WRONG: The histological changes of potassium depletion in the kidney are not very common. I know they're regarded as characteristic, but in the majority of cases I've seen with hypokalaemia, who have had biopsies or who have come to necropsy, these changes have not been present. I think these changes indicate that there must have been a very considerable potassium deficit.

Dr. COPE: I think we may well stop at this point.

We are grateful to Professor J. P. Shillingford and Dr. E. D. Williams for assistance in preparing this report, and to Mr. W. Brackenbury for the photomicrographs.

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Middle Articles

COMPUTERS IN MEDICINE

Computer Method for Deriving Hospital Inpatient Morbidity Statistics Based on the Person as the Unit

S. P. WATTS,* B.Sc. ; E. D. ACHESON,† M.A., D.M., F.R.C.P.

Brit. med. J., 1967, 4, 476-477

In a previous paper (Acheson and Barr, 1965) an account was published of the patterns of readmission from home and of transfer between hospitals for patients in the Oxford area. It was shown that within the calendar year 1962 9.5% of the patients discharged from hospital were readmitted and discharged again once or more, 4.9% were transferred once or more between hospitals, and 1.9% were readmitted and transferred.

It was also shown that for certain conditions morbidity rates calculated from discharges rather than from persons discharged were inflated to a considerable degree. The material for 1962 was based on a manual system of record linkage, and the analysis was by business machines. This paper describes a method of calculating inpatient morbidity and fatality rates by means of a computer. Each patient is counted once in any one year regardless of the number of admissions to the same or different hospitals with the same complaint.

Material and Method

The Oxford Record Linkage Study has recorded details of every birth, admission to hospital, and death occurring in the Oxford area since the beginning of 1962. Information about these events is brought together into a series of personal cumulative files. From 1963 onwards a computer system of record linkage has been employed. The basis of the system is a master file written on magnetic tape which contains the cumulative records of the persons.

Each personal file consists of identifying data, together with a record containing statistical information for each of the defined events which the person has experienced. For each new event two cards are punched; the first contains the name, date of birth, N.H.S. number (when available), and other identifying information, and the second contains statistical data. These cards are read into the computer, where they are edited and then written on magnetic tape. The data on this magnetic tape are sorted into a sequence based on soundex code of surname, sex, and initial of first forename. The identifying information on each new record is compared with the corresponding information on all records on the master file, which fall into the same soundex-sex-initial pocket. If a linkage is obtained the new statistical record is added to the person's file; if no linkage is obtained a new personal file is created. The computer used for this operation was an IBM 1401 with 16,000 characters of core store and six magnetic tape-decks.

The linked file for 1963-4 was scanned for all persons who had been discharged from hospital once or more. A new item was formed from the existing record for each episode of inpatient treatment and written on another magnetic tape. The following information was contained in the new item:

Personal identifying number, sex, age, and place of residence.
Diagnosis on discharge (four-digit code from *International Classification of Diseases*).

Month and year of discharge.

Source of admission.

Disposal, including whether living or dead on discharge from hospital.

Hospital.

Duration of stay in hospital.

Markers to denote the birth of a baby (in the case of women) or death in that year anywhere within the area, together with the month of the event.

Information concerning the delivery of a baby and death was abstracted from the relevant records in the cumulative personal file. A distinction between deaths in hospital and elsewhere was maintained.

The data on the magnetic tape were sorted into diagnostic order and by personal number within each diagnosis. From

ISC DIAGNOSIS (PRINCIPAL)		COMPUTER NUMBER	AGE	DEATH IN YEAR	BIRTH IN YEAR
325	Female	001106	96		
		005663	04		
		007842	39	*	
		009520	30		
		010748	67	*	
		010999	62	*	
		013377	11		
		013751	19		
		013778	31		
		014738	18		1
		014914	03		
		015048	28		
		015346	63		
		017459	58		
		017623	15		
		021503	03		
		022208	05		
		023683	31	*	
		023689	27	*	
		024365	61	*	
		024372	36	*	
		024846	25		1
		024847	22		
		024849	43		
		024853	10		
		024857	63		
		024858	18		
326	Male	024859	23		1
		003408	25		
		013692	17		
		020624	57		
	Female	011104	15		
		011881	25		
		014771	51		
		022208	05		

FIG. 1.—Morbidity analysis listing for 1963 in Oxford Record Linkage Study area (excluding Oxford C.B.C.).

* Computer scientist.

† May Reader in Medicine.

The Oxford Record Linkage Study, Nuffield Department of Clinical Medicine, University of Oxford.

this sorted tape two forms of output information were produced: (1) a list, in diagnostic order, giving certain data about each person discharged from hospital with that diagnosis (see Fig.); and (2) a table, in the same sequence, giving numbers of hospital discharges, of persons discharged, and of deaths in hospital from which hospital morbidity and fatality rates were calculated (see Table).

Results

The section of the list dealing with diagnostic rubrics 325 and 326 (mental deficiency and other disorders of character) is shown in the Fig. Separate lists were produced for 1963 and 1964 and for the Oxford county borough and Oxfordshire. In addition to denoting the personal number, diagnosis, age, and sex of each patient, the list indicates the fact of death if this occurred anywhere in the area in that year, whether

will shortly give place to the Hospital Activity Analysis, which entails the collection of abstracts for all spells of treatment (Benjamin, 1965). A conservative estimate of the cost of processing data on the recommended scale for the 4,900,000 episodes of inpatient treatment carried out in England and Wales in 1966 would be £1m.

This paper describes a computer system which eliminates two of the errors inherent in morbidity statistics published by the Hospital In-patient Enquiry—namely, the inflation of morbidity rates and the underestimation of hospital fatality rates. Both these errors stem from a single cause—namely that, as the abstracts are not identifiable, patients admitted more than once for the same condition are counted more than once in the tables. The Hospital Activity Analysis, in the form in which it is at present being implemented, will also be liable to these errors because the only identification data which is

Table of Discharge and Fatality Rates

Principal I.S.C. Code	Diagnosis	No. of Discharges 1963-4	No. of Persons Discharged 1963-4	No. of Deaths in Hospital 1963-4	Uncorrected Discharge Rate per 10 ⁵ per Annum	Corrected Discharge Rate per 10 ⁵ per Annum	Uncorrected Fatality Rate per 10 ³ per Annum	Corrected Fatality Rate per 10 ³ per Annum	Reduction Factor (%)
001-008	Tuberculosis of respiratory system	371	320	19	53.3	46.0	2.6	3.0	13.8
140-148	Cancer of mouth and pharynx	98	75	6	14.1	10.8	3.1	4.0	23.5
150	Cancer of oesophagus	52	37	15	7.5	5.3	14.4	20.3	28.9
151	Cancer of stomach	156	132	57	22.4	19.0	18.3	21.6	15.4
152, 153	Cancer of intestine, except rectum	210	167	41	30.2	24.0	9.8	12.3	20.5
154	Cancer of rectum	187	141	45	26.9	20.3	12.0	16.0	24.6
161	Cancer of larynx	57	30	5	8.2	4.3	4.4	8.3	47.4
162, 163	Cancer of bronchus	496	349	132	71.3	50.2	13.3	18.9	29.6
170	Cancer of breast	357	286	34	102.9	82.4	4.8	5.9	19.9
171	Cancer of cervix uteri	208	102	14	59.9	29.4	3.4	6.9	51.0
172-174	Cancer of other parts of uterus	67	52	7	19.3	15.0	5.2	6.7	22.4
177	Cancer of prostate	116	97	30	33.2	27.8	12.9	15.5	16.4
190, 191	Cancer of skin	106	78	5	15.2	11.2	2.4	3.2	26.4
196, 197	Cancer of bone and connective tissue	42	28	5	6.0	4.0	6.0	8.9	33.3
300-309	Psychoses	1,080	944	120	155.2	135.6	5.6	6.4	12.6
310-324	Psychoneuroses and disorders of personality	1,151	1,050	7	165.4	150.9	0.3	0.3	8.8
325	Mental deficiency	138	126	19	19.8	18.1	6.9	7.5	8.7
608	Stricture of urethra	126	76	0	18.1	10.9	0	0	39.7
722	Rheumatoid arthritis	181	156	5	26.0	22.4	13.8	16.0	13.8

at home or in hospital, by means of an asterisk. Delivery of a baby to females within the year is indicated by the numeral "1." Confidentiality is maintained, since no names appear on the list and the personal number which is listed has no meaning outside the computer system.

The Table shows part of the systematic tabulation which was produced. The columns from left to right give the number of discharges, the number of persons discharged once or more, and the number of deaths in hospital, together with the uncorrected and corrected discharge and fatality rates. The column on the extreme right is the factor (expressed as percentage) by which each uncorrected morbidity rate is inflated and each uncorrected fatality rate reduced on account of readmissions of the same patient for the same condition. The figures for carcinoma of the cervix illustrate an extreme instance of the inaccuracy which may occur when the number of discharges is used as the basis for calculation of morbidity and fatality rates.

Discussion

In spite of their incompleteness, statistics derived from records of spells of inpatient treatment in hospital are likely to continue for many years to be the principal source of morbidity data available on a national scale. The problems of adding data from outpatients and from episodes of domiciliary care to the material are formidable, and routine analysis of these categories of sickness are unlikely to be seen on a national scale in the near future.

It is therefore important to make the best use of the material which is likely to be available in the short term. The Hospital In-Patient Enquiry which was set up after the war (Ministry of Health and General Register Office, 1959 *et seq.*), and which required the collection and analysis of data about every tenth spell of inpatient treatment throughout England and Wales,

scheduled for processing is the filing number of the hospital or department concerned.

A further penalty of failure to include adequate identification data in the part of the abstract which is processed is that it is impossible to collate data of the subsequent fate of patients in other hospitals or elsewhere to the abstract in hand, or to relate the abstract to the previous history. At present, information about the fate of patients after discharge from hospital is defective (Hubbard and Acheson, 1967). In terms of the flow of medical information each hospital or hospital group is thus isolated in the Hospital Activity Analysis from all others and from the other branches of the Health Service (Acheson, 1967).

Summary

A computer method is described whereby hospital inpatient statistics may be derived in which the person rather than the discharge is the unit. The key to such a system is the provision of adequate data about the identity of the person treated. Results are presented which measure for selected conditions the magnitude of the errors introduced by counting, as is the practice in conventional statistics, the same person who is readmitted for the same condition more than once.

The Oxford Record Linkage Study has derived financial support from the Nuffield Foundation, Ministry of Health, and the Nuffield Provincial Hospitals Trust. It also obtains valuable assistance from the General Register Office.

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CONFERENCES AND MEETINGS

Allergology

[FROM A SPECIAL CORRESPONDENT]

The Sixth International Congress of Allergology was held in Montreal from 5 to 10 November, under the presidency of Dr. BRAM ROSE (Montreal).

The first major symposium dealt with the cells which are now regarded as the hall-marks of immune processes. J. F. A. P. MILLER (Melbourne) outlined the evolution of the progenitor stem cell from its origin in bone marrow to its final sophisticated role as an antibody-forming cell in the lymph node, via thymus lymphocyte and the circulating pool of long-living antigen-reactive and antibody-forming cells. It was possible that the simple progenitor cells were passive receptors of information, but it was still conjectural where the transfer of information took place.

G. MACKANESS (Saranac Lake) described how mononuclear phagocytes or macrophages engulfed antigenic material by pinocytosis into its pinocytic vesicles or pinosomes, and then transferred it to lysosomes. These organized packages of enzymes then degraded antigen into its constituent nucleic acids, though the fate of the latter was not clear. Anti-lymphocytic calf serum had been found to stimulate pinocytosis of macrophages and it helped to destroy antigenicity. Irradiation did likewise by causing cell lysis, and thereby the production of nucleic acid derivatives, which were powerful promoters of endocytic activity in macrophages and degradation of antigen and antigenicity. This might explain the immunosuppressive effect of irradiation in delayed-type hypersensitivity reactions and in graft reactions, in which mononuclear phagocytes had such a conspicuous role.

M. LITT (Boston) had studied the effect of inoculating the footpad of the guinea-pig with haemocyanin or chick erythrocytes, which produced eosinophils in the draining lymph nodes within minutes. This reaction was suppressed by cyclophosphamide. He felt that the prime excitant of tissue eosinophilia was an antigen-antibody complex. The eosinophilotactic property of serum, which was responsible for the activity of eosinophils, was due to a gammaglobulin.

Transplantation

Pointing out that homograft rejection followed the intimate admixture of the graft antigen with sensitized lymphocytes, R. BILLINGHAM (Philadelphia) felt that some other pharmacological factor also contributed. This lymph-node plasma factor appeared early and governed migration of macrophages; it was possibly a protein or a nucleic acid.

During the last four years Montreal's McGill University had transplanted cadaver kidneys to 79 patients with renal failure, most of whom were under 45 years old. The preparatory immunosuppressive regimen to overcome homograft rejection included local irradiation, oral corticosteroids, azathioprine, and actinomycin. Complications immediately

after operation comprised rejection, acute tubular necrosis, and vascular upsets. Immediate rejection, seen especially in multiparous women, was related to lymphotoxicity to their husbands' antigens. Other rejection processes in the first two months post-operatively developed more insidiously, with gradual progressive deterioration of renal function. Finally, sequelae attributable to prednisolone included infections, aseptic necrosis of the head of the femur, pancreatitis, and bowel perforation. In his detailed review of this considerable experience J. DOSSETOR (Montreal) pointed out that previous sensitization by haemodialysis was not deleterious to subsequent renal transplantation; in fact the opposite seemed to be the case in practice. The two-year survival rate was 40%; he felt that he could generalize that the patient who was alive at six months would also be alive at two years.

T. STARZL (Denver) emphasized the immunosuppressive value of antilymphocyte serum prepared by the subcutaneous injection of human spleen into horses. The harvested antilymphocyte serum, which was a gammaglobulin, was then inoculated intramuscularly into renal graft recipients, daily at first and then twice weekly. It behaved synergistically with oral corticosteroids and azathioprine, so that the dose of prednisone and azathioprine could be halved. Whereas there had been a survival rate of about 50% before the availability of antilymphocyte globulin, only 1 out of 20 patients had died since its introduction 17 months ago. Moreover, before July 1967 all seven patients who had received liver homotransplants had died. Since then, however, with the help of antilymphocytic globulin, three out of four patients had survived more than two months. Another advance had been the preservation of donor livers for up to 24 hours by the use of hyperbaric oxygen and hypothermia.

Since antilymphocyte globulin was a protein, it was not without its risks, which included serum sickness, anaphylactic reactions, fever, and pain at the site of injection—but so far serum-sickness nephritis had not complicated 2,500 injections in 60 patients.

Sarcoidosis

EDITH MANKIEWICZ (Montreal) reported the frequent isolation of mycobacteria and their phages from the serum and specimens resected from patients with sarcoidosis. Serum antibodies to these mycobacteriophages were readily demonstrated in patients with active tuberculosis but not in sarcoidosis patients. She claimed that the absence of antibody to mycobacteriophage was responsible for the lack of caseation and the inability to find tissue mycobacteria readily.

D. GERAINT JAMES (London) said that the cardinal feature of depression of delayed-type hypersensitivity was presumably due

to immunological bankruptcy of thymus-mediated lymphocytes. Whereas there was hyporeactivity of these antibody-carrying lymphocytes, circulating or serological antibodies were unimpaired. The other characteristic feature of sarcoidosis was the formation of torpid granulomas in all tissues, and also in response to the intradermal inoculation of human spleen sarcoid tissue.

D. G. WRAITH and K. MAUNSELL (London) reported that a mite, *Dermatophagoides*, found in house dust, was an important and widespread cause of respiratory allergy in Britain. High concentrations of the mite were noted in bed mattresses of all types, particularly if they were not regularly brushed and aired, and also in bedroom floor dust, socks, handkerchiefs, and pockets. Intradermal skin tests with mite extracts were positive in dilutions up to 1 in 10,000,000.

A. W. FRANKLAND (London) also drew attention to insect allergens which could be inhaled or injected by stings. Man responded to mosquito bites by the development of delayed-type and immediate-type reactions, both of which disappeared with desensitization. Locusts were strong sensitizers causing asthma, particularly in those who were constitutionally susceptible. He also warned of the dangers of the grain weevil in wheat causing baker's asthma, and of bee stings causing acute anaphylaxis and sudden death—especially in those who had been sensitized by previous stings.

Asthma

A. W. FRANKLAND (London) also reviewed the many factors responsible for asthma. Although asthma was influenced by corticosteroids, allergic asthma was often unimproved during pregnancy. He reiterated the possible danger of cardiac arrhythmias and even sudden death due to the abuse of atomizers containing adrenaline.

The potency of these bronchodilators was emphasized by D. BATES (Montreal), for airways obstruction was reversed and the forced expiratory volume improved within two breaths and was maximal within 20 minutes of using an aerosol. Relief of spasm of the bronchial musculature seemed too naive an explanation for such rapid reversibility. ¹³¹I administered by inhalation and intravenous radioactive xenon were now being applied to the study of respiratory function in asthma, and he paid tribute to important observations made by Dr. Wilcox at Sydney University with these techniques. Ventilation was noted to be poor in the apices and bases of the lungs of asthmatics, whereas the maximal abnormality was only at the lung bases of the chronic bronchitic smoker. Bad zones of ventilation revealed arterial oxygen tensions as low as 50 mm. mercury. Scans showed uneven distribution, and the asthmatic lung adjusted its perfusion to the abnormal ventilation. From measurements of the gradient

between mouth and oesophageal or pleural pressure the overinflated lungs of asthmatics seemed to lose their elasticity temporarily. He also drew attention to the syndrome in which bronchospasm did not coincide with exercise but instead developed when the subject was resting four minutes or so after exercise. He wondered whether metabolic acidosis led to a falling pH, which had a spastic effect on the pulmonary circulation. The post-exercise bronchospasm diminished or disappeared with adrenaline or its analogues.

Systemic Lupus Erythematosus

Using the immunofluorescent technique to demonstrate circulating antinuclear antibodies in systemic lupus erythematosus, J. T. WATSON and his colleagues (Montreal) had defined four patterns of nuclear fluorescent staining—homogeneous, mixed, composite, and peripheral. These patterns had correlated with the level of serum complement and with clinical severity of the disease. The homogeneous pattern was associated with inactive forms of disease; the peripheral pattern with the most

acute forms of disease; and a shift from homogeneous to peripheral pattern heralded an exacerbation of clinical activity and a fall in the serum-complement level. This change from homogeneous to peripheral seemed to occur stepwise, the first change being from homogeneous to mixed pattern, then from mixed to composite, and finally from composite to peripheral. Whereas this indicated a poor prognosis, the reverse sequence occurred with adequate immunosuppression. They felt that changes in pattern of this nature were useful in anticipating clinical exacerbation and in assessing the adequacy of therapy.

J. H. VAUGHAN (Rochester) reported a series of 15 patients in whom the syndrome was provoked by procainamide. Symptoms usually began after the drug had been taken for several months, but had occurred following only a fortnight's administration. Eight months after discontinuing the drug most of the patients were asymptomatic, the gamma-globulin level had fallen to normal, the Coombs test was negative, and antinuclear antibodies had disappeared from the sera of 4 of the 15 patients. This improvement upon withdrawal of the drug was one of the distinguishing features from the idiopathic disease, the others being absence of renal

involvement and normal serum-complement levels.

Cancer

S. O. FREEDMAN (Montreal) had prepared a tumour antigen from carcinoma of the human colon, and, by inoculating it into rabbits, produced a specific antiserum. Similar antigens could be made from embryonic gut, so that they were collectively referred to as carcinoembryonic antigen. A serological survey had shown that the specific circulating antibody was always absent in normal people. It was, however, present in 70% of patients with carcinomas of the alimentary tract, but absent in those with metastases—possibly because circulating antibodies were absorbed by such a large antigenic mass of cancer. Circulating antibody was sufficiently specific that it was absent in patients with tumours other than of the digestive tract, but it was always present in pregnancy because of the presence of foetal material. Another extension of this study was the ability to demonstrate fluorescence in antigen-antibody complexes in human rectal cancer. Thus by this method it should be possible to stain faeces for the presence of tumour antigen.

Television in Medical Education

[FROM A SPECIAL CORRESPONDENT]

The role of television in medical education was discussed by Professor I. R. MERRILL, of the Communications Office for Research and Teaching of the University of California, at a lecture at B.M.A. House on 16 November, with the President of the B.M.A., Mr. R. V. COOKE, in the chair.

Professor MERRILL said that it was an exciting time in the development of medical television, as financial support was now being provided for it. Television was an electronic device capable of providing either entertainment or instruction. In his view this latter role was of great benefit in medicine provided television was used with discrimination. While the process was expensive, and the value of simpler visual aids such as the slide projector should not be forgotten, there were at least five properties of television which enabled it to provide an outstanding service. Firstly, image multiplication allowed the popular lecturer or an intricate surgical operation to be seen by many audiences simultaneously. The second property, of image magnification, was the television camera's ability to present minute detail. Thirdly, image association was often of great advantage in teaching—for example, by using superimposed electrocardiographic records in the same picture as the diseased heart to which they referred. Fourthly, image transportation allowed large numbers of viewers into a sterile operating-theatre or a cramped pathology laboratory. Finally, image memory, in the form of videotape and kine-scope recording, was of obvious value for future reference.

Continuing, Professor Merrill said that he was convinced that the use of television was now established in America. Already half

the existing medical schools used it and all the future ones had plans to incorporate it in their development programmes. The growth of the use of television in San Francisco, in particular, was shown by the increase in the number of presentations—from 60 in 1960 to 585 in 1966. He thought that it was vital that medical schools be given priority for television over other university departments as the money became available. The study of medicine was much concerned with the demonstration of tissues and of practical procedures, which were all particularly well displayed on television. Nevertheless, medical teachers would do well to beware of television's deadly friends. These included the obsessive innovators (though luckily these were now mainly occupied with computers); the unscrupulous salesmen, milking the ready funds with inadequate equipment; and the faculty members who shelved the apparatus after an inadequate trial.

Postgraduate Education

Professor Merrill emphasized that the education of the postgraduate should not be forgotten. Television broadcasts to general practitioners would help them in the continual betterment of their practice, and he cited the work of A.S.M.E. and the B.B.C. and I.T.V. Medical teachers could be greatly helped by the professional television producer, but the former must be clear themselves about the aim of the programmes. Unfortunately, at present there was no useful measure of the effectiveness of television in postgraduate education, and this was not possible until the aims had been accurately defined.

Opening the discussion, with LORD COHEN OF BIRKENHEAD in the chair, Dr. CHARLES FLETCHER spoke of the broadcasts aimed at the general practitioners at home. There was a difficulty in gauging the response owing to the lack of feedback. Programmes could be shown only at "off peak" times for minority viewers. It was known in the early days of the television programmes, which had been limited to the London area, that the viewing doctors numbered 35% of the maximum possible. With expansion of the service it was more difficult to measure this figure, but he thought it was about 10%. Their aim was set at the illumination of the subject rather than at the acquisition of facts, which were much more difficult to put over satisfactorily.

Professor ROGER WARWICK (Guy's Hospital Medical School) spoke of his use of television in the context of image magnification. He considered that colour was called for only in a minority of situations. Replying to a question about whether there were any methods of testing the efficacy of television as a teaching aid, Professor MERRILL said that attempts were being made by examining patients' hospital records and the prescribing patterns in small communities following programmes. To another question, he said that three hours out of every 100 total teaching time was probably the optimum amount, while the upper limit would be five.

One speaker wondered whether the medical broadcasts might be dangerous for the lay public. He had heard of complaints from practitioners about the increase in hypochondria following these programmes. Dr. FLETCHER replied that the B.B.C. had esti-

mated their lay audience at about half a million. They had received only a handful of letters on the subject, and the overall impression from laymen was one of boredom.

Professor MERRILL was asked about the place of cinematography. He thought that there was still a place for both film and television. The former had certain advantages as regards definition, contrast, and colour reproduction, and also if the presentation was to be repeated many times or in places where only cinema projectors were available. On the other hand, television recordings were easier and more rapid to make and were immediately available for editing and show-

ing. This was a further advantage for teachers who wished to improve their lecturing technique. The rehearsal of lectures could lead to greater conciseness and effectiveness.

Another questioner spoke of televised anatomy demonstrations in Dublin in 1956 by Professor A. K. Henry, and pointed out that the ability to show in rapid sequence cadaver, diagrams, and preserved specimens made the use of television particularly effective in this subject. He asked whether the use of colour would be an asset. Professor WARWICK replied that in his experience monochrome was sufficient for 70% of demonstrations. Professor MERRILL added

that in America anatomy demonstrations on closed-circuit television were second in number only to those in pathology. Nevertheless, he felt that colour had the advantage of giving a sense of depth lacking in black-and-white.

Dr. ROGER MEYRICK (London) suggested that general practitioners might benefit more from watching a programme in a discussion group with a leader. Professor MERRILL replied that his work had been essentially with undergraduates, but that it was evident that an experienced teacher was more valuable than a complete range of expensive equipment.

NEW APPLIANCES

High Femoral Osteotomy with New Compression Plate

Mr. L. C. L. GONET, consultant orthopaedic surgeon, Putney Hospital, London S.W.15, writes: High femoral osteotomy is a well-established method in the treatment of osteoarthritis of the hip joint and sometimes for subcapital fractures of the neck of the femur. In the United Kingdom McMurray's osteotomy is commonly used for the abduction or valgus type, while on the Continent the name of Pauwels is associated with the adduction or varus procedure. In recent years compression fixation at the osteotomy site by one or other of these methods has found increasing favour. The two fragments are held more firmly together, thereby diminishing postoperative pain, allowing very early mobilization and weight-bearing, and thus reducing possible postoperative complications.

A compression plate should not only provide adequate compression and fixation between the two fragments, at least until the patient is weight-bearing, but should not be so rigid as to prevent the proper "bedding down" at the osteotomy site—for it is here that union occurs—nor so rigid as to hold the two fragments apart. It should not interfere with the reversal of the osteoarthritic process following osteotomy, but above all it should also be simple to insert with the minimum number of instruments, be cheap to produce, make x-ray control unnecessary, and its application should come within the scope of any surgeon, for only then can it be considered for universal application.

The purpose of this paper is to describe a new type of compression fixation plate which, I believe, not only meets with the above requirements but introduces a new principle in bone fixation. It has been successfully used in 69 cases, the results of which are discussed below.

Description.—The plate (Fig. 1) is a straight spline of one piece consisting of an arrowhead with a cutting edge and a flat

base, a rounded nail portion, and a flat plate with a compression screw at the end, similar to that used in the Danis principle. The plate is made in three sizes to allow for latitude in the site of osteotomy.

Technique.—The osteotomy is performed at or above the lesser trochanter in the usual way, with or without x-ray control, and the lower fragment displaced medially just enough to allow the entrance of the arrow head. The plate on its introducer is then inserted up the medullary cavity of the proximal fragment in an inward and upward direction and at right angles to the shaft and hammered through the cortex of the upper femoral neck in the region of the digital fossa (Fig. 2). The plate on the introducer is then rotated through 90° and pulled down, when it will be felt to lock over the femoral neck and the plate will fit parallel with the shaft of the femur (Fig. 3). A transverse screw is inserted through the femoral shaft at the lowest slot in the plate and the compression screw is then turned clockwise (Fig. 4). Eight to ten full turns are enough to provide a compression force of from 45 to 50 lb.

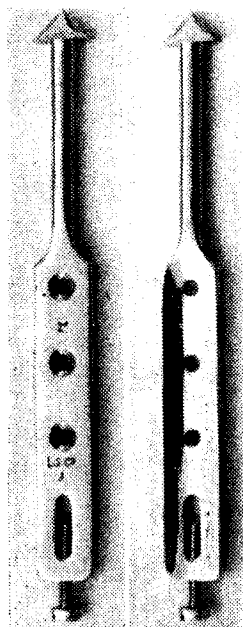


FIG. 1.—Picture of the plate in two views.

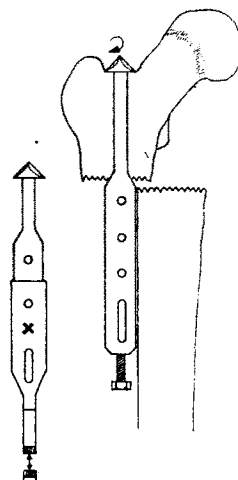


FIG. 2.—Diagrammatic representation of plate at right angles to the shaft.

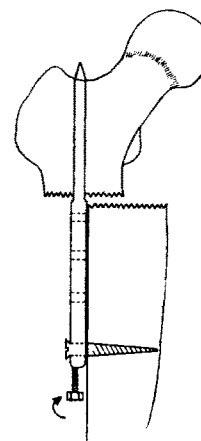


FIG. 3.—Diagrammatic representation of plate rotated through 90°. Compression not yet applied.

(20 to 23 kg.) as estimated in the Department of Clinical Measurement, Westminster Hospital, London. Three further transverse screws complete the fixation (Fig. 5). Tests carried out in the Department of Biomechanics at the Imperial College of Science and Technology, London, have confirmed the linear strength of the plate in conditions resembling surgery. The introducer and spanner are the only other instruments required.

Preoperative and Postoperative Treatment.

—All patients are given preoperative crutch-training to gain confidence for what would be expected after the operation, and the post-operative plan is explained to them. A plaster boot with an outrigger is applied after operation to prevent external rotation for the first two days, and is bivalved the next day to allow for attention to the heel. It is then

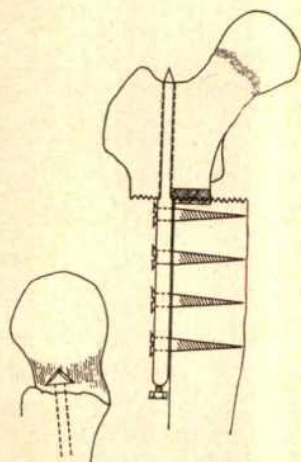


FIG. 4.—Diagrammatic representation of plate with compression applied.

applied only when the patient is in bed at night for the first five days. The patient sits out on the second day, and is allowed partial weight-bearing on crutches on the third day, going on rapidly to sticks, depending on the age and ability of the individual. Most patients by three to four weeks are self-supporting and can go up stairs.

RESULTS

Sixty-nine osteotomies have been performed. The criterion of assessment from excellent to good is based on the degree of reduction in pain and improvement in function, movement, and contracture (Van Nes, 1961). Three had had bilateral osteotomies from six weeks to 18 months after the first. Three patients have died from causes associated with their ages—79, 84, and 85 respectively. The results in nine patients between the ages of 47 and 60 can be regarded as

excellent. The older age group from 61 to 87 had gross osteoarthritis of one or both hips. All these have been greatly improved with regard to both loss of pain and increased mobility. Even in gross cases the reversal of the osteoarthritic process could be seen radiologically. In one patient the compression-screw became detached 15 months later,

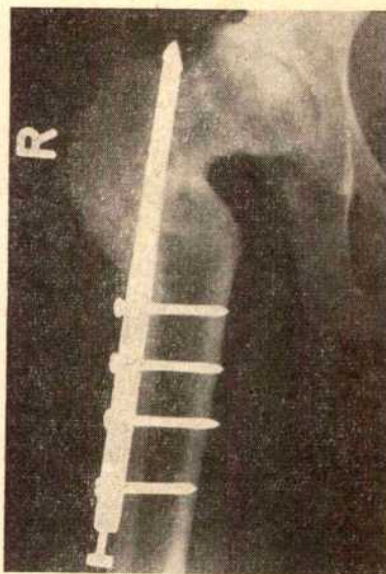


FIG. 5.—X-ray film showing anteroposterior view of completed compression plate fixation after 18 months.

but union was solid and the loose screw was easily removed. Three cases in this series showed a slight varus bend in the nail from 5 to 15°, but union was sound. In one case of a colleague, in which there were severe postoperative convulsions, the nail was bent to 60° and was later removed.

Nevertheless the overall figure of 93% excellent-to-good results compares favourably with Nissen's (1963) figures and those for Batchelor's (1963, 1966) varus osteotomy. Thus this operation almost guarantees improvement at the very least, a consideration which is often unappreciated by general practitioners, who should be made more aware of its benefits even in the chronic and very elderly.

DISCUSSION

The very early weight-bearing is in itself a help towards compression and bedding-down at the osteotomy site as the preloading compression force diminishes. Radiological union is often seen in four weeks. In some cases x-ray films four weeks to 22 months after operation show that the arrowhead has risen slightly above the femoral neck, and

in two cases quite appreciably. Thus the possibility of cutting downwards is remote. It also demonstrates that the plate does not tend to hold the fragments apart, nor does it produce a valgus tilt. In fact a varus result predominates in this series, and this can be achieved by design at operation when it is more advantageous to centre the head of the femur in the acetabulum.

The upper part of the femoral neck has a good hard cortex, which slopes posteriorly. Penetration and locking of the arrowhead can therefore occur "high" or "low." An upward slant on introduction of the plate ensures a high position. In every new method attention to small details in operative technique is important if one hopes to attain the same results.

Rotation of the plate through 90° with a locking effect opens up a new technique, which can be applied to other procedures such as arthrodesis of the hip joint and compression fixation of oblique fractures of the long bones.

Subcapital Fractures of the Femoral Neck.—Two cases of old ununited subcapital fractures of the neck of the femur have been successfully treated by osteotomy after reduction and the use of this compression plate. One fresh subcapital fracture can be classed as an excellent result, and another as a good result so far. In those cases, however, while the patient can be got up on crutches, weight-bearing is delayed for four to six weeks unless a weight-relieving calliper is fitted.

No one method of carrying out compression osteotomy is wholly better than the other, but surgeons should have the choice of alternative procedures.

"There are many roads that lead to Rome."

I acknowledge with grateful thanks the help of Mr. I. McLeod-Balkie, of Epsom District Hospital, for allowing me to review his many cases, and other orthopaedic colleagues; the Department of Clinical Measurement, Westminster Hospital; the Department of Biomechanics at the Imperial College of Science and Technology, London; the London Splint Company, who developed the plate; and Smith Kline and French for a colour film of the technique at operation.

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Correspondence

Letters to the Editor should not exceed 500 words.

Hospital Boards

SIR,—The Minister of Health has recently said that he proposes to overhaul the administrative machinery of the Health Service, and hints have been dropped that area control may well emerge as the effective pattern. Devolution to areas (rather than to regions), each responsible to the Ministry, must surely be a welcome idea in the hospital world at least.

It is no secret that, arising out of the establishment of a teaching hospital at Nottingham—that is, in a regional board's sphere of influence—a strong move is being made in certain quarters to alter completely the composition of the boards of governors of the teaching hospitals of England and Wales and possibly to bring these hospitals under the regional boards, as in Scotland. A second, and separate, issue is to increase the influence of the universities upon the administration of the teaching hospitals within which the university teachers and researchers work. Attempts are being made to integrate these two issues, and it is very important that the medical and lay staffs of the teaching hospitals should consider their own attitudes to possible changes, and to be vocal about them if necessary. The Goodenough,¹ Guillebaud,² and Porritt³ Committees have all affirmed that the teaching hospitals of England and Wales should continue to be independent of the regional boards, and recent meetings of the Teaching Hospitals' Association and of the deans of the medical schools of the English universities have said the same thing.

Taking regional boards first, one must hark back to the Health Act of 1948. In Scotland (as mentioned) the teaching hospitals have always been under the regions, and they never have had direct access to the Department of Health for Scotland. There is an almost 50-50 division of opinion in Scotland about whether this has been a good or a bad thing. Certainly the Scottish teaching hospitals started as being the favourite children of the boards, but the interposition of a board between themselves and the Department of Health has proved irksome, frustrating, and productive of delay. In England and Wales the regional boards have gradually obtained more and more power than was overtly stated in the terms of the Act—by reason of their control of finance and the appointment of consultants—and have consistently ridden roughshod over the local hospital management committees in such matters as hospital planning. Meanwhile the regions have set up imposing headquarters buildings at the taxpayers' expense, all full of administrative persons busily fulfilling Parkinson's Law. In this set-up they have always been irked by and jealous of the board of governors, and the direct access which these enjoy to the Ministry of Health. It is small wonder that they have cast covetous eyes on the teaching hospitals and that

they now possibly welcome the universities as potential allies.

Hospital consultants and administrators should consider very seriously whether in their view it would not be in the best interests of the service—and therefore of the patients—if the regional boards ceased to exist as anything but advisory bodies, rather than that they should swallow the teaching hospital boards. I believe that the Guillebaud Committee rejected this idea, but this was at a time when a situation of global war (with its inevitable regionalization) was rather more thinkable than it is now, and I submit it is a possibility which should once more be considered seriously. I can see no reason at all, for example, why any of the areas at present working through the Oxford Regional Board should not be given an area board of governors having as direct dealings with the Ministry as does the board of governors of the teaching hospital. It is argued against this sort of arrangement that it would mean greatly increasing the staff at the Elephant and Castle. Since the work of the Ministry staff turns preponderantly upon finance, a top-heavy increase of staff at that level could be avoided by giving all boards of governors a block grant of money for their year and letting them spend it to best advantage; such an arrangement might even lead to a diminution of administrative staff centrally. The present Government apparently favours decentralization of many services. Here would be an opportunity for just that.

Now one comes to consider the existing composition of boards of governors of teaching hospitals. These are made up of persons of integrity who voluntarily give their time to what is often a difficult and largely unrecognized voluntary service. The Minister has the final voice in appointing the persons forming the boards, but the universities nominate one-fifth, the medical staffs one-fifth, the regional boards one-fifth, and the Minister personally appoints two-fifths after consultation with local interests. The universities feel that they are under-represented, and I think this is so. The consultant staffs feel that they, too, are under-represented, and I believe this also to be true. Neither university nor medical nominees, however, are necessarily good business men, and it would be vital to retain the help of lawyers, bankers, and men of affairs. My suggestion for a reconstitution of teaching hospital boards of governors would be university one-third, medical staff one-third, and other persons one-third. This last category would in fact be a fusion of the three-fifths at present forming those representing the regions and the direct nominees of the Minister. In other words the influence of those who know about teaching and patients would be increased and that of politics would be diminished. This would do nothing but good. If in such reconstitution it was thought that larger boards

were needed this would be acceptable and they could act through a smaller general purposes committee, as is the habit in the regions at present.

At a time when medical education is under scrutiny it is vital that the medical schools of the universities obtain better facilities than they enjoy at present, and one way of securing these is to have a bigger representation on hospital boards; but the part-time teachers who make up the consultant service on the one hand and do most of the teaching on the other must keep a watchful eye upon the possible outcome of a potential alliance between the universities and the regions, which is unexpected and could be dangerous.—I am, etc.,

Radcliffe Infirmary,
Oxford.

R. G. MACBETH.

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- ² Report of the Committee of Enquiry into the Cost of the National Health Service, Cmd. 9663, H.M.S.O., 1956.
- ³ A Review of the Medical Services in Great Britain, Social Assey, London, 1962.

Varicose Ulcers and Use of Topical Corticosteroids

SIR,—The object of this letter is to draw attention to the harmful effects which may occur from the use of corticosteroid ointments and creams on stasis or varicose ulcers. We are seeing more and more patients in whom the application of these preparations to this type of ulcer has led to its rapid extension in diameter and depth, often with severe secondary infection from *Ps. pyocyaneus*.

In our opinion it is quite wrong to use corticosteroids on these leg ulcers, and antibiotic or bactericidal substances added to them are inadequate to control secondary infection. It is true, however, that topical corticosteroids are valuable in the treatment of stasis eczema, provided that it is possible to avoid contamination of the ulcerated area by careful application, detailed instruction, or demonstration. Also, as the starting points of these ulcers or recurrences may be scratches on such an area of eczema, the use of corticosteroids on residual eczema may be justified. However, in such cases, after abrasion occurs and becomes secondarily infected, the continued use of the application may favour extension. The newer and more powerful corticosteroids will have a greater effect in this connexion, and sprays containing corticosteroids are unlikely to be used without contaminating the ulcerated area.

In our opinion the use of topical corticosteroids on leg ulcers is never justified, whether in combination with other preparations or not. If they are used on associated eczema they must be applied with the greatest care and must not be allowed to contaminate any ulcerated area.—We are, etc.,

CLIFFORD D. EVANS.
ROGER R. M. HARMAN.
ROBERT P. WARIN.

Bristol Royal Hospital,
General Hospital Branch,
Bristol 1.

Computers in Medicine

SIR,—Your leader on computers in medicine (4 November, p. 250) was timely, and you so rightly pointed out that "the most powerful computer can originate nothing." So much in clinical medicine in the past has been padded with waffle, and in the computer age there will be no room for it. Already I have heard of examples where clinicians were unable to communicate fully with programmers. Many doctors will have to learn basic computer systems, and yet already I have experienced confusion in this field.

I recently attended the three-day introductory course at Elliott Medical Automation, University College Hospital. The lectures on the second and third day of this course were on A.L.G.O.L. programming, which is used by Elliott-Automation Computers Ltd. Two of the doctors on the course were medical officers of health and their authority had installed a Honeywell computer, which used C.O.B.O.L. language. For my own research I have been offered facilities on an I.B.M. 1401 which uses C.O.B.O.L., but part of my research involves the use of a psychiatric inventory which has a prepared programme written in F.O.R.T.R.A.N. (the I.B.M. computer language). Fortunately for me I.B.M. have gone out of their way to help me and I have no problems.

However, I do feel that there should be some rationalization in the medical computer field. We do not wish to be told what computers we should use, but I wonder whether it would be possible for the B.M.J. to run periodically a summary of what is happening in the medical computer field.—I am, etc.,

Hinckley, Leics.

PETER A. PARISH.

Cerebral Localization of Psychological Function

SIR,—May I report in the accompanying Table on three patients I have recently seen in this vicinity, all with similar psychological findings to subnormal epileptics (Dr. P. E. Sylvester and Miss E. Blundell, 4 February, p. 282), but occurring within the normal range of intellect, in adults, all with "spike and wave" E.E.G.s and abnormal personalities, but without clinical epilepsy or any previous or family history thereof.

Sex	Age	E.E.G.	Wechsler I.Q.	
			Verbal	Performance
M	17	Bilateral spike and wave during overbreathing	102	87
F	25	On photic stimulation two brief outbursts of bilaterally synchronous generalized atypical spike and wave.	85	72
M	18	Bursts of bilateral atypical spike and wave 3-5 c/s frequently throughout, usually with eyes open, and rather more frequently on photic stimulation.	96	81

These three patients' clinical personality characteristics varied from agitated labile in the first to anergic aggressive in the second and pedantic retarded in the third. All three had at one time or another in more acute exacerbations been considered borderline schizophrenics by experienced psychiatrists,

and all then responded better to phenothiazines than to anticonvulsants, on which none was kept very long.

Each patient was tested by a different senior psychologist, and the second patient's findings were essentially the same on repeat testing at an interval of six weeks, so that the results are considered reliable. The psychological finding of a significantly higher verbal than performance score was said by the psychologist testing the first and third patients to be a sign of emotional disturbance, and in the first more specifically of schizophrenic disorder, although in my experience schizophrenic disturbance, when predominantly of language function, produces the opposite test result.

While there may well be a connexion in all this between schizophrenia and the schizophrenic-like psychoses of epilepsy, the relationship of the psychological findings would seem to require further interpretation and discussion in the light of the pathological and electrical ones. Thus the E.E.G. abnormalities in my three patients were bilaterally equal, as apparently were the smallness in linear dimensions of the parietal lobes in Dr. Sylvester and Miss Blundell's epileptics, yet the psychological differences seem to suggest that the dominant cerebral hemisphere subserving language function was less affected than the non-dominant subserving spatial ability (including "performance" tests like Koh's blocks and tests with shape and pattern).

Even if bilaterally equal congenital epileptic abnormalities were invoked by way of

explanation, as interfering with clear lateralization of developing psychological function, this should affect verbal as much as performance scores. Could the observed psychological difference therefore be more an indication perhaps of global or bilateral abnormality of the sensorium, as seen in confusion or dementia? Performance tests may depend far more on "fluid" ability than "crystallized" verbal function, and thus be more affected by such intermittent generalized disorder. Unilateral localized cerebral hypogenesis might rather account for more specific psychological defects like developmental dyslexia.—I am, etc.,

Stone House Hospital,
Nr. Dartford, Kent.

J. P. CRAWFORD.

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Visuo-motor Disability in Schoolchildren

SIR,—In view of the authors' statement (4 November, p. 259) that "no formal neurological examination could be undertaken in the present inquiry . . ." it would be interesting to know whether an assessment of visual acuity, refractive error, binocular vision, or muscle balance was made in the experimental group, since a defect in any of these might have affected their performance.—I am, etc.,

Orpington,
Kent.

S. E. WHITE.

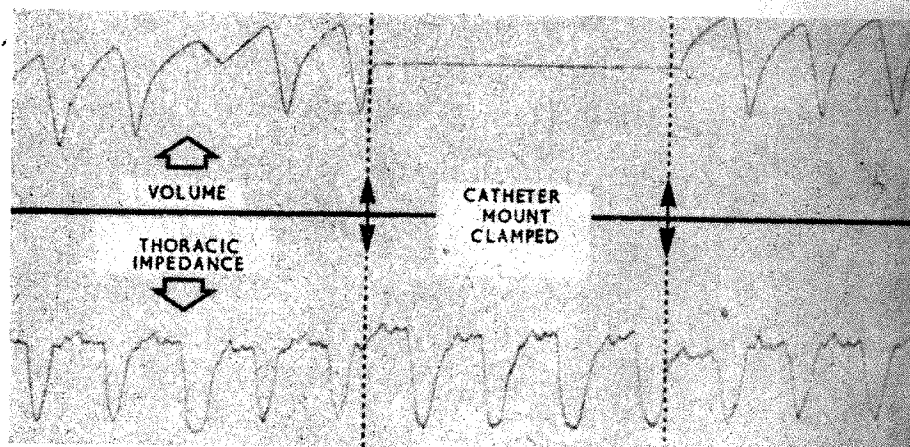
Respiratory Monitoring

SIR,—We read with interest the report by Dr. J. V. Farman and Mr. D. A. Juett on the use of impedance spirometry as a monitor of ventilation (7 October, p. 27).

Our own experience has been that the impedance "spirogram" is not always a

with the record shown in Fig. 2 of the communication by Dr. Farman.

On the evidence of the disparity between these traces and on similar experimental laboratory findings, we suggest that impedance spirometry in its present form should not be regarded as a reliable monitor of



Volume: Integrated signal from pneumotachograph head. Thoracic impedance trace: 2 electrode configuration, 30 Kc generator; indifferent electrode over sternum, measuring electrodes M.A.L.6th I.C.S. Catheter mount clamped at first arrow and released at second. Short partial occlusion at the "volume" large arrow.

reliable guide to ventilation in spontaneously breathing subjects. The record reproduced above was obtained from a lightly anaesthetized spontaneously breathing patient. Total obstruction of the catheter mount, as indicated by the arrows, produced little change in the impedance trace. This is in marked contrast

ventilation in the spontaneously breathing subject.—We are, etc.,

D. W. BETHUNE.
J. M. COLLIS.Departments of Anaesthesia
and Medical Electronics,
St. Bartholomew's Hospital,
London E.C.1.

Gastritis, Aspirin, and Alcohol

SIR,—I was interested in Dr. D. N. Croft's excellent article on gastritis (21 October, p. 164), and welcome the prominence that he gives to the role of aspirin and alcohol in provoking gastritis and haematemesis. He shows that gastritis is usually self-induced. He does not, however, mention the considerable risk of gastroduodenal haemorrhage when alcohol and aspirin are taken together, the latter often at the end of a binge in an endeavour to prevent a hangover.

Some years ago I reported to the Association of Physicians of Region No. 1 the results of a small survey of every emergency medical admission with haematemesis and melaena to this hospital in 1958 and in 1960 (unpublished). In 108 cases we found that 72 had taken aspirin in some form, as far as could be ascertained, within 24 hours of the onset of bleeding. In the year 1958, of 31 male admissions 23 had taken aspirin and 16 had taken alcohol within 24 hours of the onset, and 10 had taken both. We thought that alcohol considerably increased the risk of bleeding due to aspirin, and it was significant that male admissions with haematemesis were more frequent at week-ends and during public holidays.

Incidentally, we found that at first patients often denied aspirin ingestion, until they were carefully interrogated using several of the more popular trade names. We now hand each patient a printed list of the 321 aspirin-containing preparations they would do well to avoid in future. The most confusing was undoubtedly Alka-seltzer, none of its victims being aware of the aspirin content of this well-advertised preparation, and many thinking that it was purely an alkali and therefore taking it for gastric discomfort or pain.

Further inquiry was made into the drinking habits of the ulcer patients. There were 75 males with gastroduodenal bleeding, and 48 of these were considerable drinkers, nearly always bitter beer, and consumption varied from a mere one gallon (4.5 l.) of beer per week to as much as seven gallons per week. Of these 48 individuals 32 were considered to have a duodenal ulcer, mostly confirmed or strongly suspected. These and other figures lead one to reflect that in this district regular beer drinking, especially bitter beer, over a long number of years eventually leads to duodenal ulcer, and one speculates about whether this may explain why it is that duodenal ulcer is so much more common in men than women. If this is correct the incidence of duodenal ulcer in total abstainers should be low. It seems to me that the role of alcohol in relation to gastroduodenal troubles has hitherto been underrated, and that here is a problem which merits wider attention and further study. Also the public should be warned not to take aspirin after drinking.—I am, etc.,

North Ormesby Hospital, Middlesbrough. C. E. ASTLEY.

Body Building on Drugs

SIR,—Your leading article on the use of anabolic steroids in athletic training (11 November, p. 310) in reply to Dr. D. E. Pearson's letter (11 November, p. 353) is both timely and of importance. It may, however, be of interest to you to know that this subject has already been considered at some

length by the Medical Advisory Committee to the British Olympic Association, and that they utterly condemned the use of anabolic steroids in athletic training and pointed out the possible dangers involved in taking them. A copy of this recommendation has been sent to all the governing bodies of sport in this country.

In addition to this the International Olympic Committee has issued the following statement to the National Olympic Committees of 123 countries: "The International Olympic Committee considers the use of anabolic steroids (except for medical purposes) constitutes 'doping' from the Olympic viewpoint."—I am, etc.,

J. R. OWEN,
Honorary Medical Officer,
British Olympic Association
West Haddon,
Near Rugby.

Coagulation of Rubber Latex in the Stomach

SIR,—The common poisons used by agricultural workers in Ceylon attempting suicide are insecticides, which are easily available to them. Rubber latex is not considered to be a poisonous substance, and we report here a case of attempted suicide by ingestion of rubber latex. The only symptoms produced by the ingestion of rubber latex were due to the mechanical effects on the stomach of the coagulated rubber latex.^{1,2} This is an unusual foreign body in the stomach about which there have been no earlier reports in the literature.

A 49-year-old woman who works as a rubber tapper on a rubber estate was admitted to the medical ward with a history of having swallowed a cup full of fresh rubber latex. She had confessed to her daughter that she had taken the rubber latex with the intention of killing herself. She had ingested the rubber latex four hours prior to her admission to hospital. Although alert and conscious at the time she was brought to the hospital outpatients department she refused to answer any questions. Apart from slight abdominal pain, she had no other symptoms, and seemed reasonably comfortable. On examination the pulse was 90 a minute, regular, and blood pressure was 110/90 mm. Hg. An elongated sausage-shaped lump was palpated in the epigastrium. It was firm, but could be pitted on pressure. A plain x-ray of the abdomen did not reveal any abnormality.

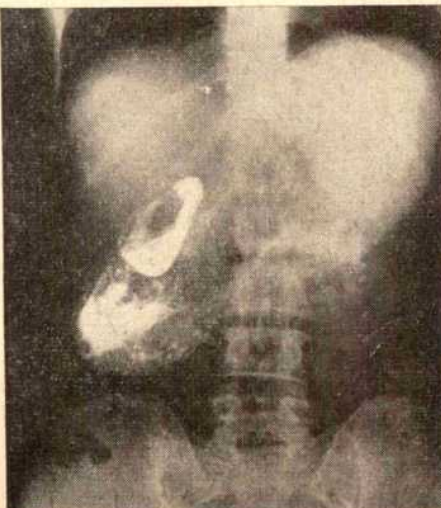


FIG. 1.—X-ray of the abdomen taken after barium showing the filling defects in the stomach and in the second part of the duodenum.

The x-ray of the abdomen taken after giving a dilute solution of barium to swallow showed two filling defects; one corresponding with the lump felt in the abdomen in the stomach and the other due to the presence of solid latex in the second part of the duodenum (Fig. 1).

At operation the solid latex, moulded to the shape of the stomach, was removed and the gastrotomy wound closed. This solid rubber was of creamy yellow colour with the impressions of the rugae of the stomach on it (Fig. 2).

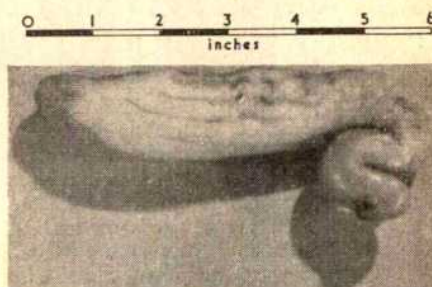


FIG. 2.—The specimen of solid rubber removed from the stomach.

When thrown on the floor it bounced like any other piece of rubber. The other latex lump was identified in the second part of the duodenum. Duodenostomy was done and the lump removed. She made an uneventful recovery. She was later seen by the psychiatrist.

Rubber latex is a milky fluid obtained by cutting the bark of the rubber tree. This latex, when coagulated, forms the solid rubber. In the rubber factories of Ceylon coagulation of rubber is obtained by adding certain chemical substances to the latex. Eight ounces (200 ml.) of 8% sodium bisulphite and 5 oz. (125 ml.) of 6% formic acid are used for 40 gallons (182 l.) of latex for it to coagulate. In this particular case the acid present in the stomach must have in some way contributed to the coagulation of the latex in the stomach.

We would like to thank Mr. M. de S. Jayasinghe, of the Photographic Department, General Hospital, Colombo, for his help with the photographs in this case.

—We are, etc.,

K. THIRUNAVUKKARASU.
K. YOHESWARAN.

General Hospital,
Ratnapura, Ceylon.

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- 1 Aird, L., *A Companion in Surgical Studies*, 1958, 2nd ed. Edinburgh.
- 2 Souttar, H., *Textbook of British Surgery*, 1956, London.

Prevention of Rh-haemolytic Disease

SIR,—My colleagues and I were interested in Dr. Sheila Murray's letter (4 November, p. 296), and the following are the replies to her queries:

The treated and control women in the Liverpool group who had subsequently Rh-positive babies were tested for antibodies immediately after delivery of the second baby. The babies were in all cases Coombs-negative, normal, and liveborn. In the clinical trials elsewhere, all we know is that the babies were also Rh-positive, normal, and liveborn, and that no treated women have made antibody, but we do not know the precise time at which the tests were carried out.

As far as we know, the 110 women remaining in the treated group have not become pregnant

again, nor is there any record of either stillbirths or abortions, except for a single case of abortion in the controls. However, complete ascertainment is extremely difficult and there may well have been a few cases which have not been reported. Our routine procedure is to give the mother a card when she is tested for antibodies six months after the birth of her first baby, and she is told to send it to us when she becomes pregnant again. As a precaution the case sheets of the mothers are also examined at intervals in case there is any indication that the woman has become pregnant.

The number of cases in the various trials has increased considerably since I gave my lecture, and the data have been sent to Dr. Murray. Our general experience in Liverpool of the time interval between first and second pregnancies does not suggest that a particularly small percentage of the women in the trial have had second babies.

The anti-Kell experiment gave inconclusive results because of difficulties with the anti-Kell antibody.

Dr. Murray speculates that suppression of D-immunization by anti-D gammaglobulin may be accompanied by some impairment of general immunity to infection. Not only have we followed up both our volunteers and trial women and found nothing to suggest this, but the gammaglobulin we inject differs from preparations used for other purposes only in that 1/500th part is anti-D, and I cannot see that its effect on general immunity can be different from that of the more usual preparations.

We have now tested for anti-Gm antibodies 62 treated women and have found positives in four, giving an incidence of 6.3%. The controls are still being studied, but we do not think that the formation of anti-Gm antibodies is likely to be damaging, for, if it were, it would make the giving of blood transfusions a most dangerous procedure, since incompatible Gm antigens must often be injected in large quantities in transfusions of whole blood.

Although in our first experiments, in about 1960, there was enhancement of immunization by IgM, which has never been satisfactorily explained, yet since that time we had not used IgM but always IgG both in our experiments and the clinical trials.

We do not understand the relevance of Dr. Murray's questions about the "ultimate relationship of anti-Gm in rheumatoid arthritis" to our work. The four women with the anti-Gm are entirely well and there is no suggestion that they have or are developing rheumatoid arthritis. Furthermore, there is no evidence that Gm antibodies, either natural or induced by immunization, predispose to rheumatoid arthritis, and the distribution of the Gm groups is normal in patients with this disease.

While agreeing that more research is needed, the most important point to us seems to be to find the smallest effective dose, and an M.R.C. working party is organizing trials to determine this. There is some very recent evidence on the subject from New York.¹ Four groups of 10 Rh-negative men were given 10 ml. of group O Rh-positive whole blood intravenously at monthly intervals for a total of three injections. Twenty-four hours following the administration of blood three of the four groups were given 1.0 ml., 0.5 ml., or 0.25 ml. respectively of an ortho preparation containing 1,200 µg.

Group	Dose of Ortho Anti-D Gamma-globulin	Number With Anti-Rh at 9 Months	% With Antibody
I	0	6 of 10 men	60
II	1,200 µg	0 " 10 "	0
III	600 "	0 " 10 "	0
IV	300 "	0 " 10 "	0

Pollack *et al.* (1967).¹

of anti-Rh (D) antibody per ml. Blood samples were obtained thereafter at monthly intervals for nine months and examined for the presence of anti-Rh. The results are summarized in the Table.

It therefore looks as though 300 µg. of ortho anti-D (approximately the amount being used in our current 1-ml. trial) is effective in protecting against a fairly large volume of injected Rh-positive blood.

Whether the treatment is "unquestionably right for national use" is a decision for the Ministry of Health, which has set up a sub-committee of its Standing Medical Advisory Committee to consider the whole matter.—I am, etc.,

Department of Medicine,
The University,
Liverpool.

C. A. CLARKE.

REFERENCE

- Pollack, W., Singher, H. O., Gorman, J. G., and Freda, V. J., Scientific Exhibit, American Association of Blood Banks Meeting, October 1967, New York.

Allergic Alveolitis

SIR,—In your leading article (16 September, p. 691) the term "extrinsic allergic alveolitis" was suggested as the appropriate general description for a group of conditions resulting from the inhalation of antigenic material and occurring in farmers, mushroom-pickers, bird-fanciers, pituitary snuff-takers, bagasse handlers, etc.

We would accept this term as appropriate if the pathology were confined to inflammatory changes in the interalveolar septa with or without an exudate into alveolar spaces, but this is not so, because at one stage a salient feature is the presence of numerous "sarcoid-like granulomata" which induced Dickie and Rankin,¹ who first described the histology in farmer's lung, to use the term "acute granulomatous interstitial pneumonitis." Another frequent feature, as indeed is pointed out in the leading article, is a bronchiolitis, the exudate of which may become organized. Further, as is to be expected in a pulmonary Arthus or Type III reaction, vasculitis occurs. Organization of the inflammatory damage often occurs in this group of diseases, leading to a chronic stage characterized by pulmonary fibrosis.

The term "extrinsic alveolitis" invites the suggestion that this fibrosis is to be compared with diffuse idiopathic fibrosing alveolitis, now apparently the term replacing idiopathic diffuse interstitial pulmonary fibrosis or "chronic Hamman-Rich disease," where the end result produces a fine interstitial fibrosis with a respiratory function profile of transfer factor defect.

In the group of diseases now under consideration, however, this is only one of the possible end-results. In many patients there is much fibrosis involving terminal conducting airways—for example, an obstructive airways disease profile is seen in about one-third of sufferers from chronic farmer's lung.² Reporting on lung-function studies in bagassosis, Weill and others³ concluded that some dyspnoeic patients in the chronic stage had obstructive airways disease which they considered was causally related to bagasse exposure.

We therefore feel that "extrinsic allergic pneumonia" is less specific and more appropriate than "extrinsic allergic alveolitis."

One of the difficulties in interpreting the published work on farmer's lung is that authors seldom make it clear whether they

are discussing the acute potentially reversible stage or the chronic stage of irreversible fibrosis. In order to obviate this situation it is suggested that the acute stage be referred to as "acute extrinsic allergic pneumonia," and the fibrotic end-result as "chronic extrinsic allergic pneumonia." The term used should describe clearly the whole clinico-pathological entity.—We are, etc.,

R. M. E. SEAL.
J. C. WAGNER.

Sully Hospital and
Medical Research Council's
Pneumoconiosis Research Unit,
Penarth, nr. Cardiff.

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- Dickie, H. A., and Rankin, J. J. *Amer. med. Ass.*, 1958, **167**, 1069.
- Hapke, E., Thomas, G. O., Seal, R. M. E., Meek, J., and Hayes, M., to be published.
- Weill, H., Buechner, H. A., Gonzalez, E., Herbert, S. J., Aucoin, E., and Ziskind, M. M., *Ann. intern. Med.*, 1966, **64**, 737.

Demonstration Aerosol Inhalers

SIR,—Dr. A. Herxheimer (28 October, p. 236) suggested that manufacturers of pressurized aerosol preparations should provide "demonstration" inhalers so that prescribing doctors could instruct their patients more effectively.

It has been our practice to provide doctors with inert aerosol inhalers from time to time, through our representatives. Our object has been to stress the desirability of correct administration, and encourage doctors to supplement the instructions in the patient's leaflet with a practical demonstration.

As part of our current efforts to avoid misuse and abuse of pressurized aerosols, our representatives are now offering inert inhalers to all doctors on whom they call. The co-operation of all prescribers is being sought in ensuring that patients are using the right technique, and thereby obtaining maximum response from minimum dosage.—I am, etc.,

H. E. LEWIS,
Medical Adviser,
Riker Laboratories.

Loughborough,
Leicestershire.

Purpura in a Patient Taking Chlordiazepoxide

SIR,—Non-thrombocytopenic purpura occurring following chlordiazepoxide (Librium) administration has been seen recently in this hospital.

The patient, a 65-year-old well-nourished Jewish woman, was investigated for a generalized purpuric rash. She had been receiving protamine zinc insulin for many years, and for at least 12 months had been receiving irregular courses of chlordiazepoxide (10 mg. twice daily) at approximately monthly intervals, each course lasting approximately a week. On admission the chlordiazepoxide was discontinued. The routine blood investigations were all normal.

The tourniquet test was positive, clot retraction was 45% (normal 48–64%), and the platelet count varied between 114,000 to 245,000/cu. mm. A peripheral blood film showed normal platelet morphology with perhaps occasional large forms. No lupus erythematosus cells were seen. The urine contained 130 mg./100 ml. protein, sugar at times, and an occasional granular cast. Serum proteins were 7.6 g./100 ml. (albumin

3.6 g./100 ml.). Protein electrophoresis showed an increase in all the globulin fractions with mild decrease of the albumin fraction.

The most likely abnormality was therefore an increase in capillary fragility, although a qualitative defect could not be outruled. The purpura gradually faded; and on discharge four weeks later the tourniquet test, though still positive, was less marked. During her hospitalization she was transferred from insulin to chlorpropamide (Diabinese) 500 mg. daily, with good control of her diabetes and no deterioration in her purpura.

She was readmitted three weeks later with right hemiparesis due to cerebral thrombosis. Chlordiazepoxide 10 mg. was given on admission. The following morning the tourniquet test was negative and the platelet count was 200,000/cu. mm. The blood urea was 44 mg./100 ml., and urinalysis showed 60 mg./100 ml. protein only. Five days after admission she was noted to be depressed, and chlordiazepoxide 10 mg. t.i.d. was prescribed. Within 48 hours the purpura reappeared and the tourniquet test was strongly positive. The platelet count was 190,000/cu. mm. The chlordiazepoxide was discontinued; the purpura gradually faded, and the tourniquet test became steadily weaker. Nine weeks later it was negative and the platelet count was 162,000/cu. mm. It was found difficult to control her diabetes with chlorpropamide and insulin therapy was recommenced, with good control and no recurrence of the purpura. She was discharged with residual hemiparesis, has remained well, and has had no further episodes of purpura.

The only reported case of purpura occurring with chlordiazepoxide administration was at a clinicopathological conference,¹ at which concurrent chloramphenicol administration was considered responsible for the purpura. Thirty-four suspected cases have been reported to the manufacturers, but no cases have been reported in the literature. It is interesting to note that the purpura did not appear when 10 mg. was administered on the evening of her second admission, and only appeared when 30 mg. per day was given later. It seems, therefore, that there is a minimum dose needed to manifest the purpura.—I am, etc.,

Mercer's Hospital, ISAAC J. COPPERMAN.
Dublin 2.

REFERENCE

¹ *Amer. J. Med.*, 1965, 39, 260.

Salmonella in Tortoises

SIR,—I was most interested to read Dr. L. T. Newman's letter on the problem of salmonella in tortoises (4 November, p. 296). It is a well-known fact that tortoises and related terrapins are excretors and carriers of salmonellas, and, as such, are a constant hazard to their owners and handlers, in particular young children.

In 1966, in conjunction with Dr. C. D. Plows, of the Sheffield Public Health Laboratory Service, we were able to identify an Arizona strain from a case of gastroenteritis in a 3-year-old Sheffield girl. A symptomless excretor of the organism (her 5-year-old brother) was also found in the same family. The source of infection was traced to a pet terrapin—a type of small turtle (genus: *Graptemys*)—purchased by the family from a pet shop in Sheffield. Full details of this investigation are to be reported in the *Journal of Hygiene* (in press).

Terrapins, like tortoises and turtles, are excretors of both salmonellas and Arizona. If the habit of keeping terrapins as pets increases, then these small innocuous animals may well become an important source of human salmonella infection. This is especially so in young children. Terrapins are more likely to act as a source of human infection than tortoises for the following reasons: terrapins are smaller and therefore easier and more tempting for young children to handle; they are usually kept indoors and in a tank of water; it has been observed that children do play with them and are in the habit of transferring them in and out of the tank at frequent intervals. If the terrapins are excretors then the water in the tank will become infected, so increasing the possibility of spread to humans or to other pets.—I am, etc.,

WILFRID H. PARRY.

Public Health Department,
Town Hall Chambers, Sheffield.

Paraquat Poisoning

SIR,—The recent report of Dr. Ch. Almog and Dr. E. Tal (16 September, p. 721) of the result of a subcutaneous injection of paraquat (Gramoxone), with the development of a right facial paresis, prompts me to record another case of facial palsy associated with Gramoxone.

This was in a male horticultural worker of 49 who presented in May this year. He had rolled a cigarette with unwashed hands after washing spray nozzles contaminated with Gramoxone. He developed a burning sensation of the tongue and examination four days later revealed nothing abnormal. Two days later, he awoke with headache and nausea, sore throat, fever, aching of the limbs, and general malaise, and by mid-afternoon had marked muscular weakness and nearly collapsed. His temperature was 101.5° F. (38.5° C). Neck stiffness was present, and there was a thin line of vesicles on the right fauces. There was a horizontal nystagmus which the patient claimed had been present for years.

He was admitted under the care of Dr. J. Campbell, and four days later developed a right lower motor neurone facial palsy with no other neurological findings. The chest, skull, and mastoid x rays were normal. The cerebral spinal fluid the day after admission showed R.B.C.s 41/cu.mm., W.B.C.s 5/cu.mm. protein 110 mg./100 ml., sugar 100 mg./100 ml. chlorides 760 mg./100 ml. A repeat lumbar puncture one week later showed R.B.C.s 8/cu. mm., W.B.C.s 39/cu.mm. neutrophils 11%, lymphocytes 89%, protein 40 mg./100 ml., chlorides 750 mg./100 ml., sugar 104 mg./100 ml; the pressure was 150 mm. with a free rise and fall. Blood count, E.S.R., blood urea, liver function tests, aspartate transaminase, and alanine transaminase were normal; the urine contained a trace of protein, many pus cells, and follow-up intravenous pyelogram suggested old right-sided pyelitis.

A follow-up chest x ray five months later showed no evidence of any active pathology in the lungs, and the heart was of normal size (Dr. Maxwell).

This sequence of contact with paraquat (Gramoxone) and facial palsy may be entirely coincidental; the minute dose of paraquat involved might suggest a hypersensitivity response in this case. It would be interesting to know of facial or other palsies occurring in others using or manufacturing paraquat.—I am, etc.,

Dereham,
Norfolk.

K. A. MOURIN.

Low Back Pain

SIR,—“Medicine Today” (11 November, p. 341) presents what is presumably a résumé of eminent authoritative exposition of the symptoms, signs, diagnosis, and treatment of this most common of complaints. Reading this, for I have not yet seen the film, it truly amazes me that these are the practices still in vogue.

What is new? What does “Medicine Today” have to offer? Let us be reasoned, and, if you like, be with it. Let us read, learn, digest, and practise, if not all, some of the teachings of Dr. James Cyriax. He after all (and a great number of his enlightened colleagues) has been thundering out for 20 years or more the signs, symptoms, and treatment of derangement of intervertebral joints (D.I.J.).

Whether you like it or not, his whole concept works—and very well at that. The problem is for the average doctor to grasp, interpret, and treat the condition.

The essence of treatment of D.I.J., no matter how severe, is immediate manipulation (apart from S.4). The acute severely immobilized patient with lumbago or sciatica is gently manipulated, not once, but daily, on alternate days, or every third day. This, together with a rigid bed, trunk extension exercises (as soon as the patient can start them), and no lumbar flexion when up and about, has been constantly found to get the patient back to work within a week or two.

Lying doggo in bed, swallowing hundreds of painkilling tablets, sweltering under a heat-tunnel, etc., is just not good enough when immediate reduction of the D.I.J. and mobilization is all that is required.—I am, etc.,

Pondwell,
Ryde, Isle of Wight.

T. HAMBLEY.

Intestinal Spirochaetosis

SIR,—Lieutenant-Colonel C. O. Burdick (11 November, p. 357) asserts that we have “misinterpreted normal intestinal microvilli cut tangentially as spirochaetes.” He presumably bases this view on the single low-powered electronmicrograph published with our paper.

We wish categorically to deny this suggestion. There can be no doubt that the condition we described (16 September, p. 718) is an infestation of the colonic mucosa by small, spiral micro-organisms. These are much larger than microvilli but smaller than bacteria. Axial filaments are clearly visible in our own material and in negatively stained preparation of the organisms prepared by Dr. J. Gordon. The organisms are motile on dark-ground microscopy.

It is of interest that this condition is quite common and can be diagnosed from routine histological preparations. The lesions must have been seen frequently by pathologists, but it seems the appearances have not been interpreted correctly in the past.—We are, etc.,

W. A. HARLAND.
F. D. LEE.

Pathology Department,
Western Infirmary,
Glasgow W.1.

SIR,—Dr. S. C. Dyke (21 October, p. 176) has referred to my work on intestinal spirochaetosis in terms which I deeply appreciate.

The reference he gave was to a précis of a lecture to the Association of Clinical Pathologists in the *Journal of Clinical Pathology*,¹ but a very much more detailed report, amply illustrated in both colour and black and white, appeared in the *British Journal of Surgery* in 1962.²—I am, etc.,

Eastbourne,
Sussex.

A. G. SHERA.

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- ¹ Shera, A. G., *J. clin. Path.*, 1953, 6, 327.
- ² — *Brit. J. Surg.*, 1962, 50, 68.

Obstetric Forceps or Vacuum Extractor?

SIR,—No doctor would wish to challenge the second sentence of the leading article on obstetric forceps or vacuum extractor (23 September, p. 753): "... the obstetrician must not only exercise his skill to deliver the baby from its obstetric dilemma but he must also protect the baby from any damage or delay caused by the operation itself." It therefore follows that, except in the very experienced hands of either a busy registrar or an active consultant, applying a vacuum extractor, either during the first stage of labour or even in the second stage where the position of the foetal skull is difficult to determine, must be considered as potentially hazardous and decidedly risky to the life or subsequent health of the foetus. Similarly there could be no objection to a widely experienced, active, and well-qualified general-practitioner obstetrician undertaking this procedure, but of course only in a specialist obstetric unit where every facility is available for readily treating any complication.

The set of the controversy "obstetric forceps or vacuum extractor" in your correspondence columns clearly takes place in the second stage of labour. Presumably no doctor disputes the vacuum extractor's place in the management of delay late in the first stage of labour, and forceps should always be banned at this time. In the second stage there are two situations where instrumental assistance is needed.

If delay occurs in the *mid-cavity* of the pelvis it is always likely that the foetal skull is in the occipitoposterior or transverse position, such a malposition as is probably the very cause of the delay. Where assistance is needed, either for delay or foetal distress, and before the instrument of choice is applied, the position of the occiput must be accurately determined—that is, if the skull and brain are to be protected from any damage. The delivery is clearly potentially difficult, so in fairness to the child (and mother) only a very experienced obstetrician should be performing. The final decision as to instrument should depend on the obstetrician's experience, enthusiasm, and considered results with its practical use. I can well understand and admire the excellent results obtained by Mr. J. A. Chalmers and others (4 November, p. 292) with the vacuum extractor, but, on the other hand, I firmly suggest that the majority of specialists, at least in this country, would prefer to use the obstetric forceps in order to achieve their best results in these obstetric situations.

A vast proportion of instrumental deliveries take place when the foetal skull has advanced beyond the mid-cavity and has now reached the *pelvic floor*; and again the indications

for their use are either foetal distress or delay in progress. It is in this group that bony disproportion is no longer a problem, and so instrumental damage to the skull and brain is unlikely, but only provided the requisite care with the application is undertaken—and this applies whatever instrument is used. It is such a case which a general-practitioner obstetrician might easily be coping with in his general-practitioner unit, and in this situation he would naturally opt for the instrument with which he is most familiar, and, perhaps even more important, the over-riding consideration he would take in making his choice would be his wish for a delivery with the least possible delay. Surely, therefore, the majority of doctors would choose the obstetric forceps, because most of us would agree with Mr. W. H. Laird (4 November, p. 292) who says: "... most obstetricians would agree that forceps delivery is preferable to vacuum extraction in cases where rapid delivery is required in the second stage of labour when foetal distress occurs with the foetal head fully engaged, because there is no doubt that the application of, and delivery with, the vacuum extractor does take longer than forceps delivery." I suggest he should continue his argument to include the potential as well as the recognized foetal distress, and, in mentioning potential foetal distress, I naturally refer to the longer second stage of labour. It is interesting that the well-known advocate of the vacuum extractor, Mr. Chalmers, also finds that forceps delivery is quicker.

I cannot agree that the vacuum extractor should be used without any anaesthetic at all, but would consider that, as with any obstetric forceps delivery, in fairness to the comfort of the patient a local anaesthetic should be administered. Only in exceptional cases would a general anaesthetic be necessary.

Finally, I could never condone the use of the vacuum extractor being applied to a foetal skull above the pelvic brim, even for a second twin.—I am, etc.,

DAVID BROWN.

Postgraduate Institute of
Obstetrics and Gynaecology,
St. John's Hospital,
Chelmsford, Essex.

Alcoholism

SIR,—Thirty years ago three diseases which were little understood, feared, and therefore not talked about were tuberculosis, insanity, and alcoholism. Enormous strides have been made in conquering the first two, but there still remains the same frightened silence about alcoholism, although it is much better understood by experts if not by the general practitioner like myself. I should therefore like to support Dr. A. Spencer Paterson (23 September, p. 798), when he says that the medical attitude is of paramount importance.

The National Council on Alcoholism states that out of 34 million who drink only half a million are alcoholics, and therefore we need only bother about them.¹ These figures are very misleading manifestly, for it implies that the very great numbers of heavy "respectable" drinkers who are inefficient and who cause unhappiness to their relatives are normal. No public health scheme to

combat disease has ever neglected prevention—as the National Council appears to be doing. If a man is going to fall over a cliff we grab hold of him rather than send for an ambulance to go to the foot of the cliff.

Prevention must be studied, and this means stopping not only direct advertising, which costs £23m., but also indirect advertising. It also means a fearless education of adolescents on the dangers of drink. Marty Mann's *Primer on Alcoholism*² should be compulsory reading, and there should be many more discussions in medical societies and journals.—I am, etc.,

London N.W.1.

J. J. MACSORLEY.

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- ² Mann, M., *Primer on Alcoholism*, 1952. London.

Hypersensitivity Reactions to Phenylbutazone

SIR,—In view of the recent interest in acute leukaemia developing after phenylbutazone therapy, it seems worth while reporting two cases seen during the past 18 months, both of which developed a blood picture with features of glandular fever following phenylbutazone administration. In one of the recent reports Dr. A. Lawrence¹ described a similar case in which "many atypical mononuclears closely resembling glandular-fever cells were seen" in the blood.

A woman aged 53 suffering from rheumatoid arthritis was treated with phenylbutazone, 600 mg. daily for one week, followed by 500 mg. daily for two weeks. A generalized maculopapular rash and a sore throat then developed, and her temperature was 100–101° F. (37.8–38.3° C.). A large soft lymph gland in the left axilla was noted, but no lymphadenopathy elsewhere, and her spleen was not palpable. The results of blood counts are shown below.

Day of Illness	W.B.C. /cu. mm.	Neutrophils /cu. mm.	Eosinophils /cu. mm.	Lymphocytes /cu. mm.
3	1,700	170 (10%)	323 (19%)	1,207 (71%)
4	2,300	40 (2%)	437 (19%)	1,817 (79%)
6	7,000	0	1,120 (16%)	5,880 (84%)
9	8,000	640 (8%)	2,960 (37%)	3,760 (47%)
11	8,000	1,840 (23%)	2,720 (34%)	2,960 (37%)
13	11,000	5,940 (54%)	2,200 (20%)	2,420 (22%)
17	8,000	4,720 (59%)	480 (6%)	2,480 (31%)

On days 3 and 4 a few of the lymphocytes were atypical, and some of these resembled glandular-fever cells. On day 6 about half the lymphocytes were atypical, and about a third of these had the character of glandular-fever cells. These atypical cells decreased in number and had disappeared from the blood by day 13. The haemoglobin level and platelet count were normal throughout the illness. Paul-Bunnell and toxoplasma dye tests were repeatedly negative. A sternal bone-marrow examination on day 7 showed no neutrophil myelocytes or leucocytes but an increase in promyelocytes and in eosinophil myelocytes and leucocytes. The increase in promyelocytes presumably represented a recovery phase rather than a maturation arrest, as neutrophil leucocytes reappeared and increased steadily in the peripheral blood shortly afterwards.

A woman aged 71 suffering from rheumatoid arthritis had been treated with phenylbutazone, 300 mg. daily for three weeks, when a general-

ized maculo-papular rash appeared, which was partly petechial on her legs. There was no lymphadenopathy and the spleen was not palpable. The results of blood counts are shown below.

Day of illness	W.B.C. /cu. mm.	Neutrophils /cu. mm.	Eosinophils /cu. mm.	Lymphocytes /cu. mm.
1	11,000	4,400 (40%)	1,210 (11%)	4,950 (45%)
3	17,000	5,780 (34%)	1,050 (5%)	10,030 (59%)
11	12,000	4,440 (37%)	3,480 (29%)	3,360 (28%)
24	9,000	6,390 (71%)	270 (3%)	1,890 (21%)

On days 1 and 3 nearly all the lymphocytes were atypical, and about half of these resembled glandular-fever cells. By day 11 the latter had disappeared and only an occasional lymphocyte was atypical. On day 24 the leucocyte picture was normal. The haemoglobin level and platelet count were constantly normal. Paul-Bunnell tests were repeatedly negative, and toxoplasma dye tests gave titres of 256 during and for three months after the illness.

It seems most unlikely that glandular-fever or toxoplasma infection was the cause of the illness in either case. Both infections are rare over the age of 50.^{2,3} Lymphadenopathy was not present, as it is invariably at some time in glandular fever³ and in cases of toxoplasmosis with glandular-fever cells in the blood.³ A toxoplasma dye titre of 256, as in Case 2, is found in 1% of adults, and the titre in the second case did not rise during or after the illness. On the other hand, the skin rashes and the marked eosinophilia, and the agranulocytosis in the first case, strongly suggest that both patients suffered a reaction to the drug phenylbutazone, and that the glandular-fever cells in the blood were part of this reaction. This was the conclusion of Dr. Lawrence as regards his case, which showed an even greater lymphocytosis of 17,820/cu. mm. with many glandular-fever cells present and an eosinophilia of 1,080/cu. mm.

I wish to thank Drs. J. Laurie, E. A. Murray, and I. D. S. Cowie for the clinical details and permission to publish these cases, and Miss J. Hutchinson for assistance.

—I am, etc.,

J. G. SELWYN.

Area Department of Haematology,
Royal Infirmary,
Dumfries.

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Elastic Band Injuries

SIR,—Deliberate production of artifact ulcers by elastic bands around the lower third of the leg is described in the paper by Mr. I. D. Kitchin and others (22 April, p. 218) and in the letter of Dr. K. Dawson-Butterworth (20 May, p. 510). Accidental production of artifact ulcers by elastic bands around the fingers and around the arm is described by Dr. J. G. B. Thurston (6 May, p. 376) and Mr. J. P. Turney (13 May, p. 445), respectively.

A widow aged 77 presented in September 1967 with a deep circumferential ulcer of the lower third of the right leg and a chronic

varicose ulcer distal to this. She reported that a tight bandage had been applied to the varicose ulcer; this was postulated as the cause of the circumferential ulcer. The day after admission to hospital an elastic band



was removed from the depths of the ulcer. On further questioning she admitted having used an elastic band to hold a dressing on the varicose ulcer some weeks before admission, and had been perplexed at its disappearance.

The photograph was taken by Mr. A. D. Ring 24 hours after removal of the band.

—I am, etc.,

GEOFFREY GLEW.

Christchurch Hospital,
Christchurch, New Zealand.

Nalidixic Acid and Intracranial Hypertension

SIR,—There have been letters in the *B.M.J.* this year describing intracranial hypertension in children treated with nalidixic acid (29 April, p. 310; 5 August, p. 370; and 9 September, p. 679).

We therefore think it of interest to report the case of a middle-aged woman, who in the third week of acute glomerulonephritis, while yet still febrile and slightly oedematous, but with good urine output and blood urea of 24 mg./100 ml., was given nalidixic acid in a dose of 1 g. four times a day for a superimposed coliform infection of the urine. At the time she was normotensive and had no papilloedema. Within 24 hours of commencement of the nalidixic acid she developed, in the night, a toxic confusional state of schizoid type with paranoid ideas and depersonalization. A day later the nalidixic acid was stopped and there was thereafter considerable improvement, although another week passed before she was completely normal. An E.E.G. at this time was essentially normal, but during the record the patient had a hallucinatory episode during which there was demonstrated an increase of theta activity, abolished by opening the eyes. A repeat E.E.G. at a later date was entirely normal, though it is probably significant that the frequency of the alpha rhythm showed an increase of one cycle per second.

It would seem possible that the administration of nalidixic acid during the oedematous phase of acute nephritis precipitated this

psychosis. Such an occurrence bears a relation to the previous reports of intracranial hypertension, although in this case there was no direct evidence.—We are, etc.,

L. KREMER.

M. WALTON.

E. N. WARDLE.

Royal Victoria Infirmary,
Newcastle upon Tyne.

Goodpasture's Syndrome and Dialysis

SIR,—The following case history supports the use of peritoneal dialysis in Goodpasture's syndrome, as mentioned by Dr. J. F. Munro and others (14 October, p. 95).

A 36-year-old woman was admitted in August 1966 with pyrexia. She had previously enjoyed good health and had borne five children with no apparent medical complication. She had noticed haemoptysis for the previous two weeks.

A postero-anterior chest x-ray showed bilateral diffuse mottling in the mid and lower zones. Haemoglobin was 6 g./100 ml. and the R.B.C.s showed the features of an iron deficiency anaemia. There was no other site of blood loss. The W.B.C. was 9,600/cu. mm.; the E.S.R. 125 mm. in one hour, and the blood urea 175 mg./100 ml.; serum proteins were 4.6 g./100 ml. with an albumin of 2.9 and a globulin of 1.7. Lupus erythematosus and rheumatoid arthritis screening tests were negative. Her sputum contained many macrophages laden with haemosiderin but no mycobacterium. The urine contained a moderate amount of protein. R.B.C.s and casts could be seen on microscopy.

Despite her sex, these features are in keeping with Goodpasture's syndrome. She was started on prednisone. Over the ensuing days haemoptysis continued and she complained of increasing dyspnoea. Her urine output fell. The blood urea slowly rose to 390 mg./100 ml., by which time she had become semi-conscious. Peritoneal dialysis was performed with dramatic subjective improvement and her urea fell to 222 mg./100 ml.

During the next two weeks she ate a low protein diet and her blood urea fell still further to 42 mg./100 ml. Haemoptysis ceased.

She then started to develop considerable oedema despite a reasonable fluid output and was prescribed frusemide. She commenced a normal diet. Average proteinuria was 1 g. per day, using Esbach's method at the time of discharge. Since that time she has remained in reasonable health up to August of this year, although her blood urea has slowly risen to 100 mg./100 ml. Episodes of haemoptysis have been infrequent.

The original peritoneal dialysis was life-saving during a critical part of her illness. She has recently been readmitted complaining of dyspnoea. Her haemoglobin is 10 g./100 ml. The blood urea has risen to 300 mg./100 ml.—I am, etc.,

General Hospital,
Burton-on-Trent.

DEREK BAINBRIDGE.

Cowpox and Paravaccinia

SIR,—I read your leading article "Cowpox and Paravaccinia" (November 11, p. 308) with great interest. How does the cow's udder become infected? What is the direct source of infection? Many country folk, and others, have quaint notions about this.

I quote from a rare copy of *Practical Observations on the Inoculation of Cowpox* by James Bryce, "one of the surgeons to the Institutions for the Gratuitous Inoculation of Cowpox, Edinburgh, 1801."

"Some have asserted that the cowpox is not generated in the constitution of the cow, but produced on her by inoculation with certain diseased fluids of the horse; while others are of opinion that this ailment is truly vaccine, being generated solely in the constitution of the cow."

"The horse, it is well known, is subject to an inflammation and swelling in the heels, which is called the grease, from which, at a certain period of the affection, there issues a very acrid thin matter; and this applied to the udder or teats of the cows . . . gives rise to a postular [sic] affection on those parts, which is the cowpox."

For all I know, Jenner himself may have proved this theory to be a scientific truth.—I am, etc.,

W. A. BRYCE.

Streetly,
Sutton Coldfield.

Percentages

SIR,—A minor annoyance in the reading of tabulated data is the habit of some authors of reporting the percentage of both positive and negative, leading the reader to check whether the figures do indeed add up to 100. This might be "planned redundancy," a common computer method of confirmation of a result or a method of emphasizing the figure.

But when a pair of figures put out by a computer do not add up to 100, as recently in the *B.M.J.* (2 September, p. 613), one wonders who or what has slipped.—I am, etc.,

R. ELSDON-DEW.

Amoebiasis Research Unit,
Institute for Parasitology,
Durban, South Africa.

** We apologize for the error in Table I in the article referred to.—ED., *B.M.J.*

Measurement of Blood Loss

SIR,—We were very interested in the paper by Dr. J. M. Holt and others (14 October, p. 86) regarding the measurement of blood loss using a whole body counter. Although this method is very convenient for the patient and the doctor, the considerable discrepancy between calculated blood loss and actual blood loss shown by the authors is alarming, and may limit the clinical usefulness of whole body counters in studying blood loss.

We have found that the method of detection of blood loss using radio-chromium-labelled red cells and faecal collections is a highly accurate way of detecting intestinal blood loss over a period of weeks. The method is sufficient to detect less than 0.5 ml. of blood and is equally applicable to menstrual blood loss.

The simplicity of this technique of faecal collection may well recommend itself for more routine clinical use, and in appropriate patients can be used as an outpatient procedure. The whole body counter is the ideal tool for iron absorption studies, but in view of the serious disadvantage in accurate detection of blood loss from our own experience

we would recommend faecal collection whenever possible using radio-chromium.—We are, etc.,

I. McLEAN BAIRD.
S. NASSER.

West Middlesex Hospital,
Isleworth, Middx.

Thiothixene in Schizophrenia

SIR,—Thiothixene (Navane, Pfizer) is a new addition to the group of tricyclic major tranquillizing and antipsychotic drugs. A number of controlled trials^{1,2} in other countries on acute and chronic schizophrenic patients have indicated a beneficial effect, principally on excitement and suspiciousness, and, in apathetic chronic schizophrenics, an activating effect. Dosages employed range from 5 to 60 mg. daily, with a mean of 30 mg. daily. Comparative studies have demonstrated a therapeutic range equivalent to thioridazine and trifluoperazine. The only consistent side-effects appear to be extrapyramidal, which respond to anti-Parkinson drugs.

We should like to report briefly an uncontrolled pilot study in 16 chronic schizophrenic patients consisting of nine females aged from 36 to 73 years, mean 55 years, and seven males aged from 25 to 48 years, mean 35 years. The duration of illness ranged from 3 to 40 years with a mean of 16 years. The psychosis took a paranoid form in six patients and a hebephrenic form in 10.

Thiothixene was given by mouth in an initial dose of 5 mg. daily, increasing gradually to a maximum of 40 mg. daily for a total period of 12 weeks. A number of target symptoms and the overall response were rated weekly and the occurrence of side-effects was noted. Weekly blood counts, liver-function tests, blood urea, and urinalysis were performed.

Overall improvement was observed in eight patients. In two patients, with duration of illness of 22 and 7 years, the response was quite dramatic, the former being able to return home and the latter being allowed into the hospital grounds without supervision for the first time. The target symptoms which showed the greatest response were excitement (six patients), suspicion (seven patients), depression (four patients), anxiety (six patients), and social inadequacy (eight patients). Extrapyramidal side-effects were observed in 11 cases, but in only two were they severe enough to warrant the use of anti-Parkinson drugs. Four patients were withdrawn from the trial before the end of the 12-week period; two because of poor clinical response, one because of uncontrolled extrapyramidal effects, and one because of a raised serum glutamic pyruvate transaminase (110 S.F. units/ml.) after three weeks.

Much of the response could be a placebo effect, but in view of the failure of these patients to respond to previous drug therapy, and the dramatic response in two patients, we think it is worth proceeding to a properly controlled trial.—We are, etc.,

K. DAVISON.
P. LEYBURN.
H. A. MCCLELLAND.

Newcastle General Hospital,
Newcastle upon Tyne.

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- Bishop, M. P., Fulmer, T. E., and Gallant, D. M., *ibid.*, 1966, 8, 509.

Therapeutic Effects of a Thunderstorm

SIR,—In Zurich, in 1732, a report was published on an unusually violent thunderstorm which had arisen in the night between 30 June and 1 July of the previous year. The report was the work of Johann Jakob Scheuchzer (1672-1733), the Swiss scientist known in the history of palaeontology as discoverer of the fossilized remains of a giant salamander. Early in the century he published accounts of his travels in the Alps, with detailed notes on the life and occupations of the people (including an illustrated description of the process of cheese-making), on flora and fauna, the movements of glaciers, and barometrical determination of altitude. Scheuchzer has been called the founder of the physical geography of the Alps. By profession a medical practitioner, he became physician in ordinary to his native city Zurich.

After a description of the storm and some theological observations characteristic of the period, Scheuchzer's report makes the following comment*:

"And how, if I were to assert that the very Thunder-storm must serve to sustain and promote our Health, inasmuch as in such mighty Perturbances not only the Mountains, Valleys, Forests, and Rocks, but also our Bodies do quake, and that the Circulation of the Blood and of all the radical Moistures is promoted and that all the Discharges are more readily effected. Moreover, the Terror itself which seizeth Men may make some Contribution, for that by its Agency the Influence of the sensitive Faculties upon the Upper Skin gains ascendancy and the littlest Vessels are compressed. To the which Cause I ascribe that various Persons of both Sexes, upon Inducement of this violent Storm, were some Days thereafter taken with a profuse Bleeding at Nose, as Instance a Widow of seventy Years, and plethorick, to whom I was summoned in the Night betwixt the third and fourth of July, and the same was freed by violent Bleeding at Nose from Giddiness and Head-akes, from the which she had suffer'd some Weeks before the Storm, and likewise eas'd of a Pursiness [or Asthma]."

Among conditions to which response may be expected Scheuchzer mentions pleurisy, running sores, rashes, "sickness of the limbs" (the term appears to have included "joint-gout," "the palsy," in general "sickness wherein there is resolution of the sinews and limbs"),† and all kinds of fever.

Beyond such details as are given in the quotation no attempt appears to be made to postulate the mechanism of the process by which the alleged cure is brought about. It may or may not be relevant to point out that Scheuchzer died some four years before the birth of Galvani and 12 years before the birth of Volta. Whether the question of electric discharge comes into the picture or not, it would perhaps seem that the Swiss physician had some inkling of the nature of shock-therapy.—I am, etc.,

WILLIAM F. MAINLAND.

The University,
Sheffield.

* There appears to be a Latin version of the report, which I have as yet been unable to consult. The present excerpt is my own translation from the German into English as nearly equivalent as possible to the vocabulary and style of Scheuchzer.

† See Christian Ludwig, *Deutsch-Englisches Lexicon*, 3rd ed., Leipzig, 1765.

Approval of Emergency Treatment Service

SIR,—The suggestion made by Dr. M. Mundy (4 November, p. 299) that the organizers of the B.M.A.-sponsored Emergency Treatment Service are unable to provide a viable service makes curious reading for those subscribers in the several cities where such a service has been running successfully for several years. That the service has so far failed to take hold in London would suggest that medico-political influences are involved, otherwise it is difficult to see why a scheme which has proved acceptable to executive councils in Bristol, Coventry, Glasgow, Leicester, Newcastle, Nottingham, and Sheffield should prove too difficult for the London Executive Council.

The criticisms that Dr. Mundy makes of the service are based on a misunderstanding of the type of service that is available, an integral part of which is that advice is given by the telephone operators (all State Registered Nurses) to a substantial proportion of the calls made to it. It is for this reason that a subscriber needs to be a member also of the Telephone Answering Service Ltd., as the staff need to have control of all incoming messages for which they are accepting responsibility. This does not mean that the subscriber loses control of his phone; he need hand over only during the time he is having cover from the E.T.S. The low cost (a guinea a month) of the Telephone Answering Service is surely sufficient answer to the allegations that this proviso is designed to make a profit. The attraction of this service is such that there are a substantial number of doctors who use it here in Bristol but who do not yet subscribe to the E.T.S.

The inefficiency of the G.P.O. transfer service is deplorable, but many of us are forced by circumstances to use it whether we use the E.T.S. or not, and criticism of this is irrelevant to the merits or otherwise of the E.T.S. But it is worth noting that even this service seems to have improved to some extent since the transfer number has been to the E.T.S. It is certainly absurd that in a so-called technological age it is not yet possible to make a transfer by simple switching; this problem must be solved by

the G.P.O. and the introduction of modern equipment.

The second complaint, that the E.T.S. is too expensive, also falls into perspective when it is realized that advice is given to a considerable proportion of calls, and if these are included in the statistics the cost per call falls to a much lower figure. I would suggest that in any case this is a highly artificial way of looking at it. What is important to the individual subscriber is not the actual number of calls done for him but the potential hours of freedom available with E.T.S. cover, even though only some of these hours may be actually used. The subscription can then be viewed in part as a type of insurance premium (with full tax relief), the total number of calls being relatively unimportant. The figure of 25 calls a month is an upper figure and irrelevant, and presumably included only to avoid the possibility of abuse of the service. It is the instant availability of the service that has proved to be its chief attraction to some of us; this advantage might seem even more cogent to potential subscribers with the advent of breathalyser tests. If the service was really so expensive, as its detractors constantly state, one would expect subscribers who found it so to resign from it; but this does not happen.

At a meeting in Bristol the financing of the service was explained very fully by the manager there, and it was made quite apparent that if you have a service which depends on the use of telephone operators who are State Registered Nurses, and locums experienced in general practice, the subscription cannot be lowered without sacrificing existing standards. Whatever may be the theoretical objections to these criteria, in practice the service is not only viable but successful. If a valid opinion is really wanted about the E.T.S. I would suggest that a survey carried out among subscribers in the cities where it operates would provide this more accurately than casual letters to the *B.M.J.*—I am, etc.,

A. DOWLING.

St. George Health Centre,
Bristol 5.

utilize its publicity outlets, and keep pressure on Divisions to ensure that the scheme was sold for both active and latent use. Surely we are not once more to wait until the apathetic mass of doctors revolt before the B.M.A. struggles to regain some form of leadership. The concept of I.M.S. may not have been to the liking of all, but at least, organized thoroughly at Division levels, we should now be in a position to face any eventuality in the political jungle without fear.—I am, etc.,

Peterculter,
Aberdeenshire.

F. L. P. FOUIN.

REFERENCE

¹ *Brit. med. J. Suppl.*, 1964, p. 91.

Casualty Staffing

SIR,—As a general practitioner and a casualty clinical assistant, I was interested to read Mr. Guy Rigby-Jones's letter on casualty staffing (11 November, p. 360).

Since the advent of Birmingham Emergency Locums Ltd.—a general-practitioner deputizing service—an interesting pattern has been emerging. Junior and senior hospital staff in their off-duty periods are largely staffing Birmingham Emergency Locums Ltd. (I understand that this is for primarily financial reasons.) General practitioners, on the other hand, are occupying what spare time they can arrange in order to staff their local casualty units.

This interchange as well as having a financial benefit also has the advantage that the general practitioner keeps in touch with the hospitals, and the hospital staffs gain first-hand knowledge of the problems of general practice. One obvious point is that this existing exchange of roles is reaching equilibrium. House-officers like to enjoy their hard-earned leisure and general practitioners like some time for relaxation. Any strain on either side results in the potential collapse of the whole. Until there are more house-officers and general practitioners available for this interchange then any stresses in the system may prejudice the whole.—I am, etc.,

Yardley,
Birmingham.

BERNARD A. JUBY.

Independent Medical Services

SIR,—With reference to your report on the proceedings of Council (*Supplement*, 4 November, p. 29), I feel we at the periphery should have something to say in this rather pathetic business of Independent Medical Services (I.M.S.).

No one who has read the Council proceedings in the past can have been other than dismayed at the apparent isolation that Dr. Ivor Jones and his Committee have found themselves in over I.M.S. Council members appear to conveniently forget their past remarks, but the records will show that many seem to prefer their own views to fully implementing the will of the profession as set down in Annual Representative Meeting resolutions.

Council must also fully realize that Dr. Ivor Jones should never have been left to promote the scheme direct to the profession. The fact that reference is made to "Ivor

Jones's Private Army" reveals a thought association with an individual, and I doubt whether Dr. Jones's image as the man who stood out against the Memorandum of Evidence to the Review Body (Doc. S.C.7)¹ endears him sufficiently to the inactivists among us to further the scheme.

Also, the Private Practice Committee is, in these days of the N.H.S., looked on as a relatively minor committee of the Association and treated as such by the majority of doctors, so why should a scheme, apparently introduced by it, carry much weight. After all, the General Practitioners Association circularized interested general practitioners with their scheme prior to I.M.S., and, on casual inspection, no great difference was apparent, in either content or sales drive, between the two.

No, it was the duty of the B.M.A. to openly proclaim its parenthood of the scheme,

Christmas Cards for Medical Charities

SIR,—As in previous years, I should like to take this opportunity of reminding all readers that Christmas cards are available for purchase from B.M.A. House, all profits from which go to medical charities. The number of applications for assistance which are received by the various funds is continuing to increase, and any support given to the funds by members of the profession to help their less fortunate colleagues or their dependants will be greatly appreciated.

Details of the design and cost of the cards may be obtained on application to the Bursar, British Medical Association, B.M.A. House, Tavistock Square, London W.C.1.—I am etc.,

R. COVE-SMITH,
Chairman, Charities Committee,
British Medical Association.

London W.C.1.

Obituary Notices

D. J. McI. IRVINE, M.B., CH.B., F.R.C.O.G.

Dr. D. J. McI. Irvine, consultant obstetrician and gynaecologist to the Edinburgh Royal Infirmary and Simpson Memorial Maternity Pavilion, died very suddenly on 12 November at his home at Newbridge, Midlothian. He was 50.

Donald James McIntosh Irvine was born at Kingussie on 13 February 1917. It was there that his deep and continuing love of the hills, of the countryside, and of the many outdoor pursuits at which he excelled began, and so coloured his life and outlook. Indeed he was out riding with his daughter when he became ill. As a student he played shinty for Edinburgh University and finally captained the team. He graduated M.B., Ch.B. from Edinburgh in 1940, and after a short time in resident hospital appointments he joined the R.A.M.C. He served with the 52nd Lowland Division, with the 150th Tank Regiment, and also in military hospitals in South-east Asia and in Belgium. After demobilization he specialized in obstetrics and gynaecology, and for a good many years held a consultant appointment at Bangour General Hospital as well as at the Edinburgh Royal Infirmary. He took a major part in developing the department at Bangour, and in establishing the obstetrical service in West Lothian. A first-class clinician and a popular and effective teacher, he yet took his full share

not only in the corporate life of the Edinburgh medical school but in the wider medical circles. He became a member of the Royal College of Obstetricians and Gynaecologists in 1950 and a Fellow in 1962. He was a Fellow and senior secretary of the Edinburgh Obstetrical Society and a member of the Gynaecological Visiting Club of Great Britain. His contributions to the literature of the subjects usually took the form of clinical surveys.

Added to and always enhancing Donald Irvine's high professional excellence was his most kindly and generous understanding, his vitality, and his gay optimism. He could never say no to any call for help or advice, be the problem great or small, professional or lay; nor did he spare himself in his giving, for he always went the second mile. He was held in the highest esteem by all who knew him, and many are those who will remember him with deep gratitude, and who, with his colleagues, now mourn his untimely passing.

His was a happy home on the outskirts of Edinburgh. This, in such little spare time as he was allowed, he could enjoy with his family and pass on to them his enduring love of nature. We offer our respectful sympathy to his widow, his daughter, and his two sons. —J. S.

K. S. KIRBY, D.SC., PH.D.

Professor K. S. Kirby, of the Institute of Cancer Research, died at his home in Amersham, Buckinghamshire, on 10 November after a long illness which he never allowed to cloud his natural cheerfulness. He was 49.

Kenneth Stanley Kirby was born in Yorkshire on 16 January 1918, and, although he spent little of his adult life in the county,



he retained a strong affection for the attitude to life of the traditional Yorkshireman. He graduated B.Sc. with first-class honours at the University of Manchester in 1940. He then worked in the Wellcome Laboratories for Tropical Medicine on the chemotherapy

of amoebiasis and on the structure of alkaloids. After the war Kirby returned to academic life and obtained his Ph.D. at Leeds in 1949. He continued to work on the structure of tannins—the subject of his thesis—when he joined the Forestal Research Laboratory in Harpenden. During this time he gained considerable experience of analy-

tical and preparative procedures necessary for the study of complex organic substances.

In 1953 Kirby joined the staff of the Chester Beatty Research Institute (of the Institute of Cancer Research, Royal Cancer Hospital). He worked firstly as a Fellow of the British Empire Cancer Campaign and subsequently on the permanent scientific staff at the Institute's research station at Pollards Wood, Chalfont St. Giles, Bucks. His previous experience and natural aptitude fitted him extraordinarily well for the contribution he was to make to the study of cellular macromolecules. He rapidly obtained international fame for his development of the phenol method for the isolation of nucleic acids. It was his thorough appreciation of the chemical problems involved in protein-nucleic acid interaction coupled with a careful experimental approach which enabled him to develop these procedures for general application to a wide variety of cell and tissue material. At the same time he was utilizing these techniques in studies of carcinogenesis at the molecular level. In this he was joined by a constant stream of visiting workers from many countries, all of whom acquired not only valuable experience but also lasting friendship.

Kirby was awarded a D.Sc. by the University of Manchester in 1964, and the title of professor of cell chemistry was conferred on him in February 1967. These were unsought honours richly deserved. He will be remem-

bered affectionately by his colleagues both for his deep chemical knowledge and for his free-ranging sense of humour and thorough enjoyment of living.

Professor Kirby leaves a widow and four children, to whom we and his many other friends extend the deepest sympathy.—A. R. C.

L. G. EDDEY, M.B., CH.B., D.P.H. D.T.M.&H.

Dr. L. G. Eddey, chief medical officer to the Ministry of Health at Blantyre, Malawi, and former W.H.O. area representative in India, died in hospital in Salisbury, Rhodesia, on 22 October. He was 64.

Leslie George Eddey was born in Devonport on 14 October 1903. He joined the Colonial Service, and in 1928 went out to the Gold Coast (now Ghana), where he worked as a superintendent health inspector. After a few years, deciding to take up medicine, he returned to Britain and entered Aberdeen University, graduating M.B., Ch.B. in 1938 and taking the D.T.M.&H. a year later. Shortly afterwards he became a medical officer on the Gold Coast, where he remained until 1946, when he left to take up the appointment of deputy director of medical services in British Guiana (now Guyana). He took the D.P.H. in London in 1949, then returned to the Gold Coast to take up the appointment of chief medical officer to the Ministry of Health there before accepting a two-year appointment with the World Health Organization in Nepal, where he helped to establish a school for the training of health assistants in Katmandu. In 1957 he joined the staff of the W.H.O. regional office for south-east Asia in New Delhi as public health administrator, becoming area representative for India from 1960 to 1963. For the next three years he was W.H.O. medical consultant for the Asian Institute for Economic Development and Planning in Bangkok, Thailand, later accepting the appointment of chief medical officer to the Ministry of Health in Malawi, Central Africa, where he was working up to the time of his death.

A colleague writes: Dr. Eddey, besides being hard-working and efficient, and of a disposition that made him enjoy whatever he was doing, was so full of enthusiasm and *joie de vivre* that he immediately made friends wherever he went. He liked people and enjoyed being with them. He loved to entertain and did it so graciously that everyone enjoyed being invited to his flat. His many friends will feel a real sense of loss.

B. B. W. writes: Leslie Eddey had the remarkable record of serving in the Gold Coast as a health superintendent, later as a medical officer of health, and finally, after a period in British Guiana, as chief medical officer. He was a bachelor, with a personality that seemed to be gentle to the point of diffidence. Gentle he certainly was, but not diffident. In the Gold Coast, and in British

Guiana, where also he was chief medical officer during the period of rapid political advance, he was faced with the position of increasing responsibility but greatly diminished power. His undoubted success was due to his ability to assess the personalities of those around him, and to get them on his side, acting as he thought best. This persuasiveness was not a deliberately developed technique, which would have earned him enemies. It came from confidence in his own knowledge combined with an earnest desire not to make others (with less knowledge or mistaken views) feel foolish. He persuaded a sanitary labourer, or a rural medical officer, in precisely the same way as a Minister of Health, and with a patent and sincere friendliness that was returned spontaneously by everyone he knew. On the rare occasions when he himself was won over by persuasion he accepted the new viewpoint without a trace of wounded vanity.

He was an excellent host and a man whose friendship lasted over the years—he sent off several hundred Christmas cards every year. When he finally left the World Health Organization his appointment as chief medical officer of Malawi seemed to be an ideal one for the country and for himself. It is indeed sad that he should have died so soon, but he would have died in harness somewhere; he was too devoted to the ideals of public health to retire.

J. T. BARR, M.B., B.S., F.F.A.R.C.S.

Dr. J. T. Barr, formerly anaesthetist to the neurosurgical unit at the Brook Hospital, Woolwich, died at his home on 31 July. He was 63.

John Templeton Barr was born on 17 November 1903, and was educated at Repton School and King's College Hospital Medical School, London, qualifying with the Conjoint diploma in 1926 and graduating M.B., B.S. a year later. He held resident posts at the Miller General Hospital, Greenwich, and was later appointed medical officer to the District Hospital at Erith, Kent. He took the diploma in anaesthetics in 1941. During the second world war he served as major in the R.A.M.C. and as anaesthetist under the Emergency Medical Service. After the war he was appointed anaesthetist to the neurosurgical unit at Joyce Green Hospital, Dartford, becoming anaesthetist to the South-east Metropolitan Regional Surgical Centre and Woolwich group of hospitals in 1946. In 1954 he was elected F.F.A.R.C.S. Ill-health forced him to retire in 1966.

G.C.K. writes: John Barr joined the staff of the South-east Metropolitan Regional Neurosurgical Unit as an anaesthetist in the early days of the development of the unit in 1946, and we were most fortunate that he did so. He worked with us for more than 20 years until the time of his retirement through failing health in 1966. He was a most excellent colleague, a man of great sympathy and charm, and a highly skilled anaesthetist who brought to the special problems of anaesthesia in neurosurgery a high standard of skill which undoubtedly contributed materially to the results obtained in this centre over a period of many years. He was unsparing of self in the care of his

patients, and continued to take part in long operations when his own health was failing through the effects of myeloid leukaemia. Such was his devotion to his work that he carried on when other men would have given up. He was a man of great personal courage whose charm endeared him to all around, and in his passing we have lost a great friend.

H. W. PALMER, M.B., B.S.

Dr. H. W. Palmer, a general practitioner in Worthing for over 21 years, died in Worthing on 29 September, aged 62.

Horace Winston Palmer was born in London on 21 June 1905, and came late into medicine after a successful commercial career. He graduated B.Sc. with first-class honours at Queen Mary's College, London, in 1926, and was instrumental in starting the analytic laboratory at Messrs. Heinz Ltd., which he conducted until he was called away to become managing director of the family business in Brighton. He held a civil pilot's licence at the outbreak of the second world war, and, on being rejected for flying duties with the R.A.F. because of age, decided to take up medicine. He entered Guy's Hospital in 1940 and graduated M.B., B.S. in 1944, taking the Conjoint diploma in the same year. After resident appointments in Pembury Hospital, Hove General Hospital, and St. Richard's Hospital, Chichester, he entered general practice in Worthing in 1946, and was hard at work in it on the day of his death.

Dr. Winston Palmer was a member of the West Sussex Medical Committee, and served on the council of the Brighton and Sussex Medico-Chirurgical Society. He was a founder member of the Royal College of General Practitioners, and was the local Treasury medical officer. A keen Mason for over 35 years, Winston Palmer's interests were many and varied, from rock-climbing and sailing to music and photography. He was a patron of drama and the arts, and was an indefatigable opera-goer. His great love, however, was always medicine, with a special interest in psychiatry. He will long be remembered with gratitude and affection for his unfailing kindness, sympathy, and patience.

In the last three years of his life Winston Palmer was often far from well, and was several times in hospital. His courage to overcome his illness, his unselfishness, and his devotion to his vocation won the admiration, respect, and affection of his many friends and colleagues. We extend to Dorothy, his widow, and their three children our sympathy in their grievous loss.—T. M.-G.

F. W. EARLE, M.R.C.S., L.R.C.P.

Dr. F. W. Earle, for many years in general practice in Garston, Liverpool, died on 11 October after a very short illness. He was 63.

Francis William Earle, son of William Kynsey Earle, was born on 18 September 1904. He was educated at Stonyhurst College and the University of Liverpool, from

which he qualified with the Conjoint diploma in 1928. He held house posts at the Royal Southern Hospital, Liverpool. After a brief period of postgraduate study in surgery, he spent much of 1931 with the New Zealand Shipping Line as ship's surgeon. It was while serving on T.S.S. *Devon* near Panama that he met with great resource the kind of desperate situation which occasionally falls to the lot of the lone doctor at sea. Help was sought from another ship for a Spanish seaman who had been stabbed in an affray. Francis Earle was rowed across to the foreign vessel, and with simple instruments and primitive facilities successfully repaired not only the abdominal wound but injured viscera as well. The letters of gratitude from the Spaniard are still treasured by his family. On returning to Liverpool Earle entered a partnership in general practice in Garston—an industrial and residential suburb of Liverpool—with its own busy accident hospital, the Sir Alfred Jones Memorial Hospital. Here he found scope for his surgical abilities, and he served the hospital with distinction until the reorganization brought about by the National Health Service. He met the formidable demands of his practice with characteristic calm, energy, and devotion, and on the death of his partner in 1961 he continued working single-handed.

After his work his absorbing interest from earliest days was in sailing. His yacht, *Spray*, was moored off Garston or off Anglesey, whence he sailed up and down the west coasts of England, Wales, and Scotland, and in Irish waters. He was a member of the Royal Mersey, Royal Dee, and Royal Anglesey yacht clubs, and often participated in the annual midnight race from the Mersey to the Isle of Man. It is characteristic of him that, ignoring menacing premonitory symptoms, he attended a navigation class on the evening before he died.

His passing is widely mourned by patients and colleagues alike. Close friends knew something of his loyal, self-sacrificing, and sustained endeavours on behalf of less fortunate colleagues. He was married to Maureen, daughter of the late Dr. W. F. McCann, of Liverpool, who survives him with a son and daughter.—R. W. B.

G. M. CLARK, M.B., B.S., D.OBST. R.C.O.G.

Dr. G. M. Clark, mission doctor in Tanzania, died suddenly on 23 October at Mnero Hospital, Tanzania. He was 40.

George Miles Clark, son of the late Dr. George Clark, of the Ministry of Health, was born on 2 February 1927, and received his medical education at University College Hospital, London, graduating M.B., B.S. in 1957, and taking the D.Obst.R.C.O.G. two years later. He held resident posts at University College Hospital, Perivale Maternity Hospital, Greenford, and Mundesley Hospital, Norfolk, before going out to Mnero Hospital, Nachingwea, Tanzania, a mission hospital in one of the more remote and poor parts of the country. His medical and surgical skill was rapidly appreciated by many grateful patients, and he was loved by a large number of the poor.

They appreciated in him a man of essential humanity, try as he often would to conceal this behind a self-effacing gruffness or a blunt Yorkshire turn of phrase.

Miles Clark was a good companion with no frills—"a foul-weather friend"—and his pithy descriptions of events which had befallen him were often masterpieces of narrative understatement. During his comparatively short life he had to fight adversity in many forms, and this he always did fearlessly, with the help of his Christian ideals coupled with a courageous sense of humour. The world, and particularly the underprivileged part where he spent his most fruitful days, can ill afford to lose so prematurely one so valuable. He truly spent himself before his time.

To his widow and his mother is extended deepest sympathy.—R. E. D.

**W. STEADMAN, M.C., M.R.C.S.
L.R.C.P.**

Dr. W. Steadman, formerly in general practice in Ledbury, Herefordshire, died in hospital on 22 October at the age of 75.

William Steadman was born on 14 December 1891, and received his medical education at University College Hospital, London, qualifying with the Conjoint diploma in 1916. He joined the R.A.M.C. and served in France, where he was awarded the Military Cross. After demobilization with the rank of captain he returned to University College Hospital and held resident posts there before entering general practice at Snettisham, Norfolk. In 1934 he joined the late Dr. Leslie Trotter in practice in Ledbury, and remained there until his retirement in 1959 to the house in Wales in which he was born.

Bill Steadman was a big kindly man, who won many friends among both his patients and his colleagues, and his hospitality and generosity were widely extended. He was a keen and a good shot, and a knowledgeable and successful collector of antique furniture. The latter years of his retirement were marred by ill-health, but were spent in the peaceful and beautiful countryside and home that he loved.

Our sympathy is offered to his wife, and to their daughter and son.—D. B.

**T. R. TROUNCE, M.R.C.S., L.R.C.P.
L.D.S.**

Dr. T. R. Trounce, a former general practitioner in Cheshunt, Herts, died on 2 October, aged 77.

Thomas Reginald Trounce was born at Waltham Abbey on 1 September 1890, and attended school at Holt House, Cheshunt, until the age of 15, when he was apprenticed to a dentist. In 1911 he qualified as a dentist, and, deciding to take up medicine, he entered Guy's Hospital, where he qualified with the Conjoint diploma in 1914. Serving as a houseman at the Royal Surrey County Hospital, Guildford, looking after casualties from France during the first world war, he met a nurse who was subsequently to become his wife—and partner in every sense of the

word. Joining the R.A.M.C., he served in Gallipoli at Suvla Bay, contracted paratyphoid in Alexandria, and was later posted to France. He was medical officer on a barge on the Somme, and later worked on an ambulance train based on Abbeville. After demobilization he returned to Guy's as house-physician and resident obstetrician. In 1919 he went into general practice as partner to Dr. Greene, of Cheshunt. The practice grew rapidly with the increase in population of the area, and there were six partners when Dr. Trounce retired in 1958.

He worked for much of his life under considerable physical handicaps, for in 1930 he developed syringomyelia affecting one hand, and received treatment at intervals throughout his life. He overcame this to such an extent that he was able to continue in practice until he retired at the age of 68. In this effort he was greatly aided by the untiring help and care given to him by his wife, who died after his retirement. As a doctor he was skilled in spite of his disability. He displayed wisdom and judgement in his decisions; he was infinitely patient, no demand, however trivial or unnecessary, upset him; he would answer a call at any time without demur. A devout Christian, with his kindness, gentle humour, and humility he had the gift of evoking affection in all who met him.—J. A. C.

S. B. REA, M.B., B.Ch., B.A.O.

Dr. S. B. Rea, anaesthetist at Carshalton War Memorial Hospital, died suddenly at Findon, in Sussex, on 24 May. He was 65.

Samuel Brown Rea was born in Belfast on 18 November 1901. He was educated at the Belfast Royal Academical Institution, and graduated M.B., B.Ch., B.A.O. at Queen's University, Belfast, in 1926. After an early appointment at the Royal Victoria Hospital, Belfast, he came to England and worked as an assistant in South London. In 1927 he went into practice in Sutton and Carshalton.

In 1941, at the relatively late age of 40, he volunteered for service and was commissioned in the R.A.M.C. From 1942 he served in the Indian and South-east Asian Commands, attaining the rank of major as a specialist anaesthetist. After demobilization he returned to his practice with the added interest of posts in anaesthesia at the Carshalton War Memorial Hospital and later at the Sutton General Hospital. Pressure of work coupled with ill-health forced him to relinquish his post of anaesthetist at Sutton General Hospital and later his general practice, but he continued his association with the Carshalton War Memorial Hospital until his final retirement.

Dr. Rea was respected by his colleagues both as an anaesthetist and as a general practitioner of the old school. He was a man of great personal integrity, and his life was moulded by a loyalty to his patients and his colleagues, and by a deep and sincere patriotism. He had an abiding interest in human relationships, and under a volatile and sometimes brusque exterior one was conscious of a deeply sensitive and even sentimental character. His relaxations were found in boating, music, and reading, and in the

company of his beloved family and of his friends. Our very sincere sympathy goes to his wife and to his daughter, who sustained this loss only a few short months after his retirement.—C. F. C.

M. B. GEE, M.B., CH.B., D.C.H.

Dr. M. B. Gee, a general practitioner at Barking, Essex, died suddenly at his home on 24 October, at the age of 38.

Michael Barnett Gee was born in London on 20 August 1929, and received his early education at Bournemouth School. He entered Bristol University, graduating M.B., Ch.B. in 1953, and held early house appointments at Southend and at the Royal Children's Hospital, Bristol, before joining the Royal Air Force and serving in Libya. After demobilization he undertook further hospital work in otolaryngology and paediatrics before taking the D.C.H. in 1958. He entered a busy partnership practice at Barking, and was also appointed school medical officer there.

In his teens Michael Gee was deeply interested in modern music, particularly that of Stravinsky and Bartok, and he became an accomplished pianist and clarinet player. He read a great deal, and introduced many of his friends to the works of the great writers and composers. Recently he had taken an interest in archaeology, becoming an associate of the Institute of Archaeology and taking part in archaeological field work. He combined many talents, but above all he was a first-rate and devoted family doctor.

He will be sadly missed by his colleagues and friends and by his patients. Our greatest sympathy is felt for his wife and three small children.—H. P.

**Sir ARCHIBALD GRAY, K.C.V.O.
C.B.E., T.D., LL.D., M.D., F.R.C.P., F.R.C.S.**

B. L. writes: His friends and admirers all over the world will feel a sharp sense of personal loss at the passing of Sir Archibald Gray (obituary, 21 October, p. 178). I knew Sir Archibald from 1933, and feel sure that my meeting with him was the vital factor in my becoming established as a dermatologist. He was so shy and modest that his almost startling integrity may have been misunderstood by some, but it was truly a godsend to anybody who, through race, creed, or sex, may have had difficulty in becoming established without his help. His courage was clearly shown towards the end of his life, when he refused to admit defeat in spite of being so greatly handicapped. Whoever had the benefit of his wonderful personality and teaching ability must give thanks for having known and loved this remarkable man.

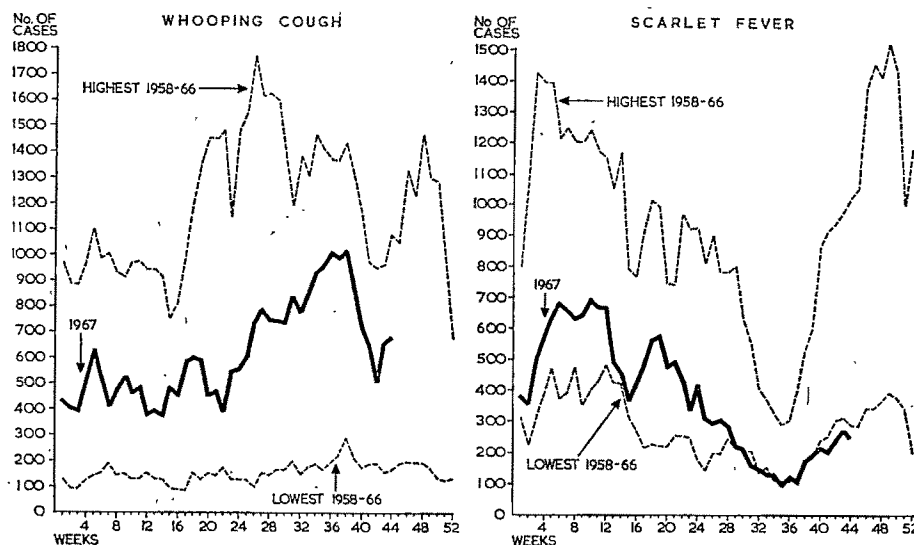
A memorial service for Dr. R. Hale-White will be held at St. Peter's Church, Vere Street, London W.1, at 12.30 p.m. on Monday, 11 December.

News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of whooping-cough and scarlet fever in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending	
	3 Nov.	10 Nov.
Dysentery		
Durham ...	9	44
Sedgefield R.D. ...	0	37
Lancashire ...	36	103
Walton-le-Dale U.D. ...	11	48
Preston R.D. ...	0	14
Warwickshire ...	18	24
Yorkshire West Riding ...	47	54
Glasgow ...	63	44
Edinburgh ...	10	15
Food-poisoning		
Buckinghamshire ...	0	22
Amersham R.D. ...	0	22
Devonshire ...	9	11
Greater London ...	29	30
Sussex ...	4	63
Hastings C.B. ...	1	63
Typhoid Fever		
Lewisham (London) ...	0	1
Bradford C.B. ...	1	2

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 4 November (No. 44) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	4	0		0	0	0	0	
Dysentery ..	246	31	129	3	6	372	71	107	8	3
Encephalitis, acute... ..	3	0		1		2	1		0	
Enteric fever: Typhoid ..	3	1	1	0		2	0	6	0	
Paratyphoid..	0	0	1B	0		3	0	1B	0	
Food-poisoning	168	29	38	4		112	24	9	0	
Infective enteritis or diarrhoea under 2 years				42	53				18	49
Measles* ..	1,338	77	24	14	68	8,804	1085	273	155	73
Meningococcal infection ..	2	0	0	0		6	1	2	1	
Ophthalmia neonatorum ..	13	1	0	0		9	2	0	0	
Pneumonia† ..	104	20	67	1	1	109	9	129	1	
Poliomyelitis, acute: Paralytic ..	0	0	0	0		0	0	0	0	
Non-paralytic ..	0	0	0	0		0	0	0	0	
Puerperal fever‡	77	24	1	2		67	28	7	0	
Scarlet fever ..	253	42	22	13	12	383	55	29	8	7
Tuberculosis: Respiratory ..	188	40	27	7		229	47	41	8	
Non-respiratory ..	26	5	1	2		35	4	8	2	
Whooping-cough	682	89	35	7	14	470	64	58	3	17
DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0	0	0		2	0	0	0	
Encephalitis, acute... ..				0						0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	0	3	0	0	0	0	0	0
Influenza ..	5	0	1	0	0	9	1	1	1	0
Measles ..	0	0	0	0	0	0	0	0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	600	107	18	9	10	650	105		14	9
Poliomyelitis, acute... ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0	0	0	0		0	0	0	0	0
Tuberculosis: Respiratory ..	27	4	2	0	4	43	3	0	0	2
Non-respiratory ..				0	2			0	0	
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	281	49	21	12	13	288	67	22	8	25
Deaths (excluding stillbirths)	10,209	1604	580	136	197	10,457	1644	562	128	181
LIVE BIRTHS	14,783	2437	833	245	498	15,472	2595	827	260	437
STILLBIRTHS	217	29	17			232	33	14		

* Measles not notifiable in Scotland whence returns are approximate

includes primary and influenza pneumonia

includes puerperal pyrexia

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then came Onadox-118...
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Paracetamol BP	500 mg
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for all conditions where relief of moderate to severe pain is required—and in the management of chronic rheumatic conditions when aspirin is contraindicated.

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Dihydrocodeine bitartrate (DF 118) has been widely used for a number of years as a powerful analgesic; it has no sedative or hypnotic properties.



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PARLIAMENT

Questions in the Commons

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Consultant Service Delays

Mr. H. BOARDMAN (Leigh, Lab.) asked the Minister of Health on 20 November if he was aware of the delays in the hospitals' consultant service and of the priority being given to fee-paying patients; and what action he proposed to ensure that priority is accorded strictly on medical grounds.

Mr. K. ROBINSON: "I am aware that there are some delays in obtaining appointments for non-urgent conditions at consultative outpatient departments, and that it may sometimes be possible to obtain a private consultation more quickly. I have no evidence, however, that patients who require hospital treatment without payment after a private consultation are allowed any priority greater than that appropriate to their medical condition, but I shall be glad to look into any particular case."

Dr. DAVID KERR (Wandsworth, Central, Lab.) asked how many part-time and full-time consultants, respectively, were appointed in each of the three latest years for which figures are available.

Mr. ROBINSON: Excluding senior hospital medical officers with allowances specially

regraded as consultants, the numbers appointed were as follows:

Year ending 30 September	Full-time	Part-time
1964	131	193
1965	194	236
1966	190	222

Hospital Doctors

Dr. JOHN DUNWOODY (Falmouth and Camborne, Lab.) asked how many doctors were employed in each grade as junior hospital doctors; and how many of each grade were on the temporary register.

Mr. ROBINSON: The numbers at 30 September 1966 were:

Grade	All staff	Staff on Temporary Register
Registrar ...	4,281	343
Junior Hospital Medical Officer	194	7
Senior House Officer	3,503	541
House Officer ...	2,374	150

Ampicillin

Mr. T. FORTESCUE (Liverpool, Garston, Con.) asked the Minister of Health whether he had yet received an assurance from a Dub-

lin firm that it had withdrawn from circulation the batch of drug labelled ampicillin but known to contain not ampicillin but penicillin V.

Mr. J. SNOW, Parliamentary Secretary: "Yes. The firm disputes the reported analysis but has informed me that each purchaser has been asked to return remaining supplies of the batch concerned and that these are being sent to independent analysts."

Questions in the Lords

Cervical Cancer Tests

LORD KENNET, speaking for the Ministry of Health in the House of Lords on 15 November, stated that the returns from hospital authorities in England and Wales showed that in June this year women were being tested for precancer of the cervix at a rate of nearly 119,000 a month, or over 1,400,000 a year. This showed an expansion of 17% over the figures for June 1966. The numbers of technicians trained in cytology, and in post in June this year, was 605, an increase of 32% in 12 months, though not all of these were employed full-time on routine cervical cytology. These numbers, he said, should be adequate to provide the service needed, but the distribution of technicians varied and there were some areas where more were needed.

MEDICO-LEGAL

No Damages for Negligence

[FROM OUR LEGAL CORRESPONDENT]

A hospital was found by the High Court to have been negligent in its treatment of a nightwatchman who had consumed arsenic, but in the absence of proof that the negligence had caused his death the nightwatchman's estate failed to recover damages from the hospital.

At about 5 a.m. on 1 January 1966 Mr. William Patrick Barnett, of West Norwood, London, drank tea with two fellow employees at the Chelsea College of Science and Technology, where he was employed as a night-watchman. The tea contained arsenic, which killed Mr. Barnett. At the inquest the verdict was murder by a person or persons unknown, no explanation of the presence of the arsenic being found.

Mr. Barnett's widow, suing as administratrix of her husband's estate, sought to establish a claim for damages against the Chelsea and Kensington Hospital Management Committee by reference to events between the tea-drinking and the subsequent death.

Within 20 minutes of drinking the tea all three men vomited and continued to vomit for three hours. At 8 a.m. Mr. Barnett drove his workmates and himself to St. Stephen's Hospital, Chelsea. There was no receptionist on duty, and they entered the

casualty department, where they saw a nurse whom they informed of their symptoms. During the interview Mr. Barnett lay across some chairs. The nurse telephoned the casualty doctor on duty, who said that he himself had been vomiting, and instructed that the men should be sent away and told to go to their own doctors.

Mr. Barnett drove the other two men back to the college, where he was seen in distress at various times in the morning by fellow employees. Finally, at 1 p.m. a fellow employee sent for the college doctor, and Mr. Barnett was sent by ambulance to St. Stephen's Hospital, but was found to be dead on arrival.

The duty owed by the hospital to these men differed from the duty owed to persons already admitted to hospital wards. No case bearing directly on the duty owed to persons presenting themselves at casualty departments before being treated or received into the wards was cited to the court. A hospital does not owe a common law duty to treat everyone or indeed anyone who presents himself to the casualty department. But this was not a case of a casualty department which had closed its doors. The men entered the department without hindrance, were interviewed by the nurse, who spoke to a doctor,

who replied with a message purporting to give advice. In these circumstances a relationship arose between the parties imposing on the hospital a duty of care toward the men.

The doctor fell short of his duty and was negligent. It was the view of the judge, on the evidence, that though a casualty doctor was not under a duty to see every caller at the department he should undoubtedly see a man who complained of vomiting for three hours. But the evidence had shown that the difficulties inherent in diagnosing arsenic poisoning would make diagnosis too slow to have done Mr. Barnett any good. If Mr. Barnett had been admitted tests might have eliminated an initial diagnosis of food poisoning in favour of a suspicion of metallic poisoning. Further tests would then have been necessary to identify the poison.

When death resulted from arsenical poisoning it was brought about by two conditions—dehydration and disturbance of the enzyme processes. In Mr. Barnett's case the principal trouble was enzyme disturbance. Only administration of B.A.L. (dimercaprol) was likely to succeed, and B.A.L. would not be used unless arsenic poisoning was specifically diagnosed. There was no real chance of it having been administered before Mr. Barnett died.

The plaintiff's action failed. (*The Times*, 9 November).

MEDICAL NEWS

O.M. for P.R.S.

Professor P. M. S. BLACKETT, President of the Royal Society, professor emeritus and senior research fellow of Imperial College, London, has been appointed to the Order of Merit.

Award of Royal Medal

Professor J. Z. YOUNG, F.R.S., has been awarded a Royal medal "for his outstanding researches correlating neural structure with function." Professor Young was demonstrator in zoology and comparative anatomy at Oxford University from 1933 to 1945. Since 1945, when he became a Fellow of the Royal Society, he has been professor of anatomy at University College, London.

The Royal medals are awarded annually by the Sovereign on the recommendation of the Council of the Royal Society.

Chair of Dermatology

Dr. PATRICK JAMES HARE has been appointed to the chair of dermatology at Edinburgh University. Dr. Hare, who is 47, received his medical education at University College, London, where he was



Andrew's Scholar, and at University College Hospital Medical School. He also studied at Johns Hopkins School of Medicine, Baltimore, as a Rockefeller Student. Graduating in 1944, he was in the Royal Army Medical Corps from 1945

to 1948 and served in Burma and Singapore. He took up his first appointment at University College Hospital as registrar in the department of dermatology in 1948. In 1951 he spent a year in postgraduate study in Paris and Zurich as a Travelling Fellow of London University. He was appointed a consultant in the department of dermatology at his parent hospital in 1952 and took charge of the department in 1958 when he also joined the staff of the Whittington Hospital. Last year he was exchange professor in the department of medicine at McGill University, Montreal. Dr. Hare is the author of *Basic Dermatology*, published in 1966. His London M.D. was awarded for a thesis on necrobiosis lipoidica. He has been editor of the *British Journal of Dermatology* since 1958. His interests include comparative pathology, embryology, and the history of medicine.

Gift to Hospital for Research

Through the Variety Club of Great Britain Mr. MICHAEL SOBELL, industrialist, is to give £100,000 to the Hospital for Sick Children, London, to promote research into the causes of congenital malformations. The club states that the gift will provide a floor of research laboratories in a new building at Great Ormond Street that will also accommodate a heart surgery unit for children. It is expected that the building will be opened in 1969.

Proposals for Hospital Transfer

At a meeting in London on 13 November the North-west Metropolitan Regional Hospital Board approved proposals that will, with the approval of the Ministry of Health, result in the transfer of Paddington General and the National Temperance Hospitals from the board's management to that of the boards of governors of St. Mary's and University College Hospitals respectively, and the transfer of New End Hospital, Hampstead, and Coppetts Wood Hospital, Hornsey, to the control of the Royal Free Hospital board of governors.

Royal College of Surgeons of Edinburgh

At a dinner held in the Royal College of Surgeons of Edinburgh on 11 November in connexion with the opening of the Lister Institute of Postgraduate Medical Education and Research earlier in the day (see *B.M.J.*, 18 November, p. 430) diplomas of Honorary Fellowship were presented to LORD FLOREY OF ADELAIDE, Provost of Queen's College, Oxford, and Chancellor of the National University of Australia, and to Professor MICHAEL M. SWANN, Principal and Vice-Chancellor of the University of Edinburgh.

Royal College of General Practitioners

The annual dinner of the Royal College of General Practitioners was held in London on 17 November. The toast of the College was proposed by the Rt. Hon. KENNETH ROBINSON, M.P., and replied to by Dr. ANNIS GILLIE. The Guests were proposed by Dr. H. N. LEVITT and replied to by LADY STOCKS.

Heberden Society

With its president, Dr. OSWALD SAVAGE, in the chair, the Heberden Society held its annual dinner at the Royal College of Physicians on 17 November. The dinner was attended by a sizable contingent of members of the Ligue Française contre le Rhumatisme with their wives. Proposing the society's toast, Sir MAX ROSENHEIM P.R.C.P., said that the Royal College of Physicians had emphasized the need for all district hospitals to have facilities for rheumatology. Dr. SAVAGE replied for the society and afterwards presented the Heberden medal. The toast of the guests was proposed by Dr. J. A. COSH, and Dr. P. ORDONNEAU, president of the Ligue, replied. Afterwards Dr. J. P. D. MOUNSEY, speaking in French, gave the visitors a short history of the College.

British Tay-Sachs Foundation

An organization has been set up to provide funds for research into Tay-Sachs disease and other allied storage conditions. Laboratory accommodation is being made available at the Hospital for Sick Children, Great Ormond Street, London W.C.1.

Anti-smoking Education Campaign

A new organization, the British Anti-Smoking Education Society (6 Coptic Street, London W.C.1), has been formed by a group of doctors to promote research into cigarette habituation. It also plans to establish a continuing programme of popular education giving the latest data on the effects of smoking on health. Other major aims include the banning of cigarette advertising and of smoking in public places. A pamphlet

initiating the campaign and inviting financial support is being sent to doctors throughout the country. Dr. J. L. BURN, medical officer of health for Salford, is president of the society. The treasurer is Mr. T. W. HURST, secretary and treasurer of Edinburgh Royal Infirmary.

Disabled at Work

Remploy Ltd., the Government-subsidized company that employs the severely disabled, now runs 87 factories in all parts of England, Scotland, and Wales. Last year it provided work for 6,852 people. According to the chairman's annual report 24% suffered from injuries and diseases of the head, trunk, and limbs; 17% from diseases of the lungs, including tuberculosis; 21% from mental and nervous disorders; and 10% from epilepsy. The company has temporarily suspended recruitment as a result of the Government's deflationary measures. Sales for the year ended March totalled £7,790,000, an increase of £72,000.

Monopoly Inquiry

Revised terms of reference, announced on 13 November by Mr. ANTHONY CROSLAND, President of the Board of Trade, confer wider powers on the Monopolies Commission in its investigation of restrictive practices affecting professional services (see *B.M.J.*, 11 February, p. 376). They enable the Commission to examine practices authorized by or under Royal Charter, or authorized by or under any statute enacted before 1 January 1956. The Board's original request, made on 30 January, excluded the investigation of practices expressly authorized by or under any enactment or Royal Charter.

People in the News

► Professor A. C. P. CAMPBELL has been reappointed dean (part-time) of the medical school at Manchester University from 1 January to 31 December 1968.

► Professor HENRY MILLER has succeeded the late Dr. HUGH GARLAND as chairman of the medical panel of the Multiple Sclerosis Society of Great Britain and Northern Ireland.

News in Brief

After 1 January 1969 all candidates for membership of the Australian College of General Practitioners will be required to take the examination of the College. The examination for membership is at present optional.

Grants and Awards

Research grants for 1967 totalling £243,198 have been announced by the National Fund for Research into Crippling Diseases.

Recent Publications

Notes on the Mental Health Act, 1959, by CECIL W. FRENCH, chief mental welfare officer to the Bedfordshire County Council: Shaw and Sons Ltd., 7-9 Fetter Lane, Fleet Street, London E.C.4, price 2s. (by post 2s. 6d.).

Taxation and Welfare, by ARTHUR SELDON, a research monograph, published by the Institute of Economic Affairs, Eaton House, 66a Eaton Square, London S.W.1, 7s. 6d.

Programmes in the Health Sciences, a bibliography of published self-instructional material for dental, medical, and nursing students. Copies can be ordered from the Secretary, National Centre for Programmed Learning, Birmingham University, 10s. (by post 10s. 6d.).

Revised edition of *A Symposium on the Role of Fluoride in Preventive Dentistry*, with references and select bibliography. Prepared by

the Oral Hygiene Service, P.O. Box 1DY, Hesketh House, Portman Square, London W.1.

The November issue of the magazine *World Health* is in the form of an illustrated calendar for 1968, W.H.O.'s 20th anniversary year. H.M.S.O., 3s. 6d. (postage 6d.).

Coming Events

Postgraduate Medicine, 1967 (T.V. Programme).—"Intrauterine Growth," Scottish Television, 27 November (11.50 p.m.), repeat 29 November (1.10 p.m.). "Advances in Therapy," Tyne Tees Television, 28 November (1.15 p.m.), repeat 3 December (10.15 a.m.).

Royal College of Physicians of London.—Christmas lectures for young people: "What it Takes to be a Doctor," by Dr. JOHN ANDERSON, 4 January, 3.30 p.m.; "The Breeding of Butterflies and Moths as a Background to Some Medical Research," by Dr. C. A. CLARKE, 9 January, 3.30 p.m. Applications by 1 December to Secretary, R.C.P., 11 St. Andrew's Place, Regent's Park, London N.W.1.

King Edward's Hospital Fund for London.—Conference, "Building and Environmental Services for Hospital Laboratories," 13 December, Hospital Centre, 24 Nutford Place, London W.1. Fee £1 (including lunch and tea). Applications by 4 December.

British Medical Association and Institute of Mathematics and its Applications.—Joint symposium on mathematical and computer methods in medicine, 6 December, 10.30 a.m., B.M.A. House. Registration fee 15s. (members), £2 (non-members). Fee includes hamper lunch and tea. Registration forms from Secretary, British Medical Association, Tavistock Square, London W.C.1.

Symposium on Blood Diseases for Consultants and Registrars.—7 December, Lewisham Hospital, London S.E.13. Details from Dr. J. S. STAFFURTH, Lewisham Hospital.

University of Cambridge School of Clinical Research and Postgraduate Medical Teaching.—Introductory course on the biology of skin, 11–16 December, Churchill College. Details and registration forms from Secretary, Cambridge University Medical School, Tennis Court Road, Cambridge.

Societies and Lectures

For attending lectures marked Ⓢ a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 27 November

CAMBRIDGE SOCIETY FOR THE STUDY OF COMPARATIVE MEDICINE.—At School of Veterinary Medicine, 8 p.m., Professor I. H. Mills: Physiological Aspects of Renal Disease.

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Dr. B. Strickland: The Deceptive Chest X-ray.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., combined staff consultation clinical meeting.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. W. R. G. Thomas: Mycoplasma; 6.30 p.m., Dr. L. O. Butler: Mode of Action of Antibiotics.

MANCHESTER MEDICAL SOCIETY: SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Manchester University Medical School, 9 p.m.,

Professor Keith Simpson: What To Do With a Dead Body.

MANCHESTER MEDICAL SOCIETY: SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital, 5.30 p.m., Professor I. Möller (Denmark): Topical Application of Fluorides.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Professor T. A. J. Prankerd: Chemical Factors in Haemolytic Anaemia.

SCOTTISH TELEVISION LTD.—11.45 p.m., Intrauterine Growth. (Sponsored by Glasgow Postgraduate Medical Board.)

Tuesday, 28 November

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. V. Eisen: Kinin Formation in Human Disease.

HACKNEY HOSPITAL POSTGRADUATE INSTITUTE.—At Nurses' Classroom, 8.45 p.m., Professor W. Linford Rees: Schizophrenia.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Dr. W. B. Robertson: Physiological Changes and Pathological Lesions in the Spiral Arteries.

LONDON UNIVERSITY.—At University College, 5.30 p.m., special university lecture in genetics—I by Dr. S. Brenner: Genetic Aspects of the Code.

NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., Dr. J. N. Harris-Jones: Diagnosis of Thyroid Disorders.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. A. G. Cox: Surgical Aspects of Malabsorption.

ROYAL STATISTICAL SOCIETY.—At Manson Theatre, London School of Hygiene and Tropical Medicine, 5 p.m., Dr. A. E. Bennett: Population Studies in Lambeth.

Wednesday, 29 November

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Professor C. D. Calnan: The Sebaceous Gland.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. N. R. Barrett: Oesophageal Hernia.

INSTITUTE OF NEUROLOGY.—6 p.m., Mr. V. Logue, and 7 p.m., Dr. H. Davison: Cerebrospinal Fluid—Hydrocephalus and Mechanics.

INSTITUTE OF UROLOGY.—5 p.m., Mr. R. T. Turner-Warwick: Urethral Stricture.

OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Dr. E. Gordon Smith and Dr. J. Holt: Changes in the Retina in Diseases of the Blood.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—5 p.m., Sir James Young Simpson memorial lecture by Professor T. C. Gray: Dilectus Suis Somnum.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 11.45 a.m., clinicopathological conference by Professor H. Miller, Professor K. Weinbren. (2) 2 p.m., Professor L. G. Whitby: Well Population Screening.

SCOTTISH TELEVISION LTD.—1 p.m., Intrauterine Growth. (Sponsored by Glasgow Postgraduate Medical Board.)

STORIE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. G. D. Hadley: Recent Advances in Gastric Diagnosis. (2) 6 p.m., Group Captain R. Mortimer: Worms.

WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Dr. A. M. Dawson: Disturbances of Carbohydrate Absorption in Man.

WHITTINGTON HOSPITAL.—At Academic Centre, Archway Wing, London N., 11.30 a.m., Professor H. E. de Wardener: Calcium Metabolism in Chronic Renal Failure.

Thursday, 30 November

ABERDEEN UNIVERSITY FACULTY OF MEDICINE.—At Large Lecture Theatre, University Medical Buildings, Foresterhill, 5 p.m., Dr. M. F. Oliver: Intensive Coronary-care Units.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. D. A. Price Evans: Genetic Factors in Drug Therapy.

DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Dr. P. D. Griffiths: Creatine Kinase in Clinical Medicine.

FACULTY OF HOMOEOPATHY.—5 p.m., Dr. Mary Y. McA. Stevenson: Comments on Foods and Related Homoeopathic Remedies.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—2.30 p.m., film, with discussion by Dr. B. W. Meade and Dr. F. R. Ellis: Long-term Care after Partial Gastrectomy.

LIVERPOOL UNIVERSITY MEDICAL STUDENTS SOCIETY.—At Anatomy Building, Surgery Lecture Theatre, Old Medical School, 5.15 p.m., B.M.A. lecture by Professor A. W. Kay: Surgical Lessons on Diarrhoea.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At 11 Chandos Street, London W., 8.15 p.m., Dr. M. H. Lessof: Immune and Autoimmune Disorders.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. I. A. Sewell: An Experimental Approach to Circulation in the Tissues.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 4 p.m., Mr. W. P. Cleland: Management of Chest Injuries. (2) 5 p.m., lecture on medical

history by Dr. E. S. Clarke: History of Microbiology.

ROYAL STATISTICAL SOCIETY: SHEFFIELD GROUP.—At Hicks Building, Sheffield University, 7 p.m., Professor D. J. Newell: Problems in Estimating the Demand for Hospital Beds.

RUNWELL HOSPITAL.—At Wickford, Essex, 8 p.m., Dr. J. W. Mack: Research into Response to Anti-depressant Drugs.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Professor J. D. Martin (Perth, W. Australia): Retarded Intrauterine Growth of the Fetus.

WESTMINSTER MEDICAL SCHOOL.—At Keene Lecture Theatre, (1) 5.15 p.m., surgical conference by Lieutenant-Colonel S. H. Janikoun: Surgery in the Far East; (2) 6.45 p.m., Dr. C. M. Conway: Comparative Studies into the Haemodynamic Effects of Some Intravenous Anaesthetic Agents.

Friday, 1 December

BROOK GENERAL HOSPITAL.—5.30 p.m., Dr. P. Blackledge: Treatment of Meningitis.

KENT POSTGRADUATE MEDICAL CENTRE AT CANTERBURY.—At Kent and Canterbury Hospital, 8 p.m., scientific lecture on man and his environment by Dr. W. R. S. Doll, F.R.S.: Environmental Cancer.

LONDON UNIVERSITY.—At University College, 5.30 p.m., special university lecture in genetics—II by Dr. S. Brenner: Genetics of Regulation in Bacteria.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—5.30 p.m., clinicopathological conference with cases from St. Thomas's Hospital.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—(1) 12 noon, Mitchell lecture by Dr. N. Lloyd Rusby: Pulmonary Tuberculosis—Present Management and Future Prospects; (2) 5 p.m., Oliver Sharpey lecture by Dr. R. W. D. Turner: Controversial Aspects of Rheumatic Heart Disease.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., The Forward Look in Operating-theatre Design. (2) 4 p.m., lecture by Professor A. S. V. Burgen.

WEST MIDDLESEX HOSPITAL.—4 p.m., Dr. G. I. M. Swyer: Sex Hormone Therapy.

Sunday, 3 December

EDGEWARE POSTGRADUATE MEDICAL SOCIETY.—At Edgware General Hospital, 10.30 a.m., Professor M. D. Milne: New Concepts of Glomerulonephritis.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—10.15 a.m., seminar for general practitioners by Mr. A. Radcliffe.

ROYAL COLLEGE OF GENERAL PRACTITIONERS: EAST ANGLIA FACULTY.—At Dukes Head Hotel, King's Lynn, 10 a.m., symposium: Practical Aspects of Abortion Law Reform.

Appointments

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—A. N. Cruickshank, M.R.C.S., F.F.A.R.C.S. (consultant anaesthetist, Ipswich group of hospitals); J. M. Collis, M.B., F.F.A.R.C.S. (consultant anaesthetist, Papworth and Addenbrooke's hospitals); Cicely Pepler, M.B., F.R.C.S. (consultant orthopaedic surgeon, Norwich, Lowestoft, and Great Yarmouth group of hospitals); J. S. R. Baxter, M.B., F.R.C.S. (consultant B.N.T. surgeon, King's Lynn, Wisbech, and Duddington areas).

KING'S COLLEGE HOSPITAL, Denmark Hill, London S.E.—M. Harris, M.B., F.D.S.R.C.S., G. H. Forman, M.B., F.D.S.R.C.S. (consultants in dental surgery); D. A. Packham, M.B., F.R.C.S. (consultant urological surgeon).

MINISTRY OF OVERSEAS DEVELOPMENT.—J. L. Craven, M.D., F.R.C.S. (senior registrar in Uganda).

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—N. N. Jaswon, M.D., M.C.Path. (consultant pathologist to Forest group of hospitals); H. L. Young, M.B. (medical assistant in B.N.T. surgery to Ilford and District group of hospitals).

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—R. A. Haddow, M.B., M.R.C.P.Ed., F.F.R. (consultant radiologist at Barnet General Hospital); Eva Hamik, M.D., F.F.A.R.C.S. (consultant anaesthetist at Central Middlesex, Acton, and Neasden Hospitals); E. D. R. Campbell, B.M., M.R.C.P., D.Phys.Med. (consultant in physical medicine at Cell Barnes Hospital); U. B. H. Baruch, M.D., D.P.M. (consultant psychiatrist at St. Bernard's Hospital and Ashford Hospital).

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—C. B. Hobbs, M.B., M.C.Path. (consultant chemical pathologist, Bath clinical area); J. J. Kelly, M.B., F.R.C.S.Ed. (consultant orthopaedic surgeon, North Gloucestershire clinical area); M. A. Voyce, M.B., M.R.C.P.Ed., D.C.H. (consultant paediatrician, West Cornwall clinical area); Eileen M. Welcher, M.B., F.F.A.R.C.S. (consultant anaesthetist, Devon and Exeter clinical area (Torquay)).

TURNER-WARWICK, R. T., D.M., M.Ch., F.R.C.S. (visiting honorary consultant urologist to King Edward VII Memorial Hospital, Bermuda).

UNITED MANCHESTER HOSPITALS.—G. Howitt, M.D., M.R.C.P. (consultant cardiologist with a special interest in cardiac physiology).

Universities and Colleges

CAMBRIDGE

M.CHIR.—I. D. Hunter-Craig.
M.B., B.CHIR.—M. T. C. Mower.
M.B.—C. H. Gallimore, *S. R. Bloom, J. F. Gordon, D. I. Johnston, D. R. Tant, *D. G. Garden.

*By proxy.

GLASGOW

M.D.—J. Guthrie (with commendation).
Ph.D.—In the Faculty of Medicine: C. G. Pierrepont.

ABERDEEN

Appointments.—Dr. F. Walker, Dr. F. L. Archer, (senior lecturers, Department of Pathology); Dr. O. A. Haugen (lecturer, Department of Pathology); Mr. W. H. H. Garvie (senior lecturer, Department of Surgery); Dr. Mary B. Hector (part-time lecturer, Department of Pathology); Dr. M. H. Wittenborg (visiting fellow, Department of Anatomy); Professor B. M. V. Shetty (visiting fellow, Department of Pathology); Dr. A. K. Webster (terminable lecturer, Department of Pathology); Dr. Violet Anderson (assistant medical officer, Student Health Service).

EDINBURGH

Ph.D.—In the Faculty of Medicine: *A. Q. S. Bukhari, *E. S. G. Hettiaratchi, I. M. Negm, A. Omer, *C. Vejbæysa.
M.B., Ch.B.—D. S. Gordon, S. MacG. Hall, I. W. Young.

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—A. P. Argyropoulos, E. R. Jay, G. E. Mylne.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—M. O. Akindele, R. L. Cundall, A. W. Kushner, S. K. Littmann, J. Oluwole.

*In absentia.

Appointments.—Drs. J. Bedel, E. W. J. Cameron, A. G. S. Tulloch, J. M. Monaghan, N. H. Hills, G. S. Watson (temporary demonstrators, Department of Anatomy); Dr. J. Wilson (lecturer, Department of Dental Surgery); Dr. L. I. Zander (lecturer, Department of General Practice); Dr. P. W. Brunt (temporary lecturer, Department of Medicine (Western General Hospital)); Dr. J. P. A. McManus (senior lecturer, Department of Medicine (Western General Hospital)); Dr. W. H. Price (half-time lecturer, Department of Medicine (Western General Hospital)); Mr. F. R. Clark (part-time lecturer, Department of Obstetrics and Gynaecology); Drs. Helen L. Cameron and D. Smith (part-time lecturers, Department of Orthopaedic Surgery); Miss Ruth Wynne-Davies (senior lecturer, Department of Orthopaedic Surgery); Dr. R. M. Milne (lecturer, Department of Pathology); Dr. E. S. Johnson (lecturer, Department of Pharmacology); Dr. R. M. Watt (demonstrator, Department of Physiology); Dr. R. C. Burgess (part-time lecturer, Department of Social Medicine); Mr. J. G. Clark (lecturer, Department of Surgical Science).

LONDON

The following have been appointed or re-appointed as representatives on schools of the University indicated in parentheses: Dr. C. F. Harris (Board of Management of London School of Hygiene and Tropical Medicine); Professor W. J. Hamilton (council of Royal Veterinary College); Dr. C. F. Harris (Council of School of Pharmacy).

Dr. J. R. May has been appointed to the readership in bacteriology tenable at the Institute of Diseases of the Chest.

Dr. P. Trexler has been appointed to the readership in veterinary gnotobiotics tenable at the Royal Veterinary College.

The following have been appointed recognized teachers of the University in the subjects indicated in parentheses: *Imperial College of Science and Technology*, Dr. C. G. Caro (experimental medicine); *Charing Cross Hospital Medical School*, Dr. R. E. W. B. Comerford, Dr. T. B. L. Roberts (anaesthetics). *King's College Hospital Medical School*, Dr. J. W. Laws (diagnostic radiology); Dr. V. Parsons (medicine); Dr. D. E. H. Tee (experimental pathology); Dr. K. J. Zilkha (neurology). *Royal Free Hospital School of Medicine*, Dr. I. A. D. Bouchier (medicine). *St. George's Hospital Medical School*, Dr. K. C. Carstairs (pathology (haematology)); Dr. H. J. W. Cleeve (chemical pathology); Dr. J. N. Harcourt-Webster (pathology); Dr. I. H. Kerr (diagnostic radiology); Dr. P. B. Storey (psychiatry); Mr. K. W. Wilkinson (sur-

gery). *St. Thomas's Hospital Medical School*, Dr. M. A. Barraclough (medicine); Dr. F. J. Imms, Dr. M. T. Jones (physiology). *University College Hospital Medical School*, Dr. C. J. Edmonds, Dr. A. N. Exton-Smith (medicine); Dr. G. M. Stern (neurology); Dr. H. H. O. Wolff (psychiatry). *Westminster Medical School*, Dr. S. Feldman (anaesthetics); Dr. J. B. MacGillivray (pathology); Dr. J. K. Oates (venereal diseases). *Royal Postgraduate Medical School*, Dr. E. D. Williams (pathology).

The Hazely Clifford postgraduate studentship for 1967-8 has been awarded to Dr. Daphne A. Roe.

The Mary Scharlieb research studentship for 1967-8 has been re-awarded to Mr. S. J. Lam.

The A. H. Bygott scholarship for 1967-8 has been awarded to Dr. Elizabeth S. Harper.

M.D.—A. D. F. Hurdle, J. C. Crawhall.
Ph.D.—In the Faculty of Medicine: R. C. D. W. D. Bandaranayake, M. A.-R. Moustafa, A. K. G. Nasser, A. Skarbek, G. T. Tucker, L. S. Wiggart.

The following candidate at the London School of Hygiene and Tropical Medicine has been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN TROPICAL PUBLIC HEALTH.—M. I. Fazal.

MANCHESTER

Appointment.—Mr. N. H. Mahindrakar (lecturer in otolaryngology); Dr. P. G. Lynch (lecturer in neuropathology); Dr. G. B. W. Tait (lecturer, clinical section of Rheumatism Research Centre).

WALES

WELSH NATIONAL SCHOOL OF MEDICINE
Appointments.—Mr. A. H. B. de Bono (lecturer in surgery); Dr. D. K. Peters (lecturer in medicine); Dr. C. J. Roberts (lecturer in social medicine).

BIRMINGHAM

The title of university clinical lecturer has been conferred on Dr. S. P. Singh, consultant cardiologist to the United Birmingham Hospitals and to the Birmingham Regional Hospital Board.

The following have been appointed honorary postgraduate clinical tutors: Dr. B. H. Bass, Good Hope Hospital, Sutton Coldfield; Mr. H. Roberts, for the Maternity and Women's Hospitals, Birmingham.

The title of assistant clinical tutor in the Department indicated in parentheses has been conferred on the following for the period of their service in the United Birmingham Hospitals: Dr. R. Cockel (medicine); Dr. J. D. Goode, Dr. G. Hall-Davies, and Mr. W. J. C. C. Rich (rheumatology); Dr. D. Riddoch (neurology); Mr. K. M. Simpson (surgery); Dr. R. A. Thompson, Dr. J. E. J. Yates (immunology).

The title of honorary research fellow has been conferred on the following for the period of their work in the university: Dr. J. A. Kiernan, who has been awarded a junior research fellowship by the Medical Research Council, tenable in the Department of Anatomy; Dr. J. F. Harrison, consultant physician at the Selly Oak Hospital who is working with Dr. J. D. Blainey in the Department of Experimental Pathology; Dr. T. A. Betts, who is working in the Department of Psychiatry, on problems of epilepsy.

Appointments.—Dr. M. J. Andrews, Dr. J. E. D. MacLaren, Dr. M. J. McMahon (temporary lecturers, Department of Anatomy); Dr. G. Harris (lecturer, Department of Experimental Pathology); Dr. P. J. K. Maskery (acting first assistant to the professor of obstetrics and gynaecology); Dr. N. Williamson (lecturer, Department of Experimental Pathology).

NOTTINGHAM

Appointments.—Dr. D. Hopwood (senior lecturer, Department of Human Morphology); Dr. P. H. Fentem (senior lecturer, Department of Physiology).

SHEFFIELD

Appointments.—Dr. D. A. Aitken (part-time clinical teacher in obstetrics and gynaecology); Dr. Gwendoline R. Barer (part-time lecturer in medicine); Dr. E. G. Oram (part-time honorary postgraduate clinical tutor (Nottinghamshire)); Dr. J. Pullar (lecturer in Student Health Service); Dr. J. Flynn (lecturer in medical microbiology).

ROYAL COLLEGE OF PHYSICIANS OF
EDINBURGH

At the quarterly meeting of the College held on 7 November 1967, the following were elected members of the College:

J. D. Dow, A. D. Forrest, I. I. Abu-Sabra, J. G. Reid, S. K. Mandal, A. Ashraf, S. K. Roy, R. Prasad, A. H. Barlas, D. M. Morgan, P. M. Barnes, S. Hazra, T. Kumarasamy, M. O. El Motasim, A. M. Hazell, S. Agarwala, S. K. Mukherjee, M. Nuruzzaman, M. A. Menon, R. Rao, M. B. Gharipour, D. V. Khare, D. L. Singh, A. Jamil, S. Mitra, C. Y. Yeung, D. P. Jham, N. Kethari, A. Ahmad, N. Arumugam, G. A. Noori, J. M. Wilner, T. O. Cole, A. J. Gordon, A. F. B. Mabadeje, P. A. Berger, R. J. Purvis.

ROYAL COLLEGE OF GENERAL
PRACTITIONERS

At the Annual General Meeting of the College held on 18 November, Dr. John H. Hunt was elected President. At the first meeting of the new Council Dr. G. Swift was elected Chairman, Dr. J. A. R. Lawson Vice-chairman, and Dr. J. Owen Deputy Vice-chairman. Dr. B. C. S. Slater was re-elected Hon. Secretary and Dr. S. Carne was re-elected Hon. Treasurer.

At the Annual General Meeting Professor J. C. van Es, of the Institute of General Practice in Utrecht, was elected an Honorary Fellow.

Dr. E. V. Kuenssberg was awarded the Foundation Council Award.

The following were elected as the first Fellows of the College.

United Kingdom: S. I. Abrahams, C. D. Baker, H. G. Barnes, C. H. D. Bartley, L. W. Batten, F. A. Bevan, A. Brown, J. F. Burdon, R. C. Durton, P. S. Byrne, L. S. Calvert, F. S. Catto, J. G. R. Clarke, J. M. Clow, S. N. Cole, J. Cottrell, R. Cove-Smith, J. D. Craig, D. Crombie, T. L. Dowell, T. S. Eimerl, H. H. Elder, S. Freeman, D. G. French, J. Fry, E. Gancz, W. S. Gardner, R. G. Gibson, N. D. Gofton, D. G. Gordon, J. H. Grove-White, N. Guest-Gornall, B. Halfpenny, J. M. Henderson, E. B. Hickson, E. G. Housden, W. V. Howells, J. H. Hunt, W. H. Hyllton, W. F. Jones, P. G. S. Kennedy, E. V. Kuenssberg, A. Lamont, L. Lamont, J. A. R. Lawson, F. H. Lee, H. N. Levitt, G. S. R. Little, Freda M. Lucas, R. M. S. McConaghey, G. L. McCulloch, T. S. MacDonald, W. S. Macgowan, M. Marcus, J. G. Ollerenshaw, J. M. Parry, D. Peebles Brown, R. A. B. Rorie, J. Sanctuary, I. M. Scott, R. A. Murray Scott, R. Scott, A. Smith, G. Swap, G. Swift, W. G. Tait, Lord Taylor, G. I. Watson, C. A. H. Watts, D. G. Wilson, F. B. Winfield; Ireland: A. S. Boyd, J. C. C. Crawford, V. G. Doyle, S. Flannery, F. Fleetwood, K. Forsythe, I. Hooper, J. M. Hunter, J. P. Little, G. Maguire, R. P. Maybin, E. J. O'Brien, R. A. M. B. Simpson, J. C. Walsh, N. D. Wright; New Zealand: A. Aitken, A. Borrie, W. H. Brockett, D. C. Campbell, T. Childs, W. N. Clay, P. Delaney, D. J. A. Gallagher, M. Kronfeld, W. R. Lang, J. D. Lough, E. J. Marshall, C. L. E. L. Sheppard, R. P. Tuckey, H. E. S. Williams, T. K. Williams; Australia: H. S. Patterson; South Africa: F. E. Hofmeyer, N. Levy, W. A. M. Miller; Kenya: T. Hedley White, R. H. Wiseman.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Atitology*, London W.C.1. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 2 DECEMBER 1967

Pointers

Renal Glucose Threshold: This varies considerably with age and is an unreliable index in diabetic detection surveys (p. 505).

Treating Arrhythmias: Beta-adrenergic drugs of value for treating cardiac arrhythmias, but do not appear to have a prophylactic effect in reducing arrhythmias after acute myocardial infarction (p. 508).

Folate Deficiency in Mentally Ill: Common enough to justify routine testing on admission (p. 512).

"Subvitaminosis C": Leucocyte ascorbic acid levels significantly low in surgical patients with gastroduodenal disorders, especially duodenal ulcer. Vitamin C supplements advised pre- and postoperatively (p. 516).

Bethanidine for Hypertension: Fair to good long-term control and relative freedom from side-effects confirmed (p. 519).

Genetic Counselling in Muscular Dystrophy: Serum level of creatine kinase found to be elevated in 50% of definite carriers of Becker type X-linked muscular dystrophy (p. 522).

Phocomelia: In twins whose mother had no thalidomide in pregnancy (p. 524).

Polyposis Coli: ABO grouping suggests that papillary adenomas have a different aetiology from adenomatous polyps (p. 526).

Foot-and-Mouth in Man: Farmer affected (p. 529). Leader on differential diagnosis (p. 503).

Other Reports: Achilles tendon reflex time and blood sugar levels (p. 528); Recurrent tetanus (p. 530); Surgery on a haemophilic with cryoprecipitate therapy (p. 531); Intestinal obstruction and perforation after eating clothing (p. 532).

Carcinoma of the Stomach: Symptoms, diagnosis, and treatment considered (p. 533).

Today's Drugs: Allantoin (p. 535).

Apothecaries' 350th Anniversary: History and pictures (p. 540).

Appointment Systems in General Practice: About one-third of N.H.S. general practitioners now use Appointment Systems Service (p. 542). Fair time-keeping by immigrants in a practice described (p. 544). Leader at p. 500.

R.C.G.P.: Annual meeting (p. 546).

A.B.P.I.: Defence of brand names (p. 549).

Motoring: Wankel rotary engine (p. 561).

G.M.S. Committee: Planning unit's proposals and drugs legislation discussed (*Supplement*, p. 59).

Jaundice of Pregnancy

Obstructive cholestatic jaundice appearing in the last trimester of pregnancy has been called idiopathic hepatopathy of pregnancy,¹ *hépatite bénigne de la grossesse*,² and idiopathic jaundice of pregnancy.³ Perhaps recurrent intrahepatic cholestatic jaundice of pregnancy is the most appropriate term.^{4 5}

Many patients experiencing generalized itching in the last weeks of pregnancy may be suffering from this condition, for jaundice is rarely deep and may be inapparent. So the physician should seek evidence of dark urine and pale stools. After delivery pruritus ceases, and in one to two weeks the jaundice disappears. The condition is apt to recur in subsequent pregnancies.

The serum shows an increase in conjugated bilirubin and alkaline phosphatase. Serum transaminase levels are normal or slightly increased, but occasionally very high values are found. Needle biopsy of the liver shows mild focal and irregular bile stasis. Hepatocellular necrosis and cellular reaction are absent. Electron-microscopy shows the dilatation, blunting, and swelling of the microvilli which is constantly found in all forms of cholestasis.⁶ The jaundice is probably due to an unusual cholestatic reaction to a steroid produced in pregnancy. Whether this is an unusual response to a natural steroid or caused by the production of an unknown cholestatic steroid remains uncertain. Changes in oestrogen metabolism are more likely to be secondary to the jaundice and the circulation of oestrogens in the liver than a primary defect.⁷

Normal women in the last trimester show increased difficulty in transfer of the test substance bromsulphalein into the biliary canaliculi. Bilirubin is in many ways analogous to bromsulphalein, and the response in recurrent cholestatic jaundice of pregnancy may be an exaggeration of the normal one. Moreover, natural oestrogens in large doses also cause abnormalities in the transfer of bromsulphalein.⁸ There is also an association between jaundice after administration of an oral contraceptive and the intrahepatic cholestasis of pregnancy. About 100 cases of jaundice from oral contraceptives have been reported. In the largest series, 50 Chilean patients, the clinical, biochemical, and microscopical findings bore a strong resemblance to those of cholestatic jaundice of pregnancy.⁹ Forty of these 50 patients had previously been pregnant, during which 17 had suffered jaundice and pruritus and ten late pruritus only. Oral contraceptives cause a fall in bromsulphalein transport when given to normal non-pregnant women,¹⁰ and they may produce the histological appearances of intrahepatic cholestasis.¹¹ A familial incidence has been reported in relation to one patient who was affected by recurrent intrahepatic cholestasis of pregnancy and who developed cholestasis when given an oral contraceptive.¹² Her mother and her sister also suffered pruritus and jaundice in pregnancy. It is interesting that reports of jaundice after oral contraceptives come from such regions as Chile and Scandinavia, where recurrent intrahepatic cholestasis of pregnancy is also common.^{9 13}

Oral contraceptives should not be given to patients who have previously suffered pruritus in pregnancy, and special care in the prescribing of them should be taken in countries where intrahepatic cholestatic jaundice of pregnancy is frequent.

In a woman's first pregnancy the differential diagnosis of idiopathic cholestatic jaundice from viral hepatitis and other conditions causing jaundice may be difficult. It might be possible to perform a diagnostic test after delivery. Serial serum-bilirubin, alkaline-phosphatase, and bromsulphalein tests are done before, during, and at the end of a one-cycle course of an oral contraceptive drug in standard dosage. Increasing cholestasis would confirm the diagnosis of intrahepatic cholestatic jaundice of pregnancy, contraindicate further use of this method of contraception, and give warning that subsequent pregnancies might be complicated by intrahepatic cholestatic jaundice. Differential diagnosis must also be made from surgical jaundice. In some cases laparotomy has been undertaken, because of the unusually long duration of jaundice and a preceding history of operation for gallstones. In a recent well-documented case report¹⁴ the liver was found not to be enlarged, but greatly dilated bile capillaries were visible on its surface. Cholangiography showed a normal appearance, and the amount of bile secreted, the secretion pressure, and its viscosity were found to be within normal limits. The patient subsequently had a normal spontaneous delivery, and the child was healthy. The aetiology of this condition is unknown, but the prognosis is nevertheless excellent. In this patient the jaundice disappeared within three weeks and hepatic histology returned to normal within three months of delivery despite the persistence of jaundice for six months of the pregnancy.

There are certainly many other causes of jaundice during pregnancy, for it has been estimated that it complicates one of every 1,500 gestations.⁴ Viral hepatitis accounts for two-fifths of cases, intrahepatic cholestasis for one-fifth, and obstruction of the common bile duct for one in 20. The acute fatty liver of the third trimester of pregnancy is a condition observed particularly in the malnourished patient with pyelonephritis treated with a tetracycline. The liver cells contain multiple fat droplets without significant necrosis or cellular infiltrate. The liver in pregnancy, when demands for protein anabolism are increased, may be more sensitive than in the non-pregnant woman to drugs which depress this function, such as the tetracyclines. The biochemical pattern is of increased serum levels of bilirubin, reduced prothrombin time, azotaemia, hyperuricaemia, and acidosis. Serum values of transaminase and alkaline phosphatase are only moderately

raised, a point of distinction from virus hepatitis. The prognosis of acute fatty liver of pregnancy is poor and there is no clear-cut course of management; caesarean section has been advocated.⁴ Corticosteroids are of no value.

Though tests of liver function in patients with toxæmia of pregnancy may give abnormal results, particularly the alkaline-phosphatase and serum-transaminase tests, jaundice is infrequent. It was present in 10 out of 90 cases of toxæmia in H. L. Sheehan's necropsy series.¹⁵ It is a grave, terminal sign of haemolysis. Histologically the liver shows periportal deposition of fibrin in the sinusoids, with haemorrhages. Centrizonal necrosis and haemorrhages reflect shock, and an inflammatory reaction is inconspicuous. In eclampsia the damage to the liver is terminal, and toxæmia of pregnancy cannot be regarded as primarily involving the liver. Toxæmia rarely enters into the differential diagnosis of jaundice in pregnancy.

Finally, drug jaundice should not be overlooked. Increased sensitivity to tetracycline has been discussed. Other drugs to be borne in mind include chlorpromazine and halothane, while the sulphonamides, novobiocin, and phenacetin should be considered as possible causes of jaundice in immature or premature babies.

Appointment Systems in General Practice

The growth of appointment systems is one symptom of the reorganization of general practice which is gathering momentum. Dr. Bruce Cardew estimates in a paper at page 542 of this week's *B.M.J.* that a third of all N.H.S. practices are now offering a complete appointment service to their patients. Thus 17,000,000 people can now consult their doctors by appointment. That the new pay system is accelerating the movement is suggested by an increase in the first nine months of this year of 2,773 in the number of doctors using the Lloyd-Hamol appointments diary, but it is noteworthy that under the Pool system 4,500 doctors had been prepared to finance appointment schemes entirely out of their own pockets.

J. M. Bevan and G. J. Draper,¹ of the Oxford University Department of Biomathematics, have recently investigated appointment systems. They had three main objectives: to find out the attitudes of doctors and patients to them; to get quantitative estimates of their effect on doctors' work load and patients' waiting time; and to determine which types of practice would find appointment systems worth while and what were the best ways of organizing them. They formed various theories from interviews with and postal surveys from doctors and patients, and tested them in an experimental study of the records of several practices before and after starting appointment systems. The vast majority of doctors and patients who had used an appointment system were satisfied with it. Nearly all doctors found that it was easy to introduce into their practices, that it evened out the work load throughout the week, and that it decreased the strain of their work and improved its quality. Patients who were elderly or of low intelligence found it difficult at first, especially if they had not been informed beforehand by circulars about its introduction and how to use it, but they liked it once they had got used to it. About half of the doctors who did not have appointment systems at the time of the survey thought them

¹ Ljunggren, G., *Nord. Med.*, 1956, 55, 373.

² Caroli, J., Puyo, G., and Rampon, *Sem. Hôp. Paris*, 1954, 30, 1692.

³ King, M. J., and Kerrins, J. P., *New Engl. J. Med.*, 1963, 268, 1180.

⁴ Haemmerli, U. R., *Acta med. scand.*, 1966, Suppl. 444.

⁵ Sherlock, S., *Diseases of the Liver and Biliary System*, 3rd ed. 1963. Oxford.

⁶ Eliakim, M., Sadovsky, E., Stein, O., and Shenkar, Y. G., *Arch. intern. Med.*, 1966, 117, 696.

⁷ Adlercreutz, H., Svanborg, A., and Anberg, A., *Amer. J. Med.*, 1967, 42, 335.

⁸ Mueller, M. N., and Kappas, A., *J. clin. Invest.*, 1964, 43, 1905.

⁹ Orellana-Alcalde, J. M., and Dominguez, J. P., *Lancet*, 1966, 2, 1278.

¹⁰ Kleiner, G. J., Kresch, L., and Arias, I. M., *New Engl. J. Med.*, 1965, 273, 420.

¹¹ Larsson-Cohn, U., and Stenram, U., *Acta med. scand.*, 1967, 181, 257.

¹² Holzbach, R. T., and Sanders, J. H., *J. Amer. med. Ass.*, 1965, 193, 542.

¹³ Thulin, K. E., and Nermark, J., *Brit. med. J.*, 1966, 1, 584.

¹⁴ Adlercreutz, H., Svanborg, A., and Anberg, A., *Amer. J. Med.*, 1967, 42, 341.

¹⁵ Sheehan, H. L., *Amer. J. Obstet. Gynec.*, 1961, 81, 427.

desirable but cited overworking of existing staff as the main reason for not starting them. Most of them did not think that reimbursement of part of the cost of ancillary staff would influence this decision, though the marked increase in appointment systems since January suggests that this was a rationalization of their reluctance to take the plunge. Patients showed a similar conservatism. Their satisfaction with the status quo, noted elsewhere by Ann Cartwright,² was reflected by the far less favourable reaction to the idea of appointment systems by patients of doctors who did not have them. Once they had experienced a successful system patients were overwhelmingly in favour of it, probably because in the average practice it halved their waiting time.

In quantitative terms the degree of success of an appointment system can be measured by the proportion of patients actually making appointments and the proportion failing to keep them. These figures varied in the practices studied from 45% to 96% and from 0% to 7%, respectively. Most patients were punctual, and of the 10% who were not only a third were more than five minutes late. As Dr. Stuart Carne points out at page 544 of this week's *B.M.J.*, an appointment system can also work in a practice with a high proportion of West Indian and West African immigrants, who on the whole are not such good timekeepers as the English and Irish patients.

The success of any system depends to a large extent on the organizing ability of the receptionists and their attitude to patients. They need to be present during all surgery sessions at least, and, on average, staff time must be increased by ten to twelve hours per week per doctor in a partnership and twice as much in a single-handed practice. Success depends also on estimating beforehand the doctor's consultation time—which may differ for each doctor in a partnership—and scheduling appointments accordingly. Doctors must be punctual themselves, because patients who repeatedly have to wait long after their appointment time get disillusioned and stop making appointments.

One of the changes which would help fewer practitioners to care effectively for more patients would be an increase in the ratio of surgery consultations to home visits. The figures from the practices, admittedly small in number, which kept records before and after an appointment system did not show any such increase, though more detailed data and a more rigorous analysis would have been needed to detect any but a very large one. That a consultation probably did acquire greater significance is suggested by the fact that about a quarter of the doctors questioned thought there had been a decrease in trivial consultations and an increase in non-trivial ones. But if an appointment system does not in itself persuade patients to come to the surgery instead of asking for a home visit it is an essential prerequisite for other means of achieving that end: by having a doctor consulting throughout the day as J. S. K. Stevenson³ found; or by receptionists pointing out the convenience of a surgery attendance at a particular time for the patient himself as well as for his doctor, as Andrew Smith⁴ has suggested.

What does emerge quite clearly from the investigation is that it is worth while for every type of practice, except probably a single-handed one, to run a system in which all sessions are by appointment and all patients are encouraged to make an appointment.

¹ Bevan, J. M., and Draper, G. J., *Appointment Systems in General Practice*, 1967, London. Oxford University Press, price 12s. 6d.

² Cartwright, Ann, *Patients and their Doctors*, 1967. London.

³ Stevenson, J. S. K., *Brit. med. J.*, 1966, 2, 515.

⁴ Smith, A., *ibid.*, 1967, 2, 369.

Reappraisal of the Austin Flint Murmur

When Alice, in *Through the Looking-glass*, was trying to reach a particular hill she found that the only way to reach her destination was to turn her back on it and walk in the opposite direction. Something of the same kind seems to be happening to our conception of the Austin Flint murmur.

In Austin Flint's original description of the murmur¹ he suggested that the likely pathogenesis was that the mitral valve leaflets became closed in early diastole as a result of over-distension of the left ventricle from free aortic incompetence, and that during atrial systole the mitral valve reopened with accompanying vibrations of the anterior cusp, producing a characteristic blubbery murmur. Recently it has been shown that in cases of free aortic incompetence reversal of the left atrioventricular gradient takes place in late diastole, left ventricular exceeding left atrial pressure by 20 mm. Hg or more.²⁻⁴ E. D. Wigle and C. J. Labrosse⁵ in 1965 found that an Austin Flint murmur was present in 9 out of 14 patients who developed sudden severe aortic incompetence and a reversal of the left atrioventricular diastolic pressure gradient. Clearly in these cases forward flow through the mitral valve in late diastole could not play any part in the production of the murmur. The next year H. E. Aldridge and his colleagues⁶ demonstrated diastolic mitral insufficiency by cineangiography in nine patients with severe aortic incompetence and reversed pressure gradients. It remained for S. Lochaya, M. Igarashi, and A. B. Shaffer⁷ to suggest that the Austin Flint murmur commonly found in severe aortic incompetence was due to diastolic mitral incompetence. They reported three cases with cineangiographic evidence of late diastolic mitral regurgitation coinciding with an Austin Flint murmur recorded in the phonocardiogram.

Given that diastolic mitral regurgitation does indeed sometimes occur in severe cases of aortic incompetence, two further problems remain. What causes the mitral valve to become incompetent in late diastole? And are the vibrations set up by this regurgitant puff responsible for the Austin Flint murmur? Lochaya and his colleagues⁷ suggest that dilatation of the mitral valve ring due to left ventricular enlargement may result in incomplete closure of the mitral orifice by the valve cusps. The normal function of the chordae tendineae might be impaired by the great ventricular dilatation, and another factor could be partial displacement of the closed or nearly closed mitral valve cusps during the atrial systole. Whether a small puff of mitral regurgitation would be sufficient to produce a loud mitral diastolic murmur is uncertain, but it is difficult to present a satisfactory alternative explanation for the murmur in patients with a reversed diastolic atrioventricular gradient.

So the Austin Flint murmur may have a different pathogenesis in individual cases of aortic incompetence, depending on the direction of the left atrioventricular diastolic pressure gradient. When the murmur occurs with less severe aortic incompetence and without reversal of the left atrioventricular

¹ Flint, A., *Amer. J. Med., Sci.*, 1862, 44, 29.

² Wright, J. L., Toscano-Barboza, E., and Brandenburg, R. O., *Proc. Mayo Clin.*, 1956, 31, 120.

³ Welch, G. H., jun., Braunwald, E., and Sarnoff, S. J., *Circulat. Res.*, 1957, 5, 546.

⁴ Dodge, H. T., Sandler, H., and Evans, T., *Circulation*, 1960, 22, 741.

⁵ Wigle, E. D., and Labrosse, C. J., *ibid.*, 1965, 32, 708.

⁶ Aldridge, H. E., Lansdown, E. L., and Wigle, E. D., *ibid.*, 1966, 34, Suppl. No. 3, 42.

⁷ Lochaya, S., Igarashi, M., and Shaffer, A. B., *Amer. Heart J.*, 1967, 74, 161.

diastolic pressure gradient the Austin Flint murmur could well be due to forward flow of blood through a functionally narrowed mitral valve, as originally suggested. In more severe cases, however, with a reversed pressure gradient, diastolic mitral incompetence seems to be a likely explanation of the pathogenesis of the murmur.

Coal Mining, Pneumoconiosis, and Lung Cancer

In 1936 N. M. Kennaway and E. L. Kennaway¹ drew attention to the low mortality from lung cancer among coal miners as compared with the general male population. Further studies by the Kennaways^{2,3} and by other workers⁴⁻⁶ led to the same conclusion; and according to the *Decennial Supplement* of the Registrar General published in 1938⁷ the standardized mortality ratio (S.M.R.) for lung cancer in men working on the coal face for the three years 1930-2 was 67 (compared with 100 for all males). The S.M.R. for lung cancer in underground workers in coal mines other than coal-face workers was lower still—namely, 36. In a more critical study conducted in South Wales W. R. L. James⁸ found lung cancer at necropsy in 5.4% of 1,531 non-miners but in only 3.3% of 1,827 coal miners. When he subdivided the miners into those with simple pneumoconiosis and those with progressive massive fibrosis (P.M.F.) the rates were 5.1% and 1.4%, respectively. More recently K. P. Goldman⁹ has analysed unpublished data collected by the Medical Research Council's Epidemiology Unit in South Wales. These data consisted of records of radiological examinations for pneumoconiosis and information on causes of death as written on death certificates for a community of 5,096 miners and ex-miners in the Rhondda Fach Valley in Glamorganshire. The results of Goldman's analysis were somewhat in conflict with the findings of James⁸: the mortality from lung cancer was highest, and equal to the national average, among miners with P.M.F., lowest in those with simple pneumoconiosis, and intermediate in those free of radiological evidence of dust disease.

Both James⁸ and R. A. Smith¹⁰ reported that survival rates are better than average in miners after surgical resection of lung cancer. Goldman¹¹ investigated this phenomenon in a careful retrospective survey of cases of primary lung cancer who attended the regional thoracic centre for South Wales between 1954 and 1960. The case material included 172 miners and 518 non-miners, and was analysed according to age, sex, smoking habits, length of time symptoms were present, respiratory function, tumour histology, method of treatment, and survival. In addition, the 172 miners were classified according to degree of pneumoconiosis as assessed radiologically. The miners as a group had a slightly reduced forced expiratory volume (F.E.V.), but differences between miners and non-miners in smoking habits, length of symptoms, average age at onset of symptoms, and spectrum of tumour types were small. Similar proportions of miners and non-miners were deemed operable, but, as noted by T. F. Nealon,¹² the immediate operative mortality was higher in the former. Survival during the five years after operation or diagnosis was similar in miners and non-miners, both for the inoperable cases and for the surgically treated cases who survived the first 28 days after operation. However, among miners, whether treated by surgery or not, survival time during the

two years after diagnosis increased with the severity of simple pneumoconiosis as determined radiologically.

It has been suggested^{10,11} that this better survival from lung cancer in the presence of pneumoconiosis may be due to the blockage of lymphatics by fibrosis and particle-laden macrophages,¹³ which serves to prevent the dissemination of cancer cells. It would be tempting to argue that the same factor could be responsible for the reduced incidence of clinically recognized lung cancers in miners, but this is unlikely in so far as Goldman found evidence of better survival from the disease only in the minority of miners with the more severe grades of simple pneumoconiosis. A mere excess of coal dust in the lungs in the absence of radiological evidence of pneumoconiosis did not affect survival time.

The difficulties of studies of this kind can scarcely be exaggerated. For instance, the diagnosis of lung cancer is rendered difficult by the presence of pneumoconiosis.^{12,14,15} A miner, particularly a pneumoconiotic, is more likely than a non-miner to be under radiological surveillance, with the result that lung cancer may be diagnosed earlier. Also one must question whether sufficient account has been taken of exposure to tobacco smoke. It is true that many workers¹⁶⁻²¹ have either failed to find much difference between miners and non-miners in relation to their smoking habits or have observed that the smoking habit is more prevalent among miners than in the general population. However, the results of three surveys¹⁷⁻¹⁹ indicated that the proportion of miners who are heavy smokers is lower than for the general population. Furthermore, according to G. F. Todd,²² though miners were smoking more than the average for all social classes in 1958, the position was reversed by 1961. An underground worker is precluded from smoking during most of his working day. The accumulated effect of these differences might be important in relation to the lowered incidence of, and better survival from, lung cancer in miners.

D. J. B. Ashley²³ has recently drawn attention to an excessive mortality from bronchitis and a reduced mortality from lung cancer in areas of England and Wales where coal mining and textile industries are prominent. He excludes the possibility that differences in exposure to general air pollutants may be responsible, but does not consider the

¹ Kennaway, N. M., and Kennaway, E. L., *J. Hyg. (Lond.)*, 1936, 36, 236.

² Kennaway, E. L., and Kennaway, N. M., *Brit. J. Cancer*, 1947, 1, 260.

³ ———, *ibid.*, 1953, 7, 10.

⁴ Gooding, C. G., *Lancet*, 1946, 2, 891.

⁵ McVittie, J. C., *Postgrad. med. J.*, 1949, 25, 618.

⁶ Chatgidakis, C. B., *Brit. J. industr. Med.*, 1963, 20, 236.

⁷ Registrar General, *Decennial Supplement, England and Wales 1931, Part IIa, Occupational Mortality*, 1938. H.M.S.O., London.

⁸ James, W. R. L., *Brit. J. industr. Med.*, 1955, 12, 87.

⁹ Goldman, K. P., *ibid.*, 1965, 22, 72.

¹⁰ Smith, R. A., *ibid.*, 1959, 16, 318.

¹¹ Goldman, K. P., *Thorax*, 1965, 20, 170.

¹² Nealon, T. F., *Arch. environ. Hlth*, 1964, 8, 882.

¹³ Heppleston, A. G., *J. Path. Bact.*, 1947, 59, 453.

¹⁴ Goldman, K. P., *Brit. J. Dis. Chest*, 1965, 59, 141.

¹⁵ Gernez-Rieux, C., Voisin, C., Balgairies, E., Delepoulle, E., and Lenoir, L., *Lille méd.*, 1961, 6, 551.

¹⁶ Higgins, I. T. T., Oldham, P. D., Cochrane, A. L., and Gilson, J. C., *Brit. med. J.*, 1956, 2, 904.

¹⁷ ——— and Cochrane, A. L., *Brit. J. industr. Med.*, 1961, 18, 93.

¹⁸ Ashford, J. R., Brown, S., Duffield, D. P., Smith, C. S., and Fay, J. W. J., *Brit. J. prev. soc. Med.*, 1961, 15, 106.

¹⁹ Todd, G. F., *Statistics and Smoking, Research Papers No. 1*, 2nd edition, Tobacco Manufacturers Standing Committee, 1959. London.

²⁰ Cross, K. W., McDowell, L. A., and Posner, E., *Brit. med. J.*, 1958, 1, 862.

²¹ Brown, S., *Report No. Sc 849/MR/41*, National Coal Board Scientific Department, 1962. London.

²² Todd, G. F., *Statistics of Smoking, Research Papers, No. 1*, 3rd edition, Tobacco Research Council, 1962. London.

²³ Ashley, D. J. B., *Brit. J. Cancer*, 1967, 21, 243.

²⁴ Old, L. L., Benacerraf, B., Clarke, D. A., Carswell, E. A., and Stockert, E., *Cancer Res.*, 1961, 21, 1281.

possible influence of differences in smoking habits. His suggestion that "the dusty lung is in a state of enhanced immunological competence and is better able to destroy the first few cells which have undergone malignant transformation than is the normal lung," though interesting, must be regarded as highly speculative. L. L. Old and his colleagues²⁴ reported that in mice B.C.G. infection non-specifically increases resistance both to isologous tumour grafts and to the induction of cancer by 3-methylcholanthrene. However, in general, the function and importance of immune mechanisms in relation to carcinogenesis are far from clear, and certainly in the present instance it would be wise to defer detailed consideration of possible mechanisms until the facts are more certain.

Foot-and-mouth Disease in Man

True foot-and-mouth disease in man is a very rare infection. During outbreaks of the disease in cattle vesicular eruptions in patients who have come into contact with infected animals naturally incur suspicion, but a diagnosis of foot-and-mouth disease confirmed by laboratory investigation is hardly ever made. Cases described have been mainly from Germany and Scandinavia, where large epizootics have been more frequent than in Britain. In 1939 A. Flaum¹ described four cases occurring during an epizootic which affected 4,300 herds of cattle in southern Sweden—a worse outbreak than that now in England, grievous though this one is. More recently W. Pilz and H. G. Garbe² have published excellent colour photographs of the hand lesions in two patients infected in the laboratory. These and nearly all previously reported cases have been due to type O virus, though one case due to type C virus has been recorded.³ Incubation periods have been from three to five days.

On page 529 in the *B.M.J.* this week a case due to type O virus in a Northumberland man is described. The signs and symptoms were similar to those in the European cases—moderate fever (up to 39.5° C. is common) preceding the eruption, inflamed throat, painful lesions on the tongue, and blisters on the hands and feet. An unusual feature, not previously described, was the recurrent crops of blisters from which no virus could be isolated. It may be that in this patient a pre-existing skin disorder may have reduced the normally very high human resistance to infection by foot-and-mouth disease virus. One of Pilz and Garbe's² patients had been subject to neurodermatitis of long standing. As in other cases, the blisters in the Northumberland man healed in a week. Also characteristically, virus in high titre was recovered from blisters, and the titres of both complement-fixing and neutralizing antibodies diminished rapidly after convalescence.

¹ Flaum, A., *Acta path. microbiol. scand.*, 1939, 16, 196.

² Pilz, W., and Garbe, H. G., *Zbl. Bakt. I., Abt. Orig.*, 1965, 198, 154.

³ Eissner, G., Böhm, H. O., and Jülich, E., *Dtsch. med. Wschr.*, 1967, 92, 830.

⁴ Verterlein, W., *Zbl. Bakt. I., Abt. Orig.*, 1955, 162, 4.

⁵ Alsop, J., Flewett, T. H., and Foster, J. R., *Brit. med. J.*, 1960, 2, 1708.

⁶ Flewett, T. H., Warin, R. P., and Clarke, S. K. R., *J. clin. Path.*, 1963, 16, 53.

⁷ Clarke, S. K. R., Morley, T., and Warin, R. P., *Brit. med. J.*, 1964, 1, 58.

⁸ Anyon, C. P., Duff, S. M. F., and Hamilton, W., *N.Z. med. J.*, 1967, 66, 599.

⁹ Higgins, P. G., Ellis, E. M., Boston, D. G., and Calnan, W. L., *Mh. Bull. Minist. Hlth Lab. Serv.*, 1965, 24, 38.

¹⁰ Froeschle, J. E., Nahmias, A. J., Feorino, P. M., McCord, G., and Naib, Z., *Amer. J. Dis. Child.*, 1967, 114, 278.

¹¹ Born, W., *Dtsch. Arztsbl.-Ärztl. Mitt.*, 1967, 64, 1703.

Human resistance is normally so high that several attempts to infect humans artificially by injecting blister fluid from animals have failed; no lesions were produced and virus could not be recovered from the volunteers' blood at any time after the injection. Subclinical infection is exceedingly rare. Antibodies have been reported in a few laboratory workers exposed over long periods to a high level of infection; in one series five workers were found to have acquired neutralizing antibodies.⁴ Only one such case is known in Britain.

Early failures to infect experimental animals from supposed cases of human foot-and-mouth disease are much more easily explained. The cases may really have been hand-foot-and-mouth disease, a not uncommon human infection first described in Britain at a time when there were numerous outbreaks of foot-and-mouth disease in cattle.⁵ This syndrome is not due to foot-and-mouth virus but is caused by a Coxsackie virus, usually type A16, occasionally A5⁶ or A10.^{7,8} The lesions differ from those of foot-and-mouth in rarely reaching 5 mm. diameter, and they never reach the size (1–2 cm. diameter) seen on hands infected with foot-and-mouth virus. In children especially, maculopapular lesions are often present on the buttocks—whence it has been suggested that a better name might be "hands, mouth, and bumps-a-daisy disease." Fever is rare; the lesions usually clear up in a week. Excellent black-and-white^{9,10} and colour¹¹ photographs have been published.

Differentiation between the two diseases is not likely to be difficult except in the early stages of the eruption. But if there is the slightest question of a human vesicular eruption infection being foot-and-mouth disease the medical officer of health should be informed and the patient should be isolated in hospital for eight days. Specimens from possible cases of human infection should not be sent to any laboratory other than the Animal Virus Research Institute at Pirbright. Both Coxsackie and foot-and-mouth viruses are easily isolated in suckling mice; and it might be all too easy for a virus as infectious to animals as foot-and-mouth to escape from a laboratory less well designed to contain it than that at Pirbright. The Pirbright laboratory staff must be working overtime at present; nevertheless, a fresh case of human infection, should one occur, might well repay investigation. None of the published descriptions mention, for example, whether virus is excreted in the urine or faeces and if so for how long. It might be important to know this.

Intestinal Absorption

The intestine has been turned inside out and back to front in order to understand the physiology of intestinal function. More recently a series of new techniques—electron microscopy, histochemistry, autoradiography, radioisotopes, chromatography—have been adapted to the investigation of the structure and function of the intestinal epithelial cell. D. H. Smyth¹ has aptly described the life of this remarkable cell as a short and merry one, if merriment is the equivalent, in cellular terms, of a range of activities possessed by few other cells in the body. Its life is brief, for the epithelial lining of the intestine is renewed every few days.

This and related topics of intestinal absorption are well reviewed in a recent *British Medical Bulletin*. Histochemical techniques have proved helpful in interpreting the absorptive

¹ Smyth, D. H., *Brit. med. Bull.*, 1967, 23, 205.

defect in steatorrhoea, and in this issue A. G. E. Pearse and E. O. Riecken demonstrate beautifully the value of histochemical and cytochemical techniques in applied research, allowing us to make assumptions about the functions of particular organelles and to suggest changes in the inter-relationship between one organelle and another.

There are also chapters on the absorption of carbohydrates, proteins, fats, salt and water, vitamins, and iron, all of which are authoritative. It is exciting, too, to learn how new techniques have thrown light on the means of transfer of these products from the intestinal lumen to the blood or lymph. The absorptive capacity of the small bowel is probably not static. It has a large functional reserve, which normally is seldom required, and R. H. Dowling shows that under stress it may respond by enhancing its absorptive capacity. Increased absorption has been found after a high-bulk diet, intermittent starvation, and in malignant disease. Resection of the small bowel in man may be followed by mucosal hypertrophy and a resultant increase in the absorptive surface area. These changes were more obvious in the ileum after proximal resection than in the jejunum when the distal small bowel was removed.

Lest readers should regard this symposium as of interest to gastroenterologists only, M. D. Milne compares defects of intestinal transport with their renal counterpart, for the mechanism of absorption of some substances by the intestine is similar to that in the renal tubules. Practical clinical implications for the general physician are further expanded by Soad Tabaqchali and C. C. Booth in reviewing the significance of intestinal flora and of the antibiotic response in patients with anatomical abnormalities. Malabsorption of vitamin B₁₂ and fat can usually be corrected within three or four days of starting treatment with a tetracycline in a patient with, say, jejunal diverticulosis. After antibiotic treatment the bacterial count in the jejunal fluid may be expected to fall, faecal fat and nitrogen become normal, absorption of vitamin B₁₂ improve, and indicanuria to be much reduced. The level of indicanuria reflects indole production in patients with a stagnant loop of bowel. Increased intestinal bacterial activity acts on the amino-acid tryptophan to produce indole. Measurement of the urinary indican may therefore be used as a gross indication of indole-producing bacteria in the gut, such as *Escherichia coli* and *Bacteroides*.

Premature Rupture of Membranes and Maternal Death

With a maternal mortality of 2.58 per 10,000 total births childbearing in Britain is now safer than ever before. The need to recognize those patients at increased risk in time to take necessary precautions has been emphasized in each Maternal Mortality Report.¹ Many recurring "avoidable factors" have been identified, but nevertheless nearly 40% of all maternal deaths are still associated with them.

It is well known that uterine sepsis can be a complication of rupture of the membranes. The identification of pathways of exogenous infection, the discovery of chemotherapeutic and antibiotic preparations, and dramatic reductions in the number of deaths from puerperal infection have contributed to a widely held but erroneous view that sepsis is no longer a serious obstetrical hazard. Its lethal role in abortion and caesarean section, particularly after prolonged labour, has

been emphasized¹ and evidence relevant to its association with premature rupture of the membranes has now been produced by G. A. Webb.² His conclusions are based on an analysis of 1,054 maternal deaths reviewed by the Maternal Mortality Committee of California. Fifty-three women died after spontaneous rupture as defined by N. J. Eastman and L. M. Hellman³: "rupture before the onset of labour." One death followed surgical induction. Eighteen died between the 16th and 30th week of gestation, ten by the 20th week. Though it is difficult to exclude interference in any abortion series cases were omitted if it was confirmed or even suspected. The ages of the women who died ranged from 18 to over 40; the highest incidence was among gravidae four-plus. Only 11 infants survived of 31 delivered after the 36th week.

Some important questions remain unanswered in Webb's paper, but there are features which merit attention. During the period of eight years premature rupture of membranes was associated with 5% of maternal deaths, and in this group sepsis was responsible in 70%. *Escherichia coli* was the most commonly identified organism; there were only three anaerobic infections, two due to streptococci and one to *Clostridium welchii*. Twenty-two women died from septic shock, but treatment led to fatal pulmonary embolism in six and acute congestive heart failure in one, emphasizing the need for constant supervision in the care of these patients.

Dangers increased with the time interval between rupture of membranes and either delivery or the onset of pyrexia, but this interval was less than 24 hours in 15 cases. Most patients were apyrexial on admission to hospital, and Webb suggests that the systemic response to uterine infection usually occurs after the onset of labour, unless infection is overwhelming. Antibiotics were given too late and in inadequate doses. A surprising feature was that seven mothers with ruptured membranes died of amniotic embolism (four were infected) and in six this followed the administration of Pitocin or Syntocinon (both oxytocin injections). The apparent association of oxytocins and embolism justifies further study.

Premature rupture of membranes precedes approximately 10% of labours. The risk of maternal death is small (Webb assesses it as one in 5,451), but the patient should be included in a high-risk category. Rupture may indicate a complication such as malpresentation, posterior position, placenta praevia, or disproportion, but should itself be regarded as an emergency requiring specialist care. Opinions differ on whether immediate antibiotic therapy is necessary, but if given it should be designed to deal with both coliform and coccal infections. Cervical culture for organisms and sensitivity is a wise precaution at the first examination and a rising pulse rate, pyrexia, hypotension, oliguria, or icterus are definite indications for intensive antibiotic treatment. If on admission the obstetrical position is otherwise favourable a carefully controlled oxytocic infusion is indicated, but if progress is unsatisfactory or if the position is unfavourable (large foetus, high head, posterior position and uneffaced cervix) caesarean section is indicated and made safer by avoiding delay.

Premature rupture of membranes should not kill the mother or the child, but the treatment which they subsequently receive may do so.

¹ Ministry of Health Report on Confidential Enquiries into Maternal Deaths in England and Wales (Reports on Public Health and Medical Subjects, No. 97 (1957), No. 103 (1960), No. 108 (1963), and No. 115 (1966)). H.M.S.O., London.

² Webb, G. A., *Amer. J. Obstet. Gynec.*, 1967, 98, 594.

³ Eastman, N. J., and Hellman, L. M., *Williams Obstetrics*, 1961, 12th ed., p. 432. New York.

Papers and Originals

Renal Glucose Threshold Variations with Age

W. J. H. BUTTERFIELD,* M.D., F.R.C.P.; H. KEEN,* M.B., M.R.C.P.; M. J. WHICHELOW,* M.A.

Brit. med. J., 1967, 4, 505-507

Each year some millions of urine samples are examined routinely for glycosuria in hospitals, clinics, and practices to screen patients for diabetes mellitus; and many more are tested by sufferers from this condition to assist in the management of their individual cases. Such tests rightly assume that there is some relation between the concentration of glucose in the blood and that in the urine. Thus the concept of the "renal threshold for glucose," though not strictly correct from a physiological point of view, retains a practical utility in these clinical situations. Despite this, surprisingly little attention is paid to its variations in populations or to its level in individual patients. In many important texts either there is no quantitative indication of the blood-sugar significance of glycosuria (Best and Taylor, 1961; Danowski, 1964; Dunlop *et al.*, 1964) or there is a choice of values for the renal threshold quoted as 170 mg./100 ml. Loeb (1959), as 180 mg./100 ml. by Lawrence (1955), Lister (1959), and Houston *et al.* (1962), and as 200 mg./100 ml. by Ellenberg and Rifkin (1962). Peters and Van Slyke (1949), who examined this question in some detail, give the normal range as 140 to 200 mg./100 ml. It has been suggested that the renal threshold may be raised in older diabetics (Lawrence, 1955; Loeb, 1959) and that it is higher in women than in men (Steinberg, 1965), while Robertson and Gray (1953) have studied some diabetics with low renal thresholds.

With regard to the management of diabetes, Lawrence (1955) and Joslin *et al.* (1959) are among the few who emphasize the importance of establishing the renal threshold in individual cases.

So far as detecting diabetes is concerned there is a widespread realization that finding glucose in a random postprandial urine sample is far from establishing directly a diagnosis of diabetes. In most cases subsequent glucose-tolerance tests will show that the glycosuric person is not diabetic (College of Gen. Pract., 1962; Butterfield, 1964; Keen, 1964; Sharp, 1964).

In contrast to the non-diabetic glycosurics, the 1962 Bedford Survey indicated clearly that there were also many hyperglycaemic people without glycosuria in the population. The possibility that unrecognized hyperglycaemia might be an important factor in vascular disease (Keen *et al.*, 1965; Ostrander *et al.*, 1965; Kingsbury, 1966), and our clinical experience with established diabetics, in whom we found renal thresholds as low as 45 and 60 mg./100 ml. and as high as 320 mg./100 ml., stimulated us to re-examine the data about glycosuria from the Bedford Survey and consider them in terms of the detection and management of diabetes.

Definitions

Test for Glycosuria.—Clinistix (Ames Co.): the appearance of a blue colour on the test strip one minute after dipping in

the specimen shows the presence of glucose exceeding 0.1 g./100 ml.

Capillary blood sugar results two hours after 50 g. of glucose by mouth (arbitrarily divided into the following groups): normal <120 mg./100 ml.; hyperglycaemic >120 mg.; borderline diabetic 120-199 mg.; diabetic >199 mg.

Methods and Material

The subjects studied were adult citizens of Bedford not known to have any disturbance of carbohydrate metabolism. All persons on the Electoral Roll were asked to provide a specimen of post-breakfast urine and 25,701 people had their urine tested, of whom, excluding known diabetics, 4% were found to have glycosuria. These were termed the glycosurics.

An age/sex stratified random sample of 535 subjects drawn from the entire co-operating population underwent standard 50-g. oral glucose-tolerance tests. Blood sugar levels were estimated by a modification of the microferricyanide reducing method in the autoanalyser (Whicelow *et al.*, 1967) on capillary samples taken fasting and at 30, 60, 90, 120, and 150 minutes after the administration of a drink containing liquid glucose equivalent to 50 g. of dextrose monohydrate. It was possible to test for glycosuria the urine passed between 60 and 120 minutes by 295 randomly selected persons. Since the presence of any small quantity of sugar-free urine in the bladder before the glucose-tolerance test could have diluted the post-glucose glycosuria, the presence of glucose and not its concentration will be considered here. It should be pointed out, under these circumstances, that from the presence of glycosuria we can only deduce that the renal threshold was lower than the peak value found, and that in the absence of glycosuria the renal threshold was higher than the peak value.

The age/sex composition of the random sample and the subsample also tested for glycosuria are shown in Table I.

TABLE I.—Structure of the Random Sample

Age	Men		Women	
	Total	No. Tested for Glycosuria	Total	No. Tested for Glycosuria
20-29	46	25	48	26
30-39	43	23	49	25
40-49	46	27	45	25
50-59	43	35	48	23
60-69	38	20	48	37
70-79	39	25	42	27

Results

During the screening survey 4% of the population were found to have glycosuria (after breakfast) whereas 30% of the random sample subjects had glycosuria during the glucose-tolerance

* Department of Medicine, Guy's Hospital Medical School, London S.E.1.

TABLE II.—Prevalence of Glycosuria at Survey and During Glucose-tolerance Test

Age	Men		Women	
	% at Survey	% at G.T.T.	% at Survey	% at G.T.T.
20-29	4.3	40	2.8	4
30-39	4.9	22	2.3	24
40-49	5.3	33	1.9	24
50-59	7.5	52	2.0	30
60-69	7.9	30	2.8	27
70-79	7.8	52	4.5	26

test. Table II shows the percentage of subjects in each group having glycosuria at the survey and during the glucose-tolerance test. At the survey, but not during the glucose-tolerance test,

women 12 had renal thresholds below 180 mg., and six below 160 mg., while 30 had peak blood sugars above 180 mg. with no glycosuria.

Discussion

Wide Variation of Renal Threshold: High Thresholds in the Elderly

It is clear that in many individuals the renal threshold was lower than 160 mg./100 ml. or higher than 200 mg./100 ml., and that it appeared to rise with age.

The postprandial blood sugars at the survey were probably much lower than after a test glucose load (Kenny and Chute, 1953) as is indicated by the higher prevalence of glycosuria after 50 g. of glucose. The prevalence of glycosuria was much higher among men than women at the survey but less so during the glucose-tolerance test (Table II). The best explanation for these findings would be that more men have on average lower renal thresholds than women, rather than that there is any difference in the sex incidence of diabetes, or that women diabetics had been removed from the survey group through the detection of diabetes at antenatal clinics, as was thought earlier.

Recognizing Diabetics in Clinical Practice

What do the foregoing results mean to the practitioner routinely testing the patients' urine to detect diabetes? Table III shows the probability that any postprandial urine test result indicates that the patient will be hyperglycaemic (see Definitions). It will be seen that young glycosurics are unlikely to have diabetes, but that, though older people are more likely to have diabetes if they have glycosuria, the absence of glycosuria does not preclude diabetes, particularly among women. If the patients are given a 50-g. glucose drink and the urine is tested for the presence of sugar between one and two hours later, not only

will the number of false positives (persons with glycosuria and normal blood sugars) be greatly increased, but there is still a 10% chance that diabetics (see Definitions) will not have glycosuria, and that their diabetes will go undetected (Figs. 3 and 4).

TABLE III.—Probability of Diabetes in Glycosuric and Non-glycosuric Subjects

Subjects	Postprandial Glycosuria	Sex	% Likely to be Hyperglycaemic (2-hr. B.S. $\geq$ 120 mg./100 ml.)
Under 50 years	Negative	Men	7%
		Women	9%
	Positive	Men	11%
		Women	17%
50 and over	Negative	Men	15%
		Women	27%
	Positive	Men	35%
		Women	73%

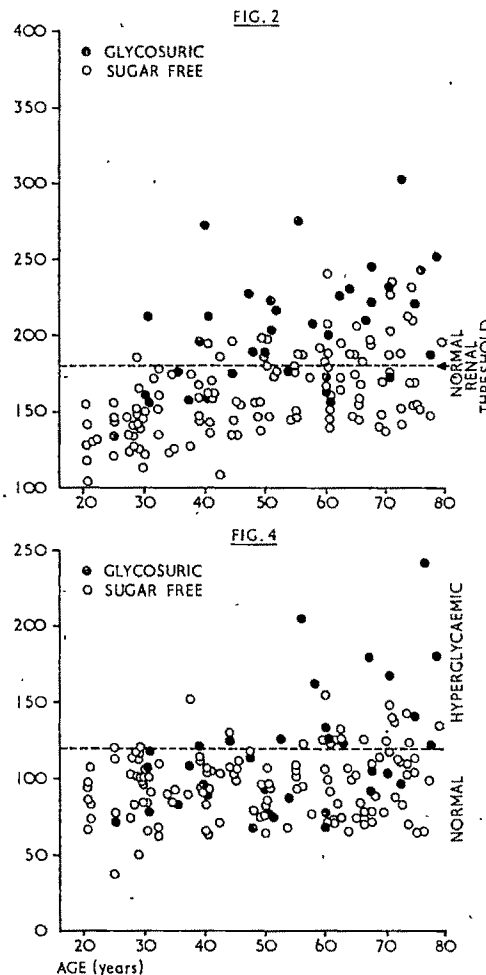
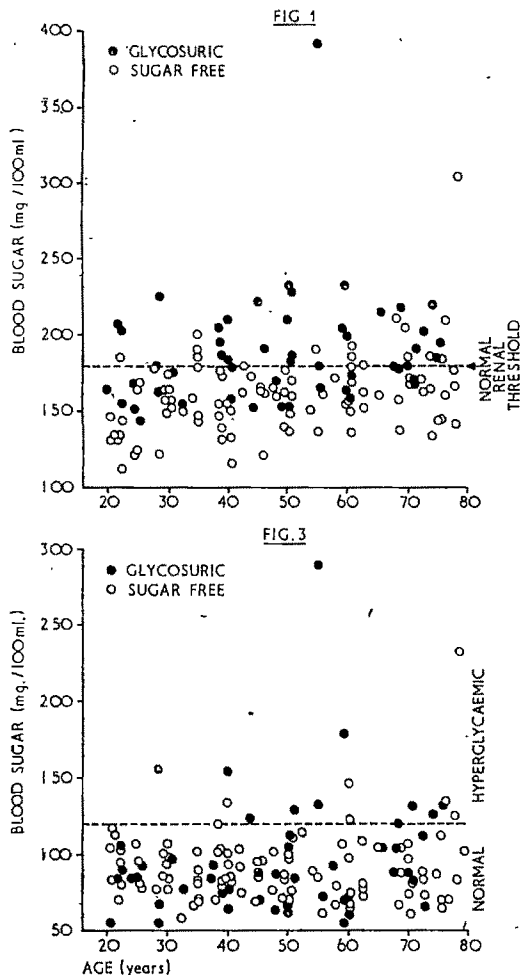


FIG. 1.—Peak blood sugar levels during glucose-tolerance tests in random sample men. FIG. 2.—Peak blood sugar levels during glucose-tolerance tests in random sample women. FIG. 3.—Blood sugar levels two hours after 50 g. of glucose in random sample men. FIG. 4.—Blood sugar levels two hours after 50 g. of glucose in random sample women.

the prevalence of glycosuria rose with age in both sexes, and also was about twice as high in the men as in the women.

Figs. 1 to 4 show the peak and two-hour blood sugar levels during glucose-tolerance tests plotted against age for both sexes, indicating those subjects with and without glycosuria. The peak blood sugar (which usually occurred at 60 minutes) rose with age (Figs. 1 and 2) and there tended to be more people, especially women, who had sugar-free urine despite high blood sugar levels (over 180 mg./100 ml.) among the older age groups. There were a large number of young persons, particularly young men, with glycosuria despite low peak levels.

It will be seen from Figs. 1 and 2 that renal threshold values as low as 130 mg. and as high as 305 mg./100 ml. were found. There were 20 men with renal threshold values below 180 mg., and 9 lower than 160 mg., whereas 14 men had peak blood sugars above 180 mg. with no glycosuria (Fig. 1). Among the

Since diabetes is defined in terms of blood sugar levels (W.H.O. Expert Committee, 1965) the only satisfactory solution to the problem of diabetes detection is to measure the blood sugar level (we have found a single estimation two hours after a 50-g. oral glucose load to be the most satisfactory). This emphasizes the need to provide the general practitioner with a quick, simple, and valid blood sugar method for the diagnosis of diabetes, preferably one which can be carried out in the surgery.

Importance of Renal Threshold in Management of the Individual Diabetic

Another question of interest to every clinician, brought to light by this study, is the proper interpretation of the results of testing for glycosuria when controlling diabetics.

It is apparent from the foregoing results that the renal glucose threshold should always be established for each diabetic at diagnosis and the results of the subsequent urine tests interpreted in the light of this threshold. From Figs. 1 and 2 it can be seen that many young diabetics may have very low renal thresholds, so that to advise them to adjust their control to keep their urine sugar-free may be to keep them in perpetual danger of hypoglycaemia, as in the two supposedly uncontrollable brittle diabetics (mentioned earlier) found to have renal threshold levels of 45 and 60 mg./100 ml. Failure to realize how low it was had resulted in one of these patients being in hospital for many weeks to the "stabilized." An even greater risk lies in the possibility that the considerable urinary glucose loss may provoke carbohydrate lack and "starvation ketosis" in the diabetic. Heavy glycosuria and ketonuria may then be misinterpreted and lead to increased insulin dosage when what is required is increased carbohydrate intake.

On the other hand, elderly diabetics with sugar-free urine may, in fact, be suffering from persistently high blood sugar levels. If the threshold is elevated in such cases, it may be more sensible to use the sensitive enzyme-impregnated test papers (Clinistix or Tes-Tape) on postprandial urine samples as an index of diabetic control, rather than copper sulphate reduction system tablets (Clinitest) on samples passed before meals, as is so often the case.

Detection of Diabetes: Epidemiological Surveys

With regard to the recognition of diabetes, either in detection drives or in epidemiological surveys, it must be stressed that the presence of glycosuria is by no means diagnostic of diabetes. Only one-third of the subjects with glycosuria at the Bedford Survey were hyperglycaemic. Also, the absence of glycosuria does not preclude diabetes, as 11% of the population we studied were hyperglycaemic, of whom about 90% were non-glycosuric. Some of these non-glycosuric subjects even had two-hour blood sugars over 200 mg./100 ml. at the subsequent glucose-tolerance test. Indeed, it can be calculated from our data that in a British population the preliminary screening by use of postprandial glycosuria will fail to detect over half the diabetics at large with blood sugars over 200 mg./100 ml. at two hours during a glucose-tolerance test. We therefore have to admit that our survey, and indeed many others based simply on glycosuria, failed to detect most of the unrecognized, mainly elderly, diabetics in the community.

Of course, attempts to detect diabetes by glycosuria have been widely used in the past because the techniques are so simple compared with blood sugar estimations. Can urine testing be made a more reliable reflection of hyperglycaemia? Testing the Bedford random sample for glycosuria after the standard oral glucose load showed that the proportion of glycosurics rose from the 4% seen among the population after a random breakfast to 30%. But unfortunately this procedure too will have its limitations; Figs. 3 and 4 show that an occasional diabetic will still be missed as well as a much larger number of borderline cases (see Definitions). Attempts to

screen all members of a community with even a modified form of the glucose-tolerance test involve a heavy burden on the laboratory.

Since the renal threshold can vary so much and reach such high values in old age, earlier ideas, that of diabetes as a disease where a high blood sugar is always associated with glycosuria and dehydration, have to be abandoned. Diabetes mellitus, the "siphoning off of sweetness into the urine," is not necessarily a concomitant of hyperglycaemia. We have to recognize that hyperglycaemia often exists without glycosuria, especially in communities where the proportion of old people is high, and that since we now define diabetes in terms of hyperglycaemia it is only by tests for hyperglycaemia that we shall be able to recognize diabetes and establish its prevalence in the community.

These points will have to be carefully considered by epidemiologists before they undertake further survey work. They will need to decide how many people are to be screened and whether or not they are to be screened for glycosuria, or for hyperglycaemia. Finally, in view of the high prevalence rates of hyperglycaemia in Western communities, the organizers of detection drives will be wise to ask themselves not only about the facilities and manpower available for the survey but also for the subsequent treatment of the cases found.

Summary

The results of testing an age-sex stratified random sample of the Bedford population for glycosuria during glucose-tolerance tests showed that the renal threshold level is very variable, and increases with age, especially among women. Renal threshold values as low as 130 mg./100 ml. were found in young subjects and as high as 300 mg. in elderly subjects. Thirty per cent. of this random sample had glycosuria during the glucose-tolerance test compared with only 4% when tested after breakfast. These findings are discussed in relation to the management of diabetic patients and the planning and execution of diabetes detection surveys.

We wish to acknowledge our thanks to the staffs of the Public Health Department, Bedford, and the Department of Experimental Medicine, Guy's Hospital, who collected and tested the urine samples, and to the Ames Company for supplies of Clinistix, and to the British Diabetic Association for financial and other support.

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Beta-adrenergic Blockade and Cardiac Arrhythmias*

GRAEME SLOMAN,[†] M.B., B.Sc., M.R.C.P., M.R.C.P.E.D., M.R.A.C.P.; MARY STANNARD,^{‡‡} M.B., B.S.

Brit. med. J., 1967, 4, 508-512

The evaluation of beta-adrenergic blockade in cardiac arrhythmias is difficult because of the complex nature of the arrhythmias and the varied modes of action of blocking drugs. Studies have confirmed the therapeutic value of the beta-adrenergic blocking drug pronethalol (Alderlin) (Vaughan Williams, 1963; Stock and Dale, 1963; Payne and Senfield, 1964; Wolfson *et al.*, 1966) and its more potent successor, propranolol (Inderal) in the management of many different atrial and ventricular arrhythmias (Harrison *et al.*, 1965; Sloman *et al.*, 1965; Stock, 1966; Harris, 1966; Szekely *et al.*, 1966; Cherchi *et al.*, 1966; Rochet and Vastesaeger, 1966; Gettes and Surawicz, 1966; Luria *et al.*, 1966; Epstein and Braunwald, 1966).

This study reports our experience in the management of patients with paroxysmal arrhythmias, acute life-threatening arrhythmias, and recurrent arrhythmias associated with prolonged cardiac arrest. An attempt has also been made to assess the prophylactic value of propranolol in reducing the high incidence of arrhythmias associated with acute myocardial infarction.

Materials and Methods

Thirty-one patients presenting with various cardiac arrhythmias were included in this study. Patients in whom full documentation was not available were not included. There

* Presented at a National Heart Foundation of Australia Symposium held in Canberra, 25-27 January 1967.

[†] Cardiac Department, Royal Melbourne Hospital, Victoria, Australia.

^{‡‡} Research assistant supported by the National Heart Foundation of Australia Grant-in-aid G. 428.

were 19 males and 12 females, with an age range from 17 to 78 (mean 50.9 years). In all these patients the arrhythmia had proved disabling; in some it was associated with prolonged cardiac arrest.

Forty-nine patients with acute myocardial infarction were studied to assess the prophylactic value of propranolol in preventing arrhythmias. The patients were divided into four major groups: group A, chronic arrhythmias, recurrent and continuous; group B, acute arrhythmias; group C, arrhythmias associated with prolonged cardiac arrest; and group D, acute myocardial infarction.

Propranolol was given intravenously or orally, depending on the urgency of the clinical situation: the details of drug therapy are discussed under each group.

Results

Group A: Chronic Arrhythmias, Recurrent and Continuous

There were 16 patients in this group (Table I). Four had atrial fibrillation, not adequately controlled by digitalis or other anti-arrhythmic drugs. In three the fibrillation was paroxysmal, frequently causing syncope at its onset. In the fourth fibrillation was continuous, but the rate could not be adequately controlled by digitalis alone. There were five patients with paroxysmal atrial tachycardia, not adequately controlled by digoxin and quinidine sulphate. Four patients had other atrial arrhythmias, while the remaining three were in sinus rhythm with frequent ventricular ectopic beats, but suffered syncopal attacks due to paroxysmal ventricular tachycardia.

TABLE I.—*Propranolol. Chronic Arrhythmias, Recurrent and Continuous*

Case No.	Age	Sex	Presenting Symptoms	Arrhythmia	Failed Therapy	Propranolol Dose	Results
<i>Atrial Fibrillation</i>							
1	52	F	Syncope	Paroxysmal	Digitalis	40 mg. 4 × /day	No syncope
2	55	F	"	"	Procainamide	10 mg. 4 × /day plus digoxin	Palpitations only. No syncope
3	56	M	"	Paroxysmal with runs of ventricular tachycardia	Quinidine. Procainamide. Digoxin. Pacemaker + digoxin	20 mg. 3 × /day plus pacemaker	No syncope
4	25	F	Dyspnoea	Continuous atrial fibrillation	Digoxin	10 mg. 4 × /day plus digoxin	Rate slowed
<i>Paroxysmal Atrial Tachycardia</i>							
5	57	M	Palpitations	Paroxysmal atrial tachycardia	Digoxin. Quinidine	5 mg. 4 × /day inc. to 60 mg. 4 × /day	Control. Occasional palpitations
6	49	F	"	" " "	Multiple. Details not known	20 mg. 4 × /day plus digoxin	Control (recent)
7	41	M	Palpitations and faintness	" " "	Digoxin. Quinidine	20 mg. 4 × /day plus digoxin	Control
8	69	M	Palpitations	" " "	Quinidine. Digoxin	10 mg. 3 × /day plus digoxin	"
9	56	M	Palpitations. Cardiac failure	" " "	Digoxin. Procainamide. Quinidine. Phenytoin sodium. D.C. shock	10 mg. 4 × /day plus procainamide	"
<i>Other Atrial Arrhythmias</i>							
10	20	M	Palpitations 6 years	Atrial tachycardia with A-V dissociation	Digoxin. Quinidine	10 mg. 4 × /day plus digoxin, quinidine, and corticosteroids	Control
11	29	M	Palpitations. Cardiac failure	" " "	Digoxin. D.C. shock	10 mg. 4 × /day plus digoxin	Rate slowed. Later reversion to sinus rhythm
12	52	F	Palpitations	Sinus tachycardia	Digoxin	10 mg. 2 × /day	Control
13	42	M	"	Atrial flutter	Digoxin. D.C. shock	3 mg. I.V. then 10 mg. 3 × /day	Slowed
<i>Ventricular Arrhythmia</i>							
14	58	M	Syncope	Frequent V.E.S. plus ventricular tachycardia	Nil	40 mg. 3 × /day	Control
15	45	M	"	Frequent V.E.S. plus ventricular tachycardia on exercise	Quinidine	10 mg. 3 × /day plus quinidine	"
16	17	F	Palpitations. Syncope	Frequent V.E.S. with coupling on exercise	Quinidine	10 mg. 4 × /day	"

V.E.S. = Ventricular extrasystoles. D.C. = Direct current.

When the arrhythmia could be produced by exercise on the treadmill (Cases 1, 3, 7, 8, 11, 14, and 16) after recording the abnormal rhythm the patient was rested, given an intravenous dose of propranolol (0.1 mg./kg. body weight with 1.2 to 2.4 mg. of atropine sulphate), and after 10 minutes the exercise study was repeated (Fig. 1). Provided the arrhythmia was controlled propranolol was continued in an oral dose, beginning with 10 mg. every six hours. The dose was increased as necessary to a maximum in this study of 60 mg. four times a day.

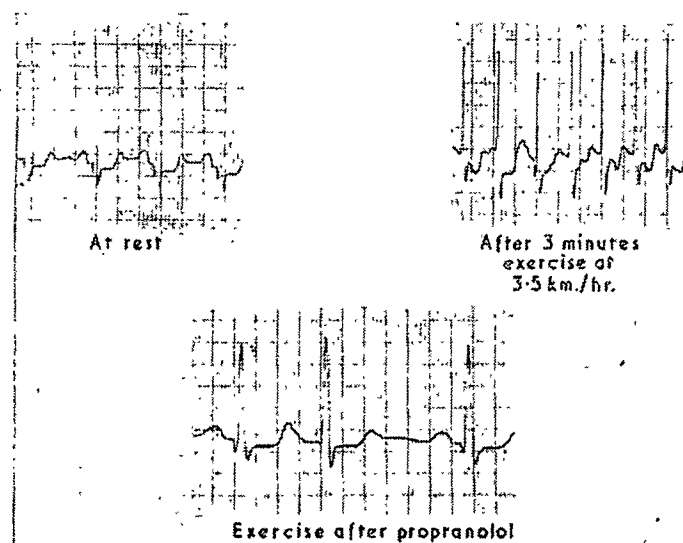


FIG. 1.—Electrocardiograms at rest and during exercise, showing the effect of propranolol in preventing atrial fibrillation.

In the four patients with atrial fibrillation symptoms were controlled in three when propranolol was added to their regimen (Cases 1, 2, and 4). In Cases 1 and 2 the paroxysms continued, but syncope did not occur. In Case 3 syncopal attacks continued to occur with exercise despite full treatment with digitalis, quinidine, and pronethalol. Endocardial pacing was then begun; however, the rhythm still alternated between a sinus mechanism and atrial fibrillation. With digitalis and pacing alone syncope continued to occur, but when propranolol was added syncope did not occur.

In the patients with paroxysmal atrial tachycardia the arrhythmia was suppressed provided the dose of propranolol was maintained, except in Case 5, where digoxin was necessary as well as the propranolol. When one patient (Case 7) discontinued treatment after three years he experienced one severe attack before resuming therapy. Two of the four patients with other atrial arrhythmias were suffering from a cardiomyopathy (Cases 10 and 11). Despite a failed direct current reversion in Case 11, both patients reverted to a sinus mechanism while receiving propranolol in addition to other medication. The patient with persistent unexplained sinus tachycardia (Case 12)

showed a satisfactory reduction in rate, as did the patient with rapid atrial flutter due to thyrotoxicosis. The arrhythmia in this case reverted to sinus rhythm when the thyrotoxicosis was controlled. In the group with ventricular ectopic beats propranolol reduced the ectopic beats and prevented the syncopal attacks.

Group B: Acute Arrhythmias

The seven patients included in this group had serious arrhythmias of acute onset associated with severe cardiac disease (Table II), and the dose and route of administration of propranolol varied with the type of the arrhythmia and the urgency of the clinical situation. In two patients the arrhythmia was associated with acute myocardial infarction and in three others coronary artery disease was associated with pulmonary embolism, digitalis toxicity, and a past history of paroxysmal atrial tachycardia respectively. Of the remaining two, one developed multifocal ventricular extrasystoles while undergoing surgery for subarachnoid haemorrhage, while the other had rapid atrial fibrillation associated with an alcoholic cardiomyopathy.

There were two patients with acute myocardial infarction. In one atrial flutter occurred (Case 17). After propranolol the ventricular rate slowed initially, and later there was reversion to sinus rhythm. In the other (Case 21) paroxysmal ventricular tachycardia was rapidly suppressed with oral propranolol (Fig. 2). Of the three patients with coronary disease propranolol proved effective in controlling both atrial and ventricular arrhythmias. In Case 18 multiple atrial and ventricular arrhythmias were controlled after quinidine, digoxin, and phenytoin sodium (Dilantin) had proved unsuccessful. In Case 23 an episode of very rapid nodal tachycardia with cardiac

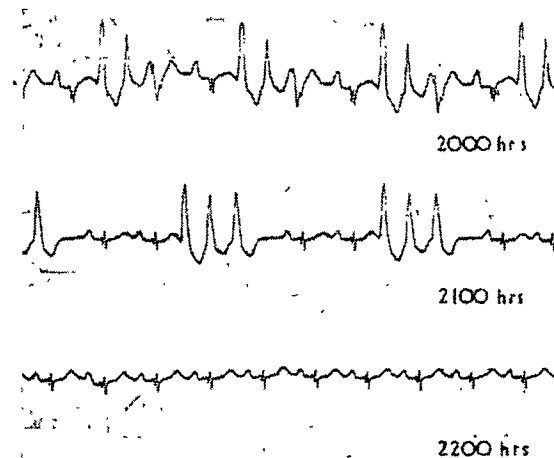


FIG. 2.—Electrocardiogram showing the effect of oral propranolol (20 mg. at 20.15 hours) on runs of ventricular extrasystoles.

TABLE II.—*Propranolol. Acute Arrhythmia*

Case No.	Age	Sex	Aetiology	Arrhythmia	Failed Therapy	Propranolol Dose and Route	Result
17	65	M	Acute infarction	Atrial flutter	Digoxin	10 mg. 4 × /day orally	Initial recurrence, but later controlled
18	66	F	Coronary artery disease. Pulmonary embolism	Atrial flutter. Atrial tachycardia. Ventricular tachycardia	Phenytoin sodium. Quinidine. Digoxin	10 mg. 4 × /day orally plus digoxin	Control
19	40	M	Subarachnoid haemorrhage. Anaesthetic	Multiple ventricular extrasystoles	Nil	2.5 mg. I.M. plus atropine 1.2 mg.	"
20	78	M	Coronary artery disease. Digitalis toxicity	Atrial tachycardia. Atrial fibrillation	Lignocaine I.V.	5 mg. I.V. followed by 10 mg. 3 × /day for 3 days	"
21	57	M	Acute infarction	Runs of ventricular tachycardia	Quinidine	20 mg. statim orally. 10 mg. 6-hourly decreasing doses	Control. Propranolol continued 7 days
22	61	M	Alcoholic cardiomyopathy	Atrial fibrillation	Digoxin	5 mg. I.V.	Control initially, but treatment not continued, and patient died
23	65	F	Coronary artery disease	Nodal tachycardia	"	Pronethalol 60 mg. I.V.	Control

failure was suppressed when intravenous pronethalol was administered to the patient in whom the arrhythmia had not been controlled with full doses of digitalis (Fig. 3). In Case 20 digitalis toxicity was present and atropine premedication produced very rapid atrial tachycardia. This was slowed with 50 mg. of lignocaine intravenously, and reverted to sinus rhythm after propranolol 5 mg. intravenously. In Case 19

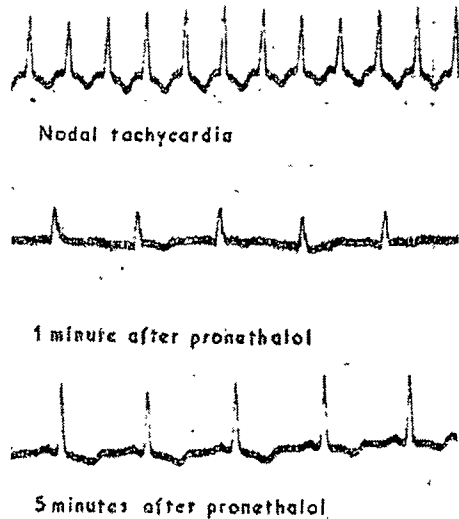


FIG. 3.—Selections from a continuous electrocardiogram taken during the administration of intravenous pronethalol.

the ventricular ectopics were rapidly controlled with intravenous propranolol. In Case 22, a patient with severe alcoholic cardiomyopathy, the ventricular rate was controlled, but the drug was inadvertently discontinued and subsequently the patient died.

Group C: Arrhythmias Associated with Prolonged Cardiac Arrest

There were eight patients in this group (Table III). In one propranolol was used initially, while in the remainder there had been prolonged cardiac arrest associated with resistant or recurrent ventricular fibrillation not responding to usual resuscitation methods, including the correction of acidosis, together with the administration of procainamide (Pronestyl) or lignocaine. In one (Case 25) 250 mg. of phenytoin sodium intravenously had also failed to maintain sinus rhythm.

In these patients the intravenous dose of propranolol ranged from 1 to 15 mg. The drug was always given cautiously in increments of 1 to 2 mg. covered by a single dose of atropine sulphate, 1.2 to 2.4 mg. intravenously. The duration of external

cardiac massage varied from 20 to 120 minutes before the administration of propranolol. In one patient (Case 24) propranolol alone was used to terminate ventricular tachycardia. In Case 25 ventricular fibrillation recurred after reversion with direct current counter shock on nine occasions (Fig. 4). Propranolol was administered after further counter shock and the patient then remained in sinus rhythm. In the other six patients (Cases 26 to 31) propranolol was given before direct current counter shock and in all cases satisfactory cardiac function was restored. All survived at least 12 hours, with four long-term survivors. Of the four deaths only one (Case 28) was due to a complication of drug therapy. This case has been

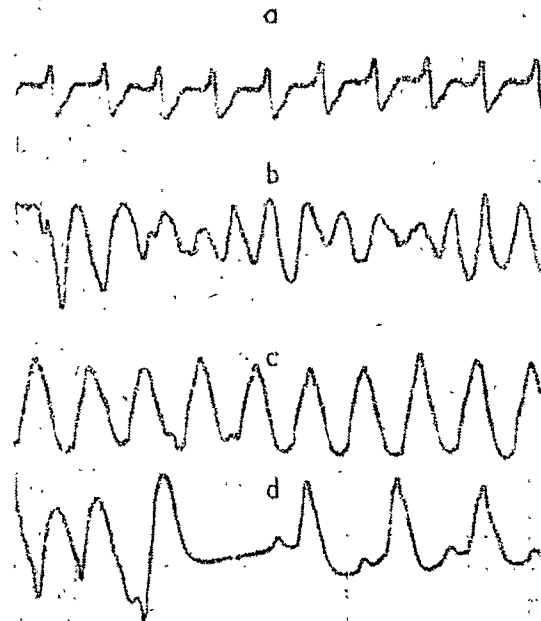


FIG. 4.—Selections from a continuous electrocardiogram taken during recurrent cardiac arrest: (a) supraventricular tachycardia; (b) ventricular fibrillation; (c) ventricular flutter; (d) ventricular fibrillation and the effect of direct current shock.

previously reported (Sloman *et al.*, 1965). Complete heart block developed while the patient was still receiving propranolol by slow intravenous infusion. The drug was not stopped, and the patient died in ventricular standstill.

Group D: Acute Myocardial Infarction

Forty-nine patients admitted to the coronary care ward with proved acute myocardial infarction were studied to assess the possible prophylactic value of propranolol in reducing the inci-

TABLE III.—Cardiac Arrest Group

Case	Age	Sex	Cause of Arrest	Duration of Cardiac Massage	Failed Treatment	Propranolol Dose and Result*	Follow-up
24	57	F	C.V.A. anoxia	20 min.	Nil	5 mg. I.V. *Sinus rhythm	Died 2 days later—C.V.A.
25	65	M	Coronary artery disease. Digoxin toxicity	Approx. 10 arrests over 2 hours	Procainamide. Phenytoin sodium. D.C. shock	2 mg. I.V. *Sinus rhythm	Survived
26	54	M	Coronary artery disease	60 min.	Lignocaine. Procainamide. D.C. shock	2 mg. I.V. + D.C. shock *Sinus rhythm	Died 2 days later of pulmonary oedema
27	61	M	Acute myocardial infarction	90 "	Digoxin. Procainamide. Sodium bicarb. Isoprenaline	5 mg. I.V. x 3 + D.C. shock *Sinus rhythm	Survived. Propranolol continued for six weeks
28	46	F	Digitalis toxicity	35 "	Sodium bicarb. Procainamide. Isoprenaline	5 mg. I.V. x 4 + D.C. shock *C.H.B.	Died—complete heart block
29	28	F	Renal failure. Pulm. embolism. Digitalis toxicity	75 "	Procainamide. Isoprenaline. Corticosteroids	2 mg. I.V. + 2.5 mg. I.M. *Sinus rhythm	Survived. Drug continued for seven days
30	60	F	Recurrent myocardial infarction	30 "	Procainamide. D.C. shock	5 mg. I.V. D.C. shock *Sinus rhythm with ventricular ectopics	Survived. V.F. recurred, but controlled by further 5 mg. I.V.
31	42	M	Aortic stenosis	40 "	Procainamide. Sodium bicarb. Isoprenaline	2 mg. I.V. + D.C. shock *Sinus rhythm	Died. Recurrent V.F. 3½ hours later

D.C. = Direct current. C.V.A. = Cerebrovascular accident. V.F. = Ventricular fibrillation. C.H.B. = Complete heart block.

dence of arrhythmias associated with acute infarction. Those with cardiogenic shock, complete heart block, or a past history of asthma were excluded from the trial. Patients were allocated to the treatment or the control group by random numbering. Twenty-six patients received propranolol, initially by the intravenous route in a dose of 0.1 mg./kg. body weight with 1.2 mg. of atropine sulphate followed by oral propranolol 10 mg. every four hours, beginning one hour after the intravenous injection and continuing for up to three weeks. Atropine sulphate 0.6 mg. intramuscularly four-hourly was continued for 12 hours and then propantheline 15 mg. eight-hourly was substituted. The control group comprised 23 patients who received treatment with analgesics, anticoagulants, diuretics, and digitalis as indicated, but no anti-arrhythmic drugs. If a significant arrhythmia developed in either group it was treated on its merits, usually with procainamide 500 mg. intramuscularly, repeated four-to-six-hourly as necessary. The patients remained in the coronary care unit for a minimum of 72 hours with continuous electrocardiographic monitoring throughout their stay. Alterations in rate or rhythm and conduction were documented by a 10-second recording of the electrocardiogram every 30 minutes, together with recordings of any arrhythmia which activated the automatic recorder or which was observed by the nursing staff. All arrhythmias were counted and the treated and control groups compared (Table IV).

TABLE IV.—*Classification, Deaths, and Incidence of Serious Arrhythmias in Propranolol Trial*

	Propranolol	Control
Mild	16	15
Severe	10	8
Shock	0	0
Deaths	3	4
No. of patients with serious arrhythmias ..	3	5
.. „ episodes of serious arrhythmias ..	4	5

Apart from atrial, nodal, and ventricular ectopic beats, which were common and of similar incidence in both groups, the incidence of serious arrhythmias was slight. In the group receiving propranolol one patient had two episodes of ventricular fibrillation and another two short episodes of ventricular tachycardia. There were three deaths in the treated group, one due to cardiogenic shock, another to brain damage following resuscitation from ventricular fibrillation, and the third due to ventricular fibrillation which occurred after the patient was discharged from the coronary care unit.

The incidence of non-specific side-effects was nil. One patient developed cardiogenic shock and another Wenckebach heart block after the administration of propranolol, but hypotension and cardiac failure were neither severe nor frequent.

In the control group two patients had short episodes of ventricular tachycardia and another prolonged slow ventricular tachycardia, which required treatment with procainamide. One patient developed ventricular fibrillation while in the coronary care unit and died, while another developed ventricular fibrillation in a general ward and was successfully resuscitated. The remaining two deaths in this group occurred in the general ward after discharge from the coronary care unit, and the mode of death is unknown. There was therefore no indication that propranolol reduced the frequency of arrhythmias in patients with acute myocardial infarction, but to reach a valid statistical conclusion much larger numbers would have to be studied.

Discussion

These clinical observations indicate that beta-adrenergic drugs have an important place in the treatment of acute and chronic arrhythmias irrespective of their origin or cause. These results are in agreement with previously published reports.

Propranolol was found to be useful in controlling the rate of ventricular response in patients with paroxysmal atrial fibril-

lation and flutter. The drug was used with digoxin, and syncope and giddiness no longer occurred. Syncope was also prevented by propranolol and digoxin when combined with endocardial pacing, supporting the work of Harris (1966), who was able to reduce the number of ventricular ectopic beats occurring during cardiac pacing by the use of oral propranolol when large doses of quinidine and procainamide had not been successful.

The efficacy of propranolol in preventing paroxysmal arrhythmias may be reliably assessed by provoking the arrhythmia by exercise on a treadmill and repeating the exercise on a treadmill after the administration of intravenous propranolol.

There appears to be a special place for the use of propranolol in patients with prolonged cardiac arrest associated with resistant, recurrent ventricular fibrillation. Propranolol has been shown to have an anti-fibrillatory effect, and we believe it should be used when standard resuscitation methods and drugs have not produced a satisfactory cardiac rhythm. It was found that a satisfactory anti-arrhythmic effect could be produced with a dose of propranolol much smaller than a recognized beta-blocking dose, supporting the work of Stickney *et al.* (1966) and Howe and Shanks (1966), who showed that the drug has a biphasic mode of action. Propranolol should therefore be given in small intravenous doses of 1–2 mg., repeated as necessary, and covered by a full dose of atropine sulphate to prevent overactivity of the unmasked parasympathetic nervous system. As propranolol appears to have an anti-arrhythmic effect which is not due to its beta-blocking effect it would therefore seem reasonable in certain circumstances to use propranolol in combination with isoprenaline. We have used this combination with success in six patients. In Cases 27, 28, 29, and 31 both drugs were used during resuscitation, and in Cases 25 and 26 isoprenaline was used after successful resuscitation without producing further ventricular fibrillation.

In Case 28 complete heart block developed after successful resuscitation. A slow intravenous infusion was continued, whereas cessation of the drug, followed by the administration of isoprenaline and perhaps endocardial pacing, may have led to a successful outcome.

Trials of the prophylactic value of propranolol in acute myocardial infarction were given impetus by the work of Snow (1965), who reported a mortality of 13% in 52 patients treated with propranolol compared with 29% mortality in a comparable control group of 55 patients. However, in our study of a relatively small group of patients monitored after infarction we found no significant difference in the incidence of arrhythmias. Studies by Clausen (1966), Balcon *et al.* (1966), and Barber *et al.* (1966) have failed to confirm any difference in mortality in patients treated with oral propranolol or to demonstrate a difference in the incidence of arrhythmias. In addition, initial favourable results prompted the arrangement of a multicentre double-blind trial which was reported by Stephen (1966). Ten centres participated, providing data on 195 patients, and no difference in mortality between treated and untreated group was demonstrated. Pentecost (1966) has questioned the amount of absorption of propranolol given orally in the early stages after myocardial infarction, as this was the mode of administration in these trials. However, in our studies the initial dose was always given intravenously, but, even so, no difference in the incidence of arrhythmias was detected.

The whole question of prophylactic treatment of cardiac arrhythmias after acute infarction is now under intense study. We accept the hypothesis of Lown and Killip (personal communications, 1966) that certain arrhythmias, particularly ventricular extrasystoles when they occur frequently, arise from multiple ventricular foci or occur in runs, are forerunners of more serious potentially lethal arrhythmias, and must be treated at once. Procainamide, propranolol, phenytoin sodium,

and lignocaine may be used by the intravenous route to suppress these arrhythmias, but why one morphological type of ventricular ectopic will respond to one of the above anti-arrhythmic drugs and not to another remains to be studied. Currently, lignocaine is the drug of choice because of its high therapeutic effect compared with its relatively slight negative inotropic effect. It is used in incremental doses up to 200 mg.

Summary

Thirty-one patients with cardiac arrhythmias were treated with beta-adrenergic blocking drugs propranolol and pronethalol. Propranolol was found to be particularly useful in the management of rapid arrhythmias when other anti-arrhythmic drugs had not been successful. Beta-adrenergic blockade was of value in reducing the ventricular rate in paroxysmal atrial fibrillation, atrial flutter, and rapid atrial and sinus rhythms. Propranolol also possessed a specific anti-arrhythmic effect not clearly related to its beta-adrenergic blocking effect, and was found to be useful in the treatment of ventricular extrasystoles, paroxysmal ventricular tachycardia, ventricular arrhythmias associated with digitalis intoxication, and recurrent and resistant ventricular fibrillation.

Forty-nine (26 treated, 23 control) patients with acute myocardial infarction were studied to assess the prophylactic value of propranolol in reducing arrhythmias in acute myocardial infarction. The drug was administered intravenously initially in a dose of 0.1 mg./kg./body weight together with atropine sulphate 1.2 mg. followed by 10 mg. of propranolol orally four-hourly for three weeks. There was no difference in the incidence of arrhythmias between the two groups.

Our thanks are due to the medical staff, Royal Melbourne Hospital, who allowed us to treat patients under their care. The propranolol used in this study was made available by Dr. Charles Proctor (Medical Director, I.C.I., Australia), to whom we are grateful. Mr. J. R. Bainbridge, Computer Centre, Monash University, advised on the statistical treatment of the results from the coronary care ward.

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Serum Folate Values in 423 Psychiatric Patients

M. W. P. CARNEY,* M.D., M.R.C.P.I., D.P.M.

Brit. med. J., 1967, 4, 512-516

With the widespread introduction of efficient ways of estimating serum folate, there have been reports of folate deficiency in malnutrition (Gough *et al.*, 1963), old age (Read *et al.*, 1965), a number of chronic physical illnesses (Batata *et al.*, 1967), neurological disease (Grant *et al.*, 1965), and patients receiving anticonvulsants, barbiturates (Klipstein, 1964; Malpas, 1966), antibiotics, and cytotoxic agents (Dr. E. J. Watson-Williams, personal communication). Folate deficiency and psychiatric conditions have also been associated—for example, anxiety/depression (Gough *et al.*, 1963) and dementia (Henderson *et al.*, 1966)—while 12 out of 43 patients with subnormal serum folate were currently attending a psychiatric department (Forshaw, 1965). Reynolds (1966, 1967) has gone so far as to suggest a causal relation between folate deficiency and certain forms of mental illness, especially affective changes and, in long-standing cases, dementia. There seems, however, to have been little systematic investigation of the incidence of folate deficiency in psychiatric populations.

These reports encouraged me to ascertain the incidence of low serum folate levels in a psychiatric population and its relation to a number of variables, including diagnosis, age, nutrition, physical state, drugs, and chronicity of illness. Though this investigation was not specifically designed to answer the question, it was felt that some clues regarding the

possible aetiological significance of folate deficiency in mental illness might appear.

Method and Material

Serum folate estimations were carried out on consecutive admissions to two psychiatric units 20 miles (32 km.) apart, one a general hospital unit and the other a mental hospital. They were all under my personal care and were admitted over a period slightly exceeding a year. Though the hospitals served the same geographical area they dealt with somewhat different psychiatric populations, the mental hospital tending to admit the more disturbed and more chronic patients. The intakes of both units were studied concurrently in order to ensure that the whole group was representative with respect to diagnosis, age, and sex of those psychiatric patients within the catchment area for whom admission to hospital was judged to be needed. Within individual subcategories of patients there was little variation in folate levels between the two hospitals.

Serum folate estimations were carried out by an adaptation of the method of Waters and Mollin (1961) by which folate activity was measured by reading turbidimetrically the growth of *Lactobacillus casei* A.T.C.C. 7469 after incubation in the sample solution for 48 hours at 37° C.: the results were calculated from a standard graph. These estimations were carried out in two different laboratories, but the procedures in both were identical.

* Consultant Psychiatrist, Blackpool and Fylde Hospital Group and Lancaster Moor Hospital.

Serum folate estimations were also carried out on nursing, medical, and clerical staff, mental welfare officers, and ambulance drivers—all volunteers. These constituted a control series; so far as was known none of them was receiving psychiatric treatment and all appeared to be physically fit.

There were 423 patients of mean age 54.04 ± 9.61 (282 females and 141 males). There were 62 controls of mean age 39.2 ± 12.65 (31 females and 31 males). Patients and controls differed significantly as regards age and sex, but since these factors were not found to be significantly associated with the folate levels within the context of the present investigation, they are probably of little importance. Only one patient had been receiving Cytamen (cyanocobalamin) previous to admission, none had received folic acid, and none was diagnosed as suffering from subacute combined degeneration of the cord.

Because of the undoubted influence of certain drugs in lowering the serum folate, blood was obtained as soon as possible after admission and nearly always before treatment was begun. Simultaneously, samples were sent to the laboratory for vitamin B₁₂ estimations. This paper does not deal with the breakdown of the B₁₂ results except where they seem to be relevant to the folate findings.

Results

The mean serum folate for the patients was 3.2 ± 1.73 $\mu\text{g./ml.}$ and for the controls 3.6 ± 1.5 $\mu\text{g./ml.}$ This difference is not quite significant ($t=1.92$; $P>0.05$). However, Fig. 1 shows a distinct clustering of the patients at the lower end of the scale not matched by the controls. If a folate level of 2 $\mu\text{g./ml.}$ is taken as the dividing point, there are only six controls as against 105 patients below this point. This difference is significant at the 1% level ($\chi^2=6.89$; $\text{d.f.}=1$). Values of serum folate below 2 $\mu\text{g./ml.}$ are hereafter referred to as "low folate."

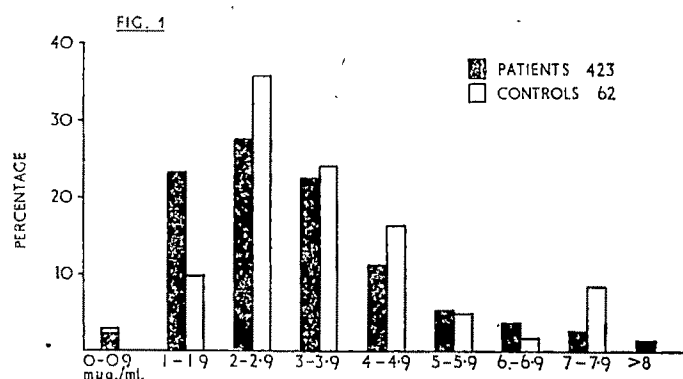


FIG. 1.—Serum folate levels: psychiatric patients compared with normal controls.

Age.—Depressed folate levels have often been found in geriatric patients. The relation between various age groups and their mean folate values is shown in Table I. There is obviously

TABLE I.—Mean Serum Folate Levels for Various Age Groups

	Age in Years							Overall Mean
	10-29	30-	40-	50-	60-	70-	80+	
Mean serum folate (μg./ml.)	3.2	3.6	3.1	3.4	3.0	3.0	3.1	3.2

no constant relation here. The mean ages of the low (53.8 ± 17.6) and normal folate (54.3 ± 17.12) patients did not differ significantly.

Sex.—The sex distribution did not alter with the serum folate level.

Haematological Findings.—A full blood count was made and a blood film taken in all patients. Of those with low folate values, 28 had haemoglobins of less than 80% and five had other abnormalities such as anisocytosis. Thus 33 (31.4%) of these patients had a haematological abnormality; of these seven showed macrocytosis and three had a low serum B₁₂. On the other hand, only 33 (10.7%) of patients with normal folate results had a haemoglobin below 80% or showed abnormality, and none had macrocytosis. The difference between the two groups is significant ($\chi^2=24.94$; $\text{d.f.}=1$; $P<0.001$).

Sternal Marrow.—A very small number of patients with evidence of anaemia, etc., were given sternal marrow puncture and a specimen of marrow was examined. Only one of these was unequivocally megaloblastic and this patient, besides having a serum folate of 1.2 $\mu\text{g./ml.}$, also had a serum B₁₂ of less than 25 $\mu\text{g./ml.}$ Thus in the present study no certain evidence of megaloblastic marrow change was found to be associated with a low folate value. This does not mean that megaloblastic marrow would not have been found if more sternal punctures had been performed. Obviously there is a limit to the frequency of this uncomfortable and sometimes frightening procedure in the psychiatric setting. Moreover, many of these patients were not very co-operative.

Folate Deficiency and Serum Vitamin B₁₂.—There have been reports that folate deficiency has resulted in subnormal serum B₁₂ levels with a return to normal after administration of folic acid (Forshaw *et al.*, 1964). In 368 of the present patients the serum B₁₂ result was available and there seems to be an association between the lower values of serum folate and a serum B₁₂ level below 150 $\mu\text{g./ml.}$ (hereafter called "low" B₁₂) (Table II). Patients with serum folate less than 2.9 $\mu\text{g./ml.}$ are significantly more liable to low serum B₁₂ than otherwise ($\chi^2=4.15$; $\text{d.f.}=1$; $P<0.05$). This finding, apart from its theoretical interest, is of practical importance. It has long been recognized that folic acid therapy in the presence of clinically occult vitamin B₁₂ deficiency can precipitate subacute combined degeneration. It seems prudent, therefore, to assess the vitamin B₁₂ status of folate-deficient patients before embarking on folic acid therapy.

TABLE II.—Incidence of Low Serum Vitamin B₁₂ (<150 $\mu\text{g./ml.}$) for Various Levels of Serum Folate

Serum folate (μg./ml.)	0-1.5 (n=56)	1.6-1.9 (n=46)	1.9-2.9 (n=100)	>2.9 (n=166)
Patients with low B ₁₂ (%)	21.4	15.2	15	10.2

Psychiatric Diagnosis

Table III shows the patients classified into diagnostic groups with mean ages, ranked in order of magnitude of mean serum folate. There is no corresponding progression of age, confirming that there is no clear-cut relation between serum folate and age. The following diagnostic groups have significantly lower

TABLE III.—Diagnostic Groups: Mean Ages and Mean Folate Levels Compared with Mean Folate Level for Controls (3.6 ± 1.5 $\mu\text{g./ml.}$)

Diagnosis	No.	Age (years)	Serum folate (μg./ml.)	Significance	
				t	P
Chronic alcoholism	27	46.4	6.3 ± 3.0	4.6	<0.001
Mania	18	54.0	4.1 ± 2.0		N.S.
Drug addiction	12	47.5	3.5 ± 1.6		N.S.
Schizophrenia	78	41.8	3.4 ± 1.6		N.S.
Neurosis (neurotic depression excepted)	30	48.9	3.3 ± 1.6		N.S.
Neurotic/reactive depression	71	47.7	3.2 ± 1.7		N.S.
Abnormal personality	15	34.5	3.2 ± 1.2		N.S.
Endogenous depression	75	55.0	3.0 ± 1.7	2.3	<0.05
Organic psychoses	90	72.9	2.9 ± 1.5	2.7	<0.01
Epilepsy	7	47.5	1.7 ± 0.8	7.2	<0.001
Total	423	54.04 ± 9.61	3.2 ± 1.73		

N.S. = Not significant.

mean serum folate values than the controls: epilepsy, organic psychoses, and endogenous depression; the only diagnosis with a mean serum folate significantly above that of the controls is chronic alcoholism.

In elucidating the relation between folate deficiency and psychiatric diagnosis, it was decided to exclude those patients with a low serum vitamin B₁₂, as this condition is thought to cause mental illness, and it has just been shown that this could have influenced the clinical picture in patients with the lower serum folate levels. Fig. 2 shows the distribution of patients with low serum folate values and normal serum vitamin B₁₂ among the various diagnostic groups ("organic" comprises dementia and delirious/subdelirious states; "others" include neurosis, abnormal personality, mania, drug addiction, and chronic alcoholism). Not unexpectedly, epilepsy has the highest proportion, with, surprisingly, depression next and organic psychoses coming only third. The distribution of diagnoses among the low folate patients is significantly different from that of patients with normal folate ($\chi^2=13.55$; d.f.=4; $P<0.01$). This situation is quite different from the distribution of diagnoses among patients with low serum B₁₂ levels, where organic states have a clear lead (Fig. 3).

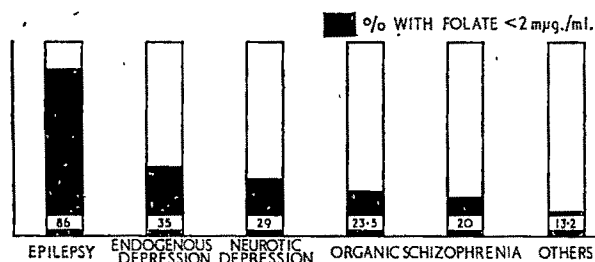


Fig. 2.—Low serum folate levels and psychiatric diagnosis in 317 patients.

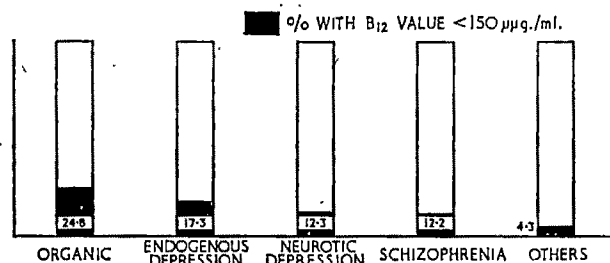


Fig. 3.—Low serum vitamin B₁₂ and psychiatric diagnosis in 377 patients.

The 19 patients with both low serum folate and vitamin B₁₂ levels tended to conform to the diagnostic pattern of the low serum B₁₂ group; thus there were eight organics, four endogenous depressives, three schizophrenics, two neurotic depressives, one other neurotic, and one chronic alcoholic.

Further Study of Low Serum Folate Group

The patients with low serum folate levels were more intensively studied for other aetiological factors, both by clinical examination and investigation and by social history-taking from relatives, etc., and consultation with the general practitioners. These last were particularly helpful in ascertaining the patients' preadmission medication (if any). The following results all refer to this group:

(a) *Drugs*.—Of the 105 patients, 79 (75%) had been on drugs in the three weeks before admission. The breakdown of these is presented in Table IV. The figures do not add up, because some patients had more than one drug. They are divided into drugs widely recognized as depressing serum folate and other drugs. Not unexpectedly barbiturates and anticonvulsants predominate among the former and phenothiazines and antidepressants among the latter. Of course any group of psychiatric patients might be expected to show this kind of drug pattern. The appropriate way of demon-

strating an association between low serum folate and drugs would be by comparing the preadmission drug intakes of low and normal folate groups. Unfortunately it was not possible to obtain this information for the normal serum folate group, but it was collected for those patients with low serum B₁₂. The preadmission drug patterns for both groups are compared in Table V, patients with simultaneous depression of serum folate and B₁₂ having been excluded. It is clear that the low folate group have had drugs far more frequently than the low serum B₁₂ patients, suggesting that psychotropic drugs are, in some way as yet unclear, associated with low serum folate levels. Of course the variation could be accounted for by other differences between the two groups.

TABLE IV.—*Drugs* and Serum Folate <2 µg./ml.*

Drugs cited as depressing serum folate:	No. of patients
Barbiturates	29
Anticonvulsants	5
Phenylbutazone	2
Antibiotics	1
Other drugs:	
Phenothiazines	22
Tricyclic antidepressants	9
Chlordiazepoxide	7
M.A.O. inhibitors	4
Others	8

* Some patients had more than one drug.

TABLE V.—*Drugs and Low Serum Folate and Vitamin B₁₂ Levels*

	No. of Cases	Drugs	No Drugs
Serum folate <2 µg./ml. and normal serum B ₁₂	86	68	18
Serum B ₁₂ <150 µg./ml. and normal serum folate	34	15	19
Total	120	83	37

$\chi^2=13.89$; d.f.=1; $P<0.001$.

(b) *Gastrectomy and Pregnancy*.—Only four of these patients had had a gastrectomy and only three were pregnant; thus these factors appeared to be relatively unimportant in the present context.

(c) *Gross Malnutrition*.—Twenty-four, or 22.9% of the group, including two food cranks and six patients with nutritional oedema, were suffering from this condition. No patient with intestinal malabsorption was found.

(d) *Physical Illness*.—An increasing number of chronic physical illnesses are being associated with folate deficiency. Might not much of the present serum folate subnormality be due to concomitant physical illness apart from gross malnutrition? Eighteen, or 17%, of the patients were physically ill: 10 with cardiovascular disease, four with chronic bronchitis, two with Parkinsonism, and one each with myxoedema and pulmonary tuberculosis. There were no examples of myeloclerosis or rheumatoid arthritis.

Thus there is little support for the idea that chronic physical illness, malabsorption, and malnutrition are solely responsible for folate deficiency. On the other hand, of 105 patients with a low serum folate, as presently defined, only 21 patients were free of a recent drug history, poor nutritional status, gastrectomy, pregnancy, and chronic physical illness. A further five had a low serum B₁₂ level, so that only 16 patients were without any recognized or suspected cause of folate deficiency. These 16 patients constitute the "idiopathic" low folate group, and one would expect these patients to show in pure culture the link, if any, between the avitaminosis and the sort of mental disturbance associated with it. However, the patients came from a broad psychiatric spectrum covering schizophrenia, dementia, chronic alcoholism, endogenous and neurotic depression, neurosis, and psychopathy. Thus the "primary" or "idiopathic" deficiency was not obviously associated with any particular mode of psychiatric presentation.

(e) *Chronicity of Mental Illness*.—In assessing chronicity very frequent episodes of illness with only brief periods of remission between, say, a week or two were counted as one period of continuous illness. The following figures relate to the interval between onset of present illness and present hospitalization: ill for less than three months, 13.4% of patients; three months to one year, 21.2%; one to three years, 21.2%; over three years, 44.2%. The proportion of chronic cases is almost certainly much higher than for the generality of hospitalized psychiatric patients. These findings raised the interesting speculation of which came first, the chronicity

or the folate deficiency? The long-term results of a trial of folic acid in the chronically mentally ill with a low serum folate might help to clear up the point.

There is evidence to suggest (Batata *et al.*, 1967) that subnormal serum folate is a nonspecific result of illness in general. It could therefore be expected that low values would occur with greater frequency with increasing duration of illness, irrespective of diagnosis; thus the syndromes with the highest proportion of depressed levels would be those with the greatest excess of chronic cases. The above findings to some extent support this idea, but can any importance be allotted to diagnosis? If chronicity were decisive the patients with low serum folate could be expected to be uniformly chronic within each diagnostic subgroup. In fact, this was found to be not so. The individual diagnoses vary widely for proportions of chronic cases; thus 66% of the subnormal folate schizophrenics had been ill for more than three years compared with 28% of the endogenous depressives. The figures for neurotics and organics were 50% and 36% respectively. This finding suggests that diagnosis has an association with low serum folate independent of duration of illness.

Discussion

This study was not designed to be a comprehensive investigation of the aetiology and biochemistry of folate deficiency: it was intended to be a preliminary screening of a representative sample of major mental illness in a defined community of population 300,000—namely, Blackpool and the Fylde. Nevertheless, within these limits some aetiological pointers emerged and certain tentative inferences can be drawn. The most striking result was the frequency of subnormal serum folate at 22.5% of the patients surveyed. However, the assumption that a low serum level of folate *invariably* indicates a folate deficiency state is not justified. Falsely low levels can occur as the result of the in-vivo and in-vitro actions of certain drugs—a possibility supported by the present findings; phenothiazines can suppress test organisms in biological assay—for example, the influence of chlorpromazine on *E. gracilis* (Herbert *et al.*, 1965)—and other laboratory artifacts can arise. In this investigation a normal control series was used to exclude some of these pitfalls. Empirically, a serum folate of 2 $\mu\text{g./ml.}$ was found to be a useful lower limit of normality, though this figure is much lower than commonly accepted levels—a finding suggesting that these levels are perhaps pitched too high.

Nevertheless, it is likely that these low serum folate values reflect a physiological imbalance, common in certain forms of mental illness, which has usually not progressed to megaloblastic anaemia. However, it does not automatically follow that the imbalance plays a causal part in psychiatric illness (see below).

The most striking associations with low serum folate were chronicity of illness, a history of medication, usually barbiturates, phenothiazines, or antidepressants, and the predominance of certain diagnoses—namely, epilepsy, endogenous depression, and organic brain syndromes. Also frequently present were malnutrition and, to a less extent, chronic physical illness. Apparently the duration of illness alone was not responsible for the associations with diagnosis.

Can drugs have played the decisive part in depressing the serum folate? The vast majority of these patients had had drugs, especially those recognized as serum-folate-depressant-like barbiturates; phenothiazines were also so prominent as to suggest they have a similar action. However, drugs, like chronicity, cannot be the whole explanation for the results, because schizophrenics and neurotics, the most chronic and probably the most medicated patients, relatively seldom had a low serum folate. On the other hand, endogenous depression and organic states, despite being of shorter duration and less likely to provoke prolonged courses of drugs, were unequivocally low in mean serum folate values. If duration of illness and drugs did not play a decisive part, what did?

It was found that malnutrition and chronic physical debility, though not invariably associated with low serum folate, were evenly distributed among the low folate patients, irrespective of psychiatric diagnosis, with the exception of organic states which, not surprisingly, had a slight excess. The most widely accepted explanation for dietary deficiencies in psychiatric patients is apathy and self-neglect, secondary to the mental state. This is probably an oversimplified view. As Reynolds (1967) points out, mental illness, self-neglect, dietary deficiency, and further mental deterioration caused by the deficiency are linked in a vicious circle. But what caused the psychiatric condition in the first place? An alternative explanation is that, in the same patient, vitamin deficiencies including folate can both cause and be caused by a psychiatric illness. The problem of investigating the interactions of these factors is thus a complex one, and prospective studies as well as long-term therapeutic trials of folic acid in patients with deficiency states are needed.

Epileptics are widely recognized as liable to folate deficiency largely due to the effects of anticonvulsant drugs (Malpas *et al.*, 1966), but here again chronicity of illness and physical deterioration certainly contribute.

An interesting finding was the difference in the diagnostic patterns among the low serum folate and low serum B_{12} patients. There is widespread agreement (Shulman, 1967) that organic psychosis is typical of vitamin B_{12} deficiency, the psychiatric counterpart of subacute combined degeneration of the cord. The present findings with regard to the low serum B_{12} patients are in accord with this observation: surprisingly, the diagnostic associations of subnormal serum folate are radically different, especially with respect to depressive states. It can fairly be deduced that this association with functional rather than organic psychosis implies a difference in the underlying pathophysiological mechanism from that of vitamin B_{12} deficiency.

Can the present investigation throw any light on the aetiological role of folate in mental illness? Despite our inability to establish a simple one-to-one relationship between "uncomplicated" low serum folate and a particular psychosyndrome, the present observations agree with Reynolds's (1967) suggestion that affective disturbances and organic psychoses are the typical psychiatric manifestations of folate deficiency, with a precision which is unlikely to be coincidental.

An unexpected finding was the significantly raised mean serum folate of the chronic alcoholics. That this may be more than a mere clinical curiosity is indicated by a report by Magnus (1966) describing a case of jejunal blind-loop syndrome, peripheral neuropathy, and high serum folate. He suggested that the raised serum folate might have caused the peripheral neuropathy even in the presence of normal serum B_{12} . The relevance of this observation for chronic alcoholism, a condition in which peripheral neuropathy is common, is obvious.

Conclusion

What are the practical implications of these results? There are three: firstly, folate deficiency would appear to be common enough in the mentally ill to justify carrying out serum folate and B_{12} estimations as routine admission procedures; secondly, it would be wise to treat patients with subnormal serum folate values with folic acid supplements, and, if indicated, cyanocobalamin, in the hope of securing mental as well as physical improvement; and thirdly, further exploratory studies as already suggested should be carried out.

Summary

Serum folate estimations were carried out on 423 psychiatric inpatients, consecutive admissions to a general hospital and a

mental hospital unit, and 62 normal controls. Serum vitamin B₁₂ estimations were also done on 368 of the patients. Though patients and controls did not differ on mean serum folate, there were significantly more patients with values below 2 $\mu\text{g./ml.}$ ("low folate") than controls. Patients with epilepsy, organic psychoses, and endogenous depression had significantly lower mean serum folate, and chronic alcoholics significantly higher mean serum folate, than the controls; the former conditions also predominated among patients with low folate, a diagnostic pattern significantly at variance from that of patients with normal folate values and those with serum B₁₂ <150 $\mu\text{g./ml.}$ Low folate patients had more haematological abnormalities, including low serum B₁₂, than other patients; 75.2% had received drugs during the three weeks before admission, 22.9% showed evidence of malnutrition, 17% were physically ill, and 44.2% had been continuously ill for more than three years.

I wish to thank Drs. F. Yates, P. Harvey, and F. Hayes, Messrs. Orrell, Curd, Singleton, and Kilgariff, and Sisters Hetherington

and Morton for advice and co-operation; and Mrs. J. Taylor and Mrs. E. Jackson for clerical assistance.

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Ascorbic Acid Nutrition in Gastroduodenal Disorders

MAX M. COHEN,* M.B., CH.B.; ANNE M. DUNCAN,† B.SC.

Brit. med. j., 1967, 4, 516–518

Frank clinical scurvy is a rare disease, but subclinical deficiency of ascorbic acid, as defined by low dietary intake of ascorbic acid and low blood levels, is common. Thus the significance of "subvitaminosis C" has been the subject of controversy since it was first described by Hess (1917). However, it is probably now accepted that, while under normal circumstances a low intake of ascorbic acid is harmless (Dahlberg, Engel, and Rydin, 1944), at times of stress, when there is increased utilization of ascorbic acid by the tissues generally (Faulkner and Taylor, 1937) and especially by wounded tissues (Crandon, Landau, Mikal, Balmanno, Jefferson, and Mahoney, 1958), dietary deficiency may render the patient vulnerable to infection (Heise and Martin, 1936) and the low blood ascorbic acid level may make the surgical patient more liable to wound dehiscence (Crandon, Lennihan, Mikal, and Reif, 1961).

Attention has recently been drawn to the low levels of leucocyte ascorbic acid seen in large numbers of surgical patients (Crandon *et al.*, 1961), in elderly patients (Bowers and Kubik, 1965), and particularly in patients with peptic disorders (Cohen, 1967).

The fundamental importance of vitamin C in the healing process has been demonstrated in guinea-pigs (Bourne, 1944; Penney and Balfour, 1949; Gould, 1958; Ellis, Harrison, and Hugh, 1965) and in humans (Hunt, 1941; Boyd and Campbell, 1950), the two animal species known not to synthesize ascorbic acid. It is therefore important to understand the significance of the low blood levels of ascorbic acid consistently found in patients with peptic ulcer (Harris, Abbas, Yudkin, and Kelly, 1936; Platt, 1936; Archer and Graham, 1936; Lazarus, 1937; Portnoy and Wilkinson, 1938), as in these patients surgery is often the treatment of choice.

In this investigation we have attempted to assess the extent of ascorbic acid deficiency in surgical patients, and in particular in those with duodenal ulcer, using the leucocyte ascorbic acid level, as this is now accepted as the best available index of ascorbic acid nutrition (Bartley, Krebs, and O'Brien, 1953), and to relate these findings to dietary intake of ascorbic acid.

Method

Leucocyte ascorbic acid levels were estimated by the method of Denson and Bowers (1961). Particular care was taken to avoid delays of more than several minutes between venepuncture and beginning the initial fractionation of the blood, as white blood cells take up ascorbic acid from the plasma on standing. Simultaneous estimations were made of the white blood cell count and platelet count to allow any necessary conversion factor to be applied (Gibson, Moore, and Goldberg, 1966); but in fact all of these counts fell within the accepted normal range and thus no conversion factor was necessary. The levels of ascorbic acid quoted subsequently represent the total ascorbic acid present in the white cells plus the platelets, though conventionally expressed as microgrammes per hundred million white blood cells ($\mu\text{g./10}^8$ W.B.C.).

The leucocyte ascorbic acid levels were estimated in 14 normal healthy young adults, all of whom were known to have an intake of ascorbic acid of at least 30 mg./day, the level of intake recommended by the Medical Research Council (Bartley *et al.*, 1953) and adopted by the British Medical Association.

A random sample of 50 patients admitted to a general surgical unit in a large city teaching hospital was investigated. All were admitted during November or December, a time of year when the autumn peak of ascorbic acid nutrition (National Food Survey Committee, 1966) would still be reflected in the leucocyte ascorbic acid level and above average levels could reasonably be expected. Dietary histories were obtained from all patients and normal subjects by one of us (M.M.C.) using a questionnaire based on the tables of McCance and Widdowson (1960).

Of the 50 patients investigated 14 were found to be suffering from some gastroduodenal disorder, and in all 14 the diagnosis was confirmed at laparotomy. Fourteen surgical patients with no known alimentary disease, matched for age and sex, were used as controls.

Nine of the 14 patients with gastroduodenal disorders had duodenal ulcer alone; all were treated surgically by total vagotomy and pyloroplasty. Eight of them were reviewed five months after surgery (one patient being lost to follow-up).

* Department of Surgery, Glasgow Royal Infirmary. Present appointment: Surgical Registrar, Western Infirmary, Glasgow W.I.

† Department of Biochemistry, Glasgow Royal Infirmary, Glasgow C4.

Results

(1) *Normals*.—In 14 normal young adults (eight male, six female) with a mean age of 22 years (S.D. ± 1.7) and on an adequate diet, the mean leucocyte ascorbic acid level was $21.7 \mu\text{g./}10^8 \text{ W.B.C.}$ (S.D. ± 4.6). The range of values was 15.0–29.0 $\mu\text{g./}10^8 \text{ W.B.C.}$ The mean dietary intake of ascorbic acid was 48 mg./day (S.D. ± 19.5), the range of values being 30–101 mg./day. In these subjects there was no correlation demonstrable between the level of intake of ascorbic acid and the leucocyte ascorbic acid level (Fig. 1).

(2) *Control Patients*.—In 14 control patients (seven male, seven female) with a mean age of 50 years (S.D. ± 17.0) and with no known alimentary disease the mean leucocyte ascorbic acid level was $22.9 \mu\text{g./}10^8 \text{ W.B.C.}$ (S.D. ± 5.9). The mean dietary intake of ascorbic acid in this group was 39 mg./day (S.D. ± 17.3). A strong correlation was observed between the ascorbic acid intake and the leucocyte ascorbic acid level (Fig. 2).

(3) *Gastroduodenal Disorders*.—The mean leucocyte ascorbic acid level in 14 patients (seven male, seven female) with gastro-duodenal disorders (mean age 50 years, S.D. ± 17.0) was $11.0 \mu\text{g./}10^8 \text{ W.B.C.}$ (S.D. ± 4.4). The mean dietary intake of ascorbic acid was 27 mg./day (S.D. ± 12.5). In this group there was fair correlation between the leucocyte ascorbic acid level and the dietary intake of ascorbic acid (Fig. 3).

(4) *Duodenal Ulcer Before Surgery*.—The mean leucocyte ascorbic acid level in the eight patients (five male, three female) with duodenal ulcer who were subsequently reviewed was $8.7 \mu\text{g./}10^8 \text{ W.B.C.}$ (S.D. ± 1.3). The mean dietary intake of ascorbic acid was 27 mg./day (S.D. ± 10.7), no correlation being demonstrable between this and the leucocyte ascorbic acid level (Fig. 4).

(5) *Duodenal Ulcer After Surgery*.—Five months after surgery, when the eight patients (five male, three female) with duodenal ulcer were reviewed, the mean leucocyte ascorbic acid level was found to be $12.8 \mu\text{g./}10^8 \text{ W.B.C.}$ (S.D. ± 4.3) and the mean dietary intake of ascorbic acid was 53 mg./day (S.D. ± 27.9). The relation between ascorbic acid intake and leucocyte ascorbic acid is shown in Fig. 4.

The results demonstrate no significant difference between the leucocyte ascorbic acid levels or ascorbic acid intakes of normal subjects and control patients. The dietary intake of ascorbic acid was significantly lower in patients with gastroduodenal disorders than in control patients ($P > 0.05$). No difference was demonstrated between the ascorbic acid intake of patients with duodenal ulcer and those with gastroduodenal disorders in general. The leucocyte ascorbic acid levels in patients with gastroduodenal disorders, and particularly duodenal ulcer, were significantly lower than in controls ($P > 0.01$).

While patients with duodenal ulcer had lower leucocyte ascorbic acid levels than patients with gastroduodenal disorders in general, this was not significant. After surgery for duodenal

ulcer, however, there was a significant rise in the leucocyte ascorbic acid level ($P > 0.05$) and in the dietary intake of ascorbic acid ($P > 0.01$).

In no patient was there any obvious clinical evidence of scurvy. None of the patients had clinical evidence of steatorrhoea or malabsorption, and in no patient was there any gross upset of haemoglobin level or of the plasma proteins. The patients who were reviewed after surgery for duodenal ulcer were well, offered no dyspeptic symptoms on specific questioning, and in particular none had post-vagotomy diarrhoea.

Discussion

The leucocyte ascorbic acid level has been shown to be significantly lower in patients with gastroduodenal disorders, and, in particular, in duodenal ulcer than in a control group. These patients have also been shown to subsist on a dietary intake of ascorbic acid below the 30 mg./day recommended by the British Medical Association (1950) at a time of year when dietary ascorbic acid could normally be expected to be above average. None of the patients subsisted on a "scurbutogenic" diet of less than 10 mg./day (Bartley *et al.*, 1953).

In patients with gastroduodenal disorders and in controls a correlation has been shown to exist between the dietary intake of ascorbic acid and the leucocyte ascorbic acid level. There was, however, no such correlation demonstrable in normal young adults on high intakes of ascorbic acid nor in patients with duodenal ulcer after surgery.

Low leucocyte ascorbic acid levels have been found in elderly patients (Bowers and Kubik, 1965), and this has been attributed to a reduced dietary intake of ascorbic acid (Andrews and Brook, 1966). Williamson, Goldberg, and Moore (1967) have found low leucocyte ascorbic acid levels in patients with malabsorption and after various gastric operations, in association with a normal intake of ascorbic acid, and they postulate the possibility of this being due to increased utilization of ascorbic acid in these circumstances.

Our findings suggest that the low leucocyte ascorbic acid level found in the patients with gastroduodenal disorder is due to dietary deficiency of ascorbic acid rather than to any increased utilization or malabsorption of ascorbic acid. This correlates well with everyday experience of the dietary habits of patients with dyspepsia.

Experiments in guinea-pigs have shown that ascorbic acid is essential for the formation of mature collagen in wounds (Robertson and Schwartz, 1953; Gould, 1958), and, in addition, that there is a definite correlation between the dietary intake of ascorbic acid and the rate of collagen formation (Robertson, 1961). It has also been shown that a dose of less than 5 mg. of ascorbic acid per day (5 mg. daily is roughly five times the amount necessary to protect the guinea-pig from

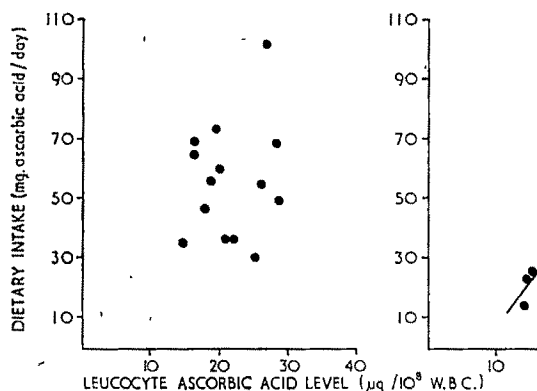


FIG. 1

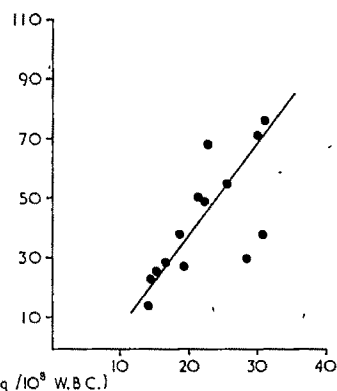


FIG. 2

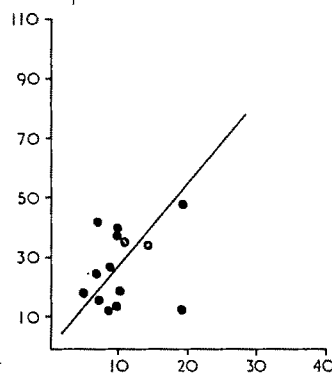


FIG. 3

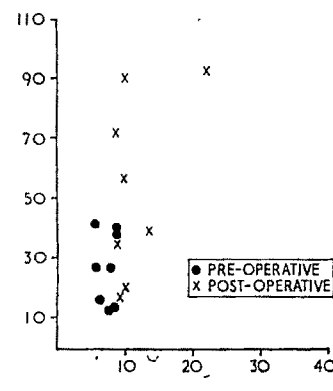


FIG. 4

FIG. 1.—Relation of ascorbic acid intake to leucocyte ascorbic acid in 14 young adults. FIG. 2.—Relation of ascorbic acid intake to leucocyte ascorbic acid in 14 control patients. FIG. 3.—Relation of ascorbic acid intake to leucocyte ascorbic acid in 14 patients with gastroduodenal disorders. FIG. 4.—Relation of ascorbic acid intake to leucocyte ascorbic acid in eight patients with duodenal ulcer.

scurvy) is not adequate to permit a maximal collagen concentration in guinea-pig experimental carrageenin granulomas (Robertson, 1966).

Because of the technical difficulty of studying human wound healing it is not yet known whether there is a critical level of ascorbic acid nutrition below which wound healing is impaired. But the evidence from guinea-pig experiments, together with the evidence of a high incidence of poor ascorbic acid nutrition in patients suffering the complication of complete wound dehiscence (Crandon *et al.*, 1958), must make us view with concern the low leucocyte ascorbic acid levels we have shown in patients with gastroduodenal disorders.

Until it is shown conclusively that patients with low leucocyte ascorbic acid levels are at no greater risk of impaired wound healing it would appear mandatory that all patients who could be expected to have such low levels be given routine ascorbic acid supplements before surgery and during the phase of early wound healing. This can be done easily and very cheaply by means of oral ascorbic acid tablets, and in emergencies saturation can be achieved by the intravenous route. There are no known hazards of ascorbic acid therapy, and overdosage is therefore of no practical importance.

We have shown that after successful surgery for duodenal ulcer there was the expected return to a normal diet with an adequate intake of ascorbic acid. It is very interesting, however, that though the leucocyte ascorbic acid levels significantly improved after surgery they did not return to normal levels even after five months had elapsed. The turnover half-life of labelled ascorbic acid is approximately 20 days (Baker, Saari, and Tolbert, 1966), so no improvement in ascorbic acid nutrition could be expected with the further passage of time. A possible explanation of this finding is that after vagotomy and pyloroplasty there is a relative malabsorption of ascorbic acid. The absorption of ascorbic acid is impaired by achlorhydria (Alt, Chinn, and Farmer, 1939), so it may be that the therapeutic hypochlorhydria achieved by complete vagotomy is responsible for the failure of a normal diet to correct completely the abnormal leucocyte ascorbic acid levels found in patients with duodenal ulcer.

Summary

Fourteen patients with gastroduodenal disorders had significantly lower levels of leucocyte ascorbic acid than 14 control patients and 14 healthy young adults. The mean leucocyte ascorbic acid level in the test patients was $11.0 \mu\text{g./}10^8 \text{ W.B.C.}$ and in the control patients was $22.9 \mu\text{g./}10^8 \text{ W.B.C.}$ ($P > 0.01$).

Eight patients with proved duodenal ulcer had a reduced dietary intake of ascorbic acid and a low level of leucocyte ascorbic acid (mean $8.7 \mu\text{g./}10^8 \text{ W.B.C.}$). After vagotomy and pyloroplasty the dietary intake returned to normal and the

leucocyte ascorbic acid level increased significantly ($P > 0.05$) though normal levels were not achieved.

The significance of these findings was discussed, and it was recommended that patients with peptic ulcer should have routine supplements of ascorbic acid before surgery is performed and during the period of postoperative convalescence.

We are indebted to Mr. John Hutchison for his encouragement and permission to study patients in his wards, and to Professor H. G. Morgan and Sir David Cuthbertson for helpful advice and criticism. We are grateful to Dr. G. MacDonald for haematological estimations and to Miss Catherine M. Smith for assistance with the dietary investigations.

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Clinical Experience with Bethanidine in Treatment of Hypertension*

JULIAN BATH, M.B., B.Sc., M.R.C.P.ED.; DOUGLAS PICKERING, M.B., M.R.C.P.ED.

RICHARD TURNER, M.D., F.R.C.P., F.R.C.P.ED.

Brit. med. J., 1967, 4, 519-521

At the present time probably most patients with high blood pressure in this country are being treated with guanethidine or methyl dopa with or without the addition of an oral diuretic. Because of certain disadvantages of these two drugs in our experience (Lowther and Turner, 1963; Johnson *et al.*, 1966) we have largely confined our attention during the past three years to debrisoquine (Kitchin and Turner, 1966) and bethanidine. Experience with the latter drug is the subject of this paper.

Pharmacology

Bethanidine is a post-ganglionic adrenergic neurone-blocking agent which exerts a marked postural hypotensive effect (Boura *et al.*, 1961; Boura and Green, 1963; Fewings *et al.*, 1964). In man sympathetic blockade begins about two hours after a single dose, is maximal in four to five hours, and fades in 8 to 12 hours, but the duration of action depends on the dose administered (Smirk, 1963; Johnston *et al.*, 1964; Wilson *et al.*, 1965). The absorption and excretion of ¹⁴C bethanidine in man was studied by Doyle and Morley (1965), who showed that after oral administration absorption was rapid and almost complete. Excretion is almost entirely in the urine, the rate depending on the glomerular filtration rate. Other studies have shown the renal clearance of inulin and of para-aminohippuric acid to be slightly reduced in patients given bethanidine (Esch and Krammer, 1965).

The precise mechanism whereby bethanidine causes blockade of adrenergic neurones is unknown (Boura and Green, 1965). An initial sympathomimetic effect has been demonstrated in man and animals, possibly due to release of catecholamines, for it is blocked by phenoxybenzamine (Fewings *et al.*, 1964), and increased sensitivity to noradrenaline after bethanidine further suggests peripheral release of catecholamines by this drug. Bethanidine resembles bretyliumtosylate and debrisoquine in that blockade is achieved without early depletion of tissue catecholamines, in this respect differing from guanethidine and guanoclor. However, large doses of bethanidine over long periods reduce catecholamines in some tissues (Boura *et al.*, 1961). Unless administered in very high concentration bethanidine does not block cholinergic or motor-neurone activity (Boura and Green, 1963).

Material and Methods

Between September 1964 and March 1967 70 patients were treated with bethanidine for periods ranging from six to 24 months: 23 were followed up for six to 12 months, 10 for 13 to 18 months, 22 for 19 to 24 months, and 15 for 25 to 30 months. In addition 12 patients stopped treatment earlier for reasons discussed below. Ages ranged from 21 to 66 years. Of the 82 patients 41 were male and 41 female. Table I includes the age distribution related to severity of the disease.

Indications for treatment, selection of patients, methods of blood pressure measurement, criteria of severity, and classification of results were similar to those we have already described in relation to the other drugs except that this series includes more relatively young patients without evidence of secondary changes in the heart or fundi.

Half the patients had previously received treatment with other antihypertensive drugs. Most new patients were admitted to hospital for assessment of the severity and type of their hypertension and the initiation of appropriate treatment. In some who had been fully assessed previously and treated for

a period with other drugs the change-over was arranged on an outpatient basis. The usual reason for change was difficulty in controlling the blood pressure, undue postural hypotension, or side-effects.

TABLE I.—Clinical Features

	Severe Hypertension	Moderate Hypertension	Total
Patient age group:			
30-40	4	7	11
41-50	11	8	19
51-60	13	21	34
61-70	11	7	18
Mode of presentation:			
Left ventricular failure ..	6	2	8
Cerebrovascular accident ..	13	6	19
Headache	2	6	8
Dizziness	4	7	11
Visual disturbance	2	0	2
Angina	1	7	8
Routine examination	11	15	26
Blood urea:			
< 40 mg./100 ml.	28	35	63
> 40 mg./100 ml.	11	8	19
E.C.G.:			
L.V. hypertrophy present ..	34	8	42
L.V. hypertrophy absent ..	5	35	40
Retinal changes:			
Normal	0	11	11
Grade I-II	21	27	48
Grade III	15	5	20
Grade IV	3	0	3
Resting diastolic pressure before treatment:			
105-129 (mm. Hg)	15	22	37
130-149	18	14	32
150+	6	7	13

The initial dose of bethanidine was usually 5 mg. twice daily. Increments were made every third day in hospital patients and every week in those being treated at home until an adequate response was obtained. Frequency of attendance at the clinic depended on the degree of control or the presence of side-effects. The daily dose ranged from 10 to 120 mg., with an average of 32.5 mg. in the initial stages and 43 mg. later on.

As in previous studies of antihypertensive drugs the aim of treatment was to reduce the standing diastolic pressure to as near normal levels as could be achieved without undue side-effects. In patients with cerebral or coronary atherosclerosis or with a persistently raised blood urea the blood pressure was lowered more cautiously and reduction to a standing diastolic level of 100-105 mm. Hg was regarded as a satisfactory result. Only the fall in pressure achieved and maintained has been considered in classifying the results of treatment. A "good" result signifies a fall in diastolic pressure to below 100 mm. Hg. A "fair" result signifies a fall of diastolic pressure to between 100 and 110 mm. Hg. A "poor" result denotes failure to maintain a diastolic pressure below 110 mm. Hg. It will be appreciated that a precise classification is not possible because in some patients the deliberate aim has been to achieve a fair result as defined by reduction in blood pressure.

The results have been tabulated for each patient at intervals of six months.

Results

Of the original 82 patients, four died, seven discontinued bethanidine because of side-effects, and one defaulted before the end of six months. The remaining 70 all completed at least six months of treatment (Table II).

After six months one patient discontinued the drug because of side-effects, two defaulted, and seven died. At the end of

* University Department of Medicine and the Cardiac Department of the Western General Hospital, Edinburgh 4.

TABLE II.—Results

	Control	Patients		Total	
		Moderate	Severe	No.	%
At 6 months	Good	15	15	30	43
	Fair	13	8	21	30
	Poor	9	10	19	27
At 12 months	Good	12	12	24	52
	Fair	10	3	13	28
	Poor	3	7	10	20
At 18 months	Good	13	8	21	56
	Fair	5	3	8	22
	Poor	2	6	8	22
At 24 months	Good	4	5	9	60
	Fair	3	1	4	27
	Poor	1	1	2	13

six months 73% of patients had good or fair control of their blood pressure. Results improved with continued treatment and adjustment of dosage with or without the addition of an oral diuretic, the proportion having good or fair control rising to 80% after 12 months and to 87% in the 15 patients who had been treated for two years. Most of the poor results were in patients with severe hypertension.

Of the 19 patients in whom initial control was unsatisfactory 13 continued treatment for 12 months or more. Good or fair control was achieved in five by increasing the dose and in three more by the addition of an oral diuretic. Of the five patients in whom control was persistently poor two had severe cerebral atherosclerosis, one uraemia, one asthma requiring corticosteroid therapy, and one cor pulmonale. Temporary failure of control was attributed to tolerance in two patients and to side-effects in two others. Of nine patients with only fair control throughout, two had severe cerebral atherosclerosis, five side-effects, and one a rising blood urea.

Deaths

Eleven patients died during treatment, but in none was this thought to be attributable to the drug being used or to failure to maintain reasonable control over the blood pressure or to side-effects. Three died from myocardial infarction, three from cerebral haemorrhage, and two from uraemia. In addition, one died from rupture of an aortic aneurysm and one suddenly from an unknown cause.

Four patients had been under treatment for three months or less, four for 8 to 14 months, and three for approximately 18 months. Seven had previously shown evidence of coronary or cerebral atherosclerosis.

Side-effects

Thirty-one patients (38%) had symptoms from postural hypotension, but in most cases this was relieved by adjustment of dosage while still maintaining satisfactory control over the blood pressure. A few had syncope and in five bethanidine had to be discontinued.

As is usual with drugs which lower blood pressure by sympathetic blockade the lowest readings were recorded first thing in the morning or when special readings were taken during what are normally sleeping hours. It is of interest in this connexion that several patients complained of syncope or dizziness after rising at night to pass urine.

Transient focal neurological disturbances associated with postural hypotension were recorded in two patients, but in none of the six whose death was attributable to a cerebral vascular accident or in the two patients who died of renal failure had there been excessive hypotension.

Five patients complained of muscular weakness soon after starting treatment and in two the drug was discontinued. Two who complained of impotence had previously experienced this symptom when taking other antihypertensive drugs. There was no case of diarrhoea or of mental depression. Two patients developed cardiac failure while on treatment, but this was attributable to the underlying heart disease.

The incidence of side-effects bore no obvious relation to the initial severity of hypertensive disease, the presenting symptoms, associated atherosclerosis, the degree of blood pressure control, or subsequent death. As with other antihypertensive drugs the incidence between individuals was most variable.

Oral Diuretic Supplements

In order to facilitate comparison with other drugs it had been intended, if possible, to treat all patients with bethanidine alone. However, it became necessary to add an oral diuretic in 28 cases on account of difficulty in controlling the pressure, side-effects, or fluid retention.

As can be seen from Table III the mean daily dose of bethanidine was gradually increased for most patients. In 19 cases the dose was increased to improve control and in seven to regain control on account of tolerance. An oral diuretic was added to improve control in six and to regain control in two patients. The fact that supplementary oral diuretics were used in 34% of all patients reflects the difficulty experienced in achieving satisfactory control with freedom from excessive postural hypotension when using bethanidine alone. In a few cases a diuretic was used from the start because rapid control of the blood pressure or a diuresis was required. Diuretics were used in a proportionately larger number of patients the longer treatment continued, because of an increased tendency to make this addition whenever difficulty with control or side-effects was experienced.

TABLE III.—Average Dose of Bethanidine According to Duration of Treatment

Duration of Treatment (months)	No. of Patients	Average Dose Bethanidine (mg.)
3	77	32.5
6	70	37
12	47	40
18	37	43
24	15	45

Comparison of Guanethidine, Methyldopa, Debrisoquine, and Bethanidine

Since the treatment of hypertension with guanethidine, methyldopa, and debrisoquine has previously been described from our unit some comparison between these drugs can be made. Recently, however, there has been a decreased incidence of severe hypertensive disease and a progressive tendency to treat patients who have relatively mild hypertensive disease. It is no longer thought desirable to carry out double-blind trials of different drugs in the same patient because of greater ease of controlling the blood pressure. All that is required is to change treatment to another preparation in any patient not doing well on a particular drug.

Table IV shows the results of treatment in groups of patients thought to have hypertensive disease of comparable severity according to the criteria described. Seventy-three with severe hypertension were treated with guanethidine, 37 with methyldopa, 31 with debrisoquine, and 26 with bethanidine, all for more than six months and many for as long as 18 months. The same criteria were used in classifying results on the basis of blood pressure control. It will be seen that there is no striking difference in the results of treatment with the four

TABLE IV.—Comparison of Long-term Results and Supplementary Use of Oral Diuretics in Treatment of Severe Hypertension with Guanethidine, Methyldopa, Debrisoquine, and Bethanidine

Control	Guanethidine 73 Patients	Methyldopa 37 Patients	Debrisoquine 31 Patients	Bethanidine 26 Patients
Good ..	40%	54%	71%	70%
Fair ..	40%	33%	22%	15%
Poor ..	20%	13%	7%	15%
Supplementary diuretics ..	56%	41%	65%	38%

preparations. About 50% of patients on guanethidine, about 40% each with methyl dopa and bethanidine, and about 65% with debrisoquine, required the addition of an oral diuretic. This probably reflects a somewhat greater degree of tolerance to debrisoquine, but on the other hand, as discussed below, postural symptoms and side-effects were least with this preparation.

Discussion

The rapid onset of the antihypertensive effect after oral administration of bethanidine and the short duration of action are obvious advantages when reduction of blood pressure is required as an emergency or when an excessive hypotensive effect has to be counteracted quickly. In the two instances in which we have used oral bethanidine to gain rapid control of malignant hypertension a satisfactory response was obtained within the first 24 hours.

In long-term treatment fair or good control was obtained in 73 to 87% of patients, depending on the duration of treatment. These results are similar to those reported by Montuschi and Pickens (1962), who used supplementary oral diuretics in over half their patients, and by Johnston *et al.* (1964), who used oral diuretics in less than 20% of cases. In the report by Smirk (1963) the assessment of results was rather different, but approximately 60% of 56 patients were controlled with bethanidine alone. Esch and Krammer (1965) obtained a satisfactory result in 35 out of 40 outpatients, using supplementary oral diuretics only occasionally.

The chief difficulty we have encountered is postural hypotension, which is most likely to occur in the initial phases of treatment when quite pronounced fluctuations of standing blood pressure may occur. Postural symptoms may be particularly troublesome in the morning, and in those who for any reason have to get out of bed at night. The fall in pressure which follows micturition may be an additional factor in some cases. Postural hypotension is also particularly apt to develop after the addition of an oral diuretic unless care is taken to make an adequate reduction in the dose of bethanidine. We have the impression that this may occur more readily than with other antihypertensive drugs but that smoother control may sometimes be achieved by suitable timing of the doses of bethanidine given three or four times during the 24 hours, depending on individual requirements. Since bethanidine has considerable advantages in other respects persistence is well worth while because satisfactory control can usually be achieved.

Possibly each patient should first be treated for three to four weeks with an oral diuretic, after which time it is known that there is no further reduction in exchangeable sodium and that plasma and extracellular fluid volumes rise to previous levels, though the antihypertensive action of the diuretic persists (Peters, 1966).

However, the long-term administration of oral diuretics in the treatment of hypertension depletes the body not only of sodium but of potassium and other ions, including magnesium, so that many would prefer not to use them routinely. In all cases it is only sensible to reduce the intake of salt.

The dose of drug required to maintain control increased in many patients after they left hospital, but tolerance with bethanidine is not a serious problem and can always be overcome. After three to six months, when smooth control had been obtained, a further increase in dosage or the addition of an oral diuretic was required in about one-third of patients, but increments were usually small and after 18 months the need for a further increase was exceptional. It would therefore appear that tolerance is less of a problem in long-term management of hypertension with bethanidine than with debrisoquine. On the other hand, good control of the blood pressure during the first six months of treatment was achieved in a higher proportion of patients with debrisoquine and there was a lower incidence of side-effects. If in the first few months

control can be achieved with bethanidine without undue postural effects it is likely to remain satisfactory.

In our experience the disadvantages of guanethidine included the difficulty in adjustment of dosage because increments were so critical, the frequency and disabling nature of side-effects, postural hypotension and syncope of effort, and the development of tolerance. With methyl dopa side-effects were usually milder and less persistent, but many patients did not feel well; also a number of severe toxic effects have now been reported, including Parkinsonism, hyperpyrexia, jaundice, and haemolytic anaemia.

Tolerance with debrisoquine and postural hypotension with bethanidine are relative disadvantages but less troublesome and disabling than the difficulties encountered with guanethidine or methyl dopa.

There would now seem to be no case for beginning treatment with guanethidine or methyl dopa in any new patient, but either may be useful in any patient in whom treatment with one of the newer preparations is unsatisfactory.

There can be no question that with the principal antihypertensive drugs in common use today, and with due attention to detail, the blood pressure can almost always be controlled satisfactorily, but some patients do better on one preparation than on another. It may be that instead of adding an oral diuretic there should be greater experiment with drugs in combination, and if any individual patient is not doing sufficiently well on debrisoquine or bethanidine a combination of these two preparations may well prove effective. Further experience is clearly required.

Summary

Seventy patients with hypertension were treated with bethanidine for periods ranging from six months to two years with satisfactory control of the blood pressure in about three-quarters of them.

Toxicity was not seen and side-effects, apart from postural hypotension, were rare. Tolerance was not a problem.

Postural symptoms were experienced by 38% of all patients but could usually be overcome by adjustment of dosage and timing of drug administration or by combination with an oral diuretic.

For various reasons an oral diuretic was added in 34% of cases.

An attempt was made to compare the efficacy of guanethidine, methyl dopa, debrisoquine, and bethanidine in groups of patients of similar severity as regards hypertensive disease.

It is concluded that bethanidine is a most useful addition to the drugs available for the treatment of hypertension, and, like debrisoquine, has advantages which outweigh relative disadvantages in comparison with guanethidine or methyl dopa.

We thank Dr. N. L. Stokoe for reports on the retina of these patients; Miss M. Baker and Mrs. S. Heggie for carrying out numerous blood pressure readings; and Dr. A. D. Munro-Faure, of the Wellcome Foundation, for pharmacological advice.

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Detection of Carriers of Benign X-Linked Muscular Dystrophy

ALAN E. H. EMERY,* M.D., M.Sc., Ph.D., M.R.C.P.Ed.; ENID R. CLACK†; SYBIL SIMON,‡ M.B.
JOHN L. TAYLOR,§ M.B., B.Sc., M.R.C.P.

Brit. med. J., 1967, 4, 522-523

From the point of view of genetic counselling carrier detection is most important in X-linked disorders. Okinaka *et al.* (1959) were the first to employ the serum level of creatine kinase to detect female carriers of X-linked Duchenne muscular dystrophy. Since then many investigators have confirmed the usefulness and reliability of this test. So far results on over 200 carriers have been reported, and of these approximately two-thirds were found to have significantly raised levels of serum creatine kinase (Emery, 1967).

Besides the severe Duchenne type of muscular dystrophy, another X-linked form of muscular dystrophy has been recognized by Becker (1955, 1957, 1962). This type of muscular dystrophy is clinically similar to Duchenne muscular dystrophy in that weakness begins in the pelvic girdle musculature, only later affecting the upper limbs, and there is pseudohypertrophy of the calf muscles. However, it differs from Duchenne muscular dystrophy because the disease does not manifest itself until the teens or early twenties, and affected individuals usually become chair-ridden only after 25 to 30 years. This report is concerned with the usefulness of serum enzyme studies for detecting carriers of this benign Becker type X-linked muscular dystrophy.

Subjects and Methods

Carriers.—All the carriers belonged to four large families, in each of which were several affected males. A definite carrier has been defined as a daughter of an affected man or a woman with an affected son and a family history of other male relatives having been similarly affected—for example, a brother or maternal uncle.

Controls.—Enzyme determinations were carried out on 50 normal women with no history of any neuromuscular disease and of comparable age to the carriers.

Methods.—Blood samples were taken during everyday activity. In most cases enzyme determinations were carried out within an hour or so of the blood sample being taken. In the few instances where this was not possible the serum was frozen and kept at -20°C . until the following day. No specimens were stored for more than 24 hours. Serum levels of creatine kinase were estimated according to the method of Tanzer and Gilvarg (1959), using a Hilger and Watts Uvispek spectrophotometer with temperature control. Cysteine was incorporated in the reaction mixture to a final concentration of $1\text{ }\mu\text{M}/\text{ml}$. The incorporation of cysteine has been shown to increase the accuracy and reproducibility of assay methods for serum creatine kinase and to prevent the loss of enzyme activity which occurs when serum is stored (Hughes, 1962; Okinaka *et al.*, 1964; Kar and Pearson, 1965; Finley and Anderson, 1966). With cysteine incorporated in the reaction mixture the values obtained were not appreciably affected by storing serum samples for

several days at -20°C . However, without cysteine the values obtained after storage were significantly less than those obtained with fresh serum. It would seem, therefore, that if stored serum is used cysteine should be incorporated in the reaction mixture.

Results are expressed in international units, one unit being that amount of enzyme which catalyses the transformation of $1\text{ }\mu\text{M}$ of creatine per 1,000 ml. of serum per minute at 25°C . and pH 9. Duplicate determinations were carried out on each sample of serum.

Results

The values for the serum levels of creatine kinase in the controls were not normally distributed, but the cumulative

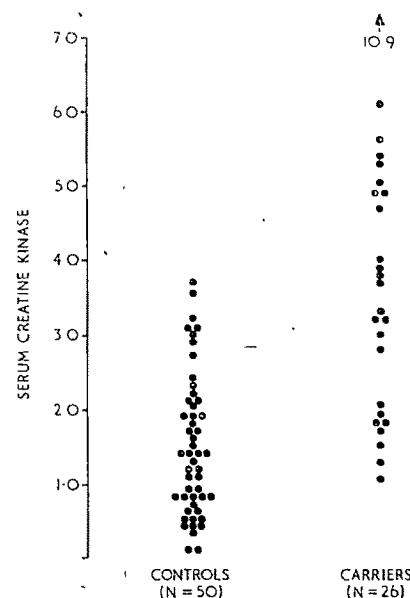


FIG. 1.—Serum creatine kinase levels in controls and carriers, actual values.

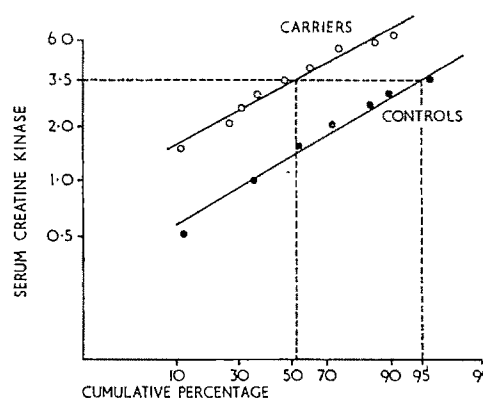


FIG. 2.—Serum creatine kinase levels in controls and carriers, cumulative percentage frequency of the logarithms of the values.

* Reader, University Department of Medical Genetics, Manchester Royal Infirmary.

† Field Worker, University Department of Medical Genetics, Manchester Royal Infirmary.

‡ Research Fellow, University Department of Medical Genetics, Manchester Royal Infirmary.

§ Consultant Physician, the Infirmary, Rochdale, Lancs.

distribution produced a close approximation to a straight line on a log. probability plot, and from this curve the normal 95 percentile was estimated to 3.5 units. Of the 26 definite carriers who have been tested 13 (50%) had serum levels of creatine kinase which exceeded the normal 95 percentile (Fig. 1). From the cumulative log. probability plot approximately 48% of carriers would be predicted to have values more than 3.5 units (Fig. 2). There was no significant correlation ($r = +0.04$) between age and the serum level of creatine kinase.

Enzyme determinations were carried out on 14 possible carriers. These were women who were sisters of affected males, sisters of definite carriers, or daughters of definite carriers. Except for two boys who were not available for testing, all the sons of these possible carriers were examined and their serum level of creatine kinase was determined, but none was found to be affected. Five (36%) of these possible carriers had raised serum creatine kinase levels.

None of the 26 definite carriers or any of the 14 possible carriers had enlarged calves or any evidence of muscle weakness.

Discussion

A benign form of X-linked muscular dystrophy was first recognized by Becker (1955, 1957, 1962). Other investigators have also reported families in which the onset was later and the progression slower than in the classical X-linked Duchenne

Serum Creatine Kinase in Carriers of Benign X-linked Muscular Dystrophy

Assay Method (± Modifications)	Total No.	Abnormal		Reference
		No.	%	
Hughes (1962)	1	1	100	Hughes (1963) Wilson <i>et al.</i> (1965) Rotthauwe and Kowalewski (1966b)
	9	6	67	
	23	11	48	
Tanzer and Gilvarg (1959)	4	2	50	Mabry <i>et al.</i> (1965) Emery and Dreifuss (1966) Present study
	11	4	36	
	26	13	50	
	74	37	50	

type of muscular dystrophy (Levison, 1951; Lamy and de Grouchy, 1954; Walton, 1955-6, 1956-7; Blyth and Pugh, 1958-9; Emery, 1964; Rotthauwe and Kowalewski, 1966a). Mabry *et al.* (1965) and Emery and Dreifuss (1966) have described families with benign forms of X-linked muscular dystrophy which appeared to differ clinically from the Becker type, and these investigators have suggested that there may be at least three different types of benign X-linked muscular dystrophy.

So far there have been few published reports of serum enzyme studies in carriers of benign X-linked muscular dys-

trophy (see Table). The findings of the present study are in good agreement with those of Rotthauwe and Kowalewski (1966b) in showing that approximately 50% of carriers have significantly elevated levels of creatine kinase. The test may therefore be useful in genetic counselling in this form of muscular dystrophy.

Summary

The serum level of creatine kinase has been found to be significantly elevated in 13 out of 26 (50%) definite carriers and 5 out of 14 (36%) possible carriers of benign (Becker type) X-linked muscular dystrophy. The test may therefore be useful in genetic counselling in this form of muscular dystrophy.

Grateful thanks are due to Dr. J. Timson and Dr. D. Gardner-Medwin for valuable help in tracing members of certain families and to Miss Valerie Hodson for technical assistance. The work was supported by a research grant from the Muscular Dystrophy Group of Great Britain. S. S. was in receipt of an M.R.C. research scholarship.

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Congenital Phocomelia in Monozygotic Twins

S. G. I. HAMILTON,* M.A., M.CHIR., F.R.C.S.

Brit. med. J., 1967, 4, 524-526

Phocomelia is the congenital absence of legs and arms, resulting in the hands and feet being in close proximity to the trunk. Occasionally deformed intermediate segments may be demonstrated radiologically (Carey, 1919), though the limb girdles and digital elements may appear normal.

In the past decade interest has been taken in abnormalities showing phocomelia as a result of thalidomide taken by the mother during pregnancy. It has been shown (Lenz and Knapp, 1962) that a critical period of sensitivity, 34 to 50 days after the last menstrual cycle or 20 to 36 days' ovulation age, exists in the human in those cases having thalidomide deformities. These results have recently been reproduced in mammals, including primates (Hendricks *et al.*, 1966).

Similar defects are known to have existed many years before the use of this drug. Two paintings, one entitled *Handschriften* depicting the armless town clerk of Nuremberg at the end of the sixteenth century (Oertel, 1962), and the other by Goya in the Louvre (Smithells, 1966), must surely refer to the same defect.

The case discussed below is unrelated to thalidomide therapy, though the deformity, particularly of the arms, resembles in many respects that seen after thalidomide therapy.

Case Report

A married woman aged 30 had a history of primary infertility of five years' standing and was found on examination to have an enlarged, blocked left uterine tube. Radiology was not undertaken during the pregnancy, and only routine investigations had been made previously.

History of Pregnancy.—Tubal insufflation was carried out three weeks after a normal menstrual period. No further vaginal loss

occurred until the fourteenth week of her pregnancy, when she had a threatened miscarriage. She was found to be group O Rhesus-negative with no antibodies. A normal pregnancy persisted until 38 weeks, when mild pre-eclampsia developed, but still no antibodies were present. She was treated by bed rest, and was admitted to hospital in labour at 39 weeks. She had an assisted vaginal delivery of stillborn malformed "locked twins," sharing a single placenta.

Description of Twins (Fig. 1).—Both twins were male. Twin 1 showed a normal head and trunk. The hands were set directly into the shoulder region, both appearing like flippers with no division into fingers. The feet were appended to the lower end of the trunk and pointed laterally. The right and left feet had five toes each. Twin 2 had a normal head and trunk, but there was a complete absence of arms. The feet were attached directly on to the lower end of the trunk and showed division into toes: six on the right foot and only four on the left foot. **Radiologically** their appearance was stated as follows. **Twin 1** (Fig. 2): The skull, vertebrae, ribs, and pectoral girdle are normal. There is complete absence of any bone in the upper limbs apart from a metacarpal and phalanx representing one digit. The pelvic girdle is normal. The lower limb skeleton is represented only by a talus, a calcaneum, and metatarsals and phalanges of five digits on each foot. **Twin 2** (Fig. 3): Again the skull, vertebrae, and ribs are normal. The pectoral girdle is normal, with complete absence of any upper-limb skeleton. The pelvic girdle is normal. The lower limb shows only the presence of a talus, a calcaneum, and six metatarsals and phalanges on the right side, and a talus and four metatarsals and phalanges on the left side.

Development of Limbs.—Limb buds in the human make their appearance at about 30 to 32 days' estimated age, 28 to 30 somite stage, or 5 mm. crown-rump length, and the digits at a later stage (40 mm. crown-rump length) (Fig. 4). The arm buds appear opposite the fifth to seventh cervical somites at the level of the pericardial swelling and the leg buds appear some 48 hours later opposite the second lumbar to the third sacral segments and lie just caudal to the attachment of the umbilical cord. The first evidence of a limb bud is of a condensation of mesenchymal cells, showing frequent mitotic figures in the body wall, throwing up a slight

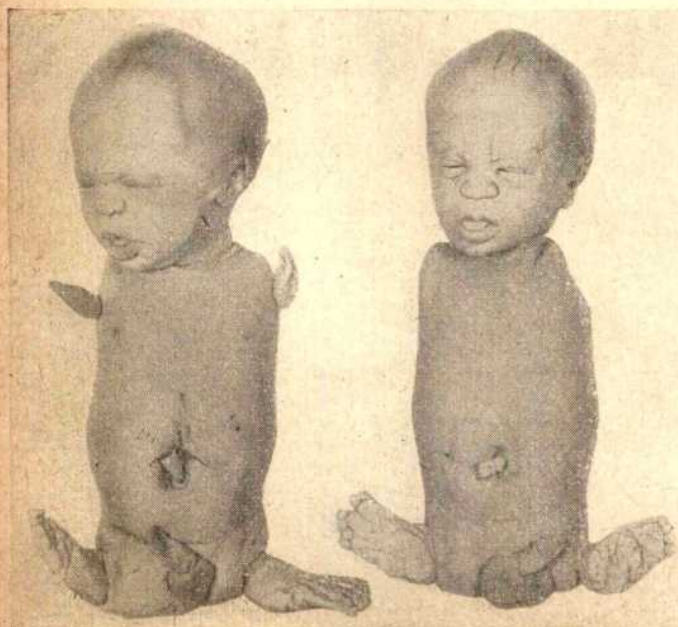


FIG. 1.—Twins 1 (left) and 2 (right) showing limb deformities.

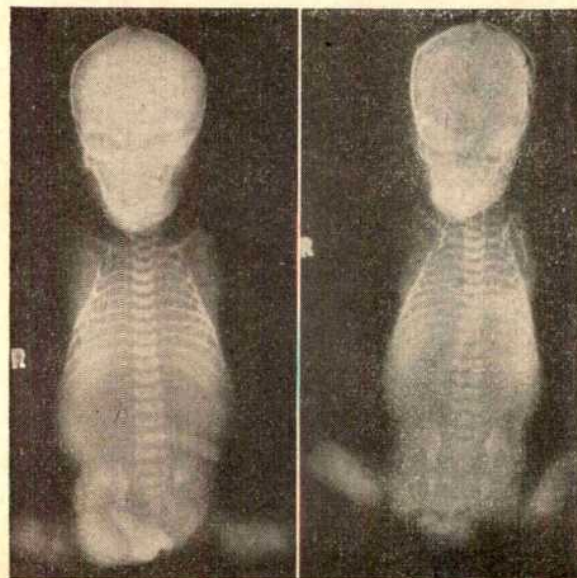


FIG. 2

FIG. 3

FIG. 2.—Radiograph of Twin 1, showing normal pectoral and pelvic (rotated) girdles. FIG. 3.—Radiograph of Twin 2.

* Senior Registrar, Royal Devon and Exeter Hospital, Exeter, Devon.

longitudinal ridge on the surface of the embryo. At the apex of this condensation the ectoderm is thickened (Fig. 5)—the apical ectodermal ridge (Boyd, 1960). In the mesenchymal tissue vasculogenesis occurs, forming a fine-meshed plexus between the cells, tapping the segmental artery at the base of the limb bud and draining into a marginal vein. All the structures of the limb are derived from the ectodermal and mesenchymal cells of the limb bud except the nerves, pigment cells, and possibly the larger vessels. Except for these structures the limb is a "self-differentiating system."

The limb buds develop before there is any differentiation of anterior horn cells in the spinal cord, and in one case (Curtis and Helmholtz, 1911) there was no cervical enlargement and no lateral portion of the anterior horn cells.

Experimental Embryology

Most experimental work on limb development has been performed on amphibians and birds, though similar processes have been shown to exist in mammals (Milaire, 1965).



FIG. 4.—Photograph of a portion of a human embryo (10 mm. crown-rump length) to show the development of a limb bud. Note the peripheral sinus around the tip of the limb bud.

It would seem that for normal limb growth to occur both limb mesenchyme and an apical ectodermal ridge must be present, and the latter's persistence depends on a "maintenance factor" from the mesenchyme, distributed asymmetrically. Abnormal development may thus result from interference with this "inductive" mechanism either by loss of capacity for inducing or loss of response from the subjected tissue, or failure of the one from reaching and reacting with the other (Beck and Lloyd, 1966). Of the experiments leading to this conclusion one appears to be pertinent in the present context: if *non*-limb mesenchyme is covered with limb ectoderm, including the apical ridge, the structure so formed does not develop into a limb, but if a fragment of limb mesenchyme is introduced beneath the ectodermal jacket at the apical ridge the latter maintains its thickened structures and an elongated outgrowth forms (Zwilling, 1956). The mesenchyme acts, therefore, as an inductor force on only a limited area of the ectodermal ridge and is insufficient in capacity to cause the formation of a normal limb.

Normally development progresses in a proximo-distal differentiation, and in bilateral organs this differentiation may occur at slightly different times, giving a discrepancy in size between the two sides (Stockard, 1931).

Discussion

Much attention has been focused recently on the effect of drugs, particularly thalidomide, on limb skeletal abnormalities. The twins described were born after a pregnancy in which no drug therapy had been employed, no fever had interrupted, and only possible hypoxia as a result of insufflation and perhaps temporary disestablishment of implantation had resulted. Several cases have been mentioned, and six patients who have

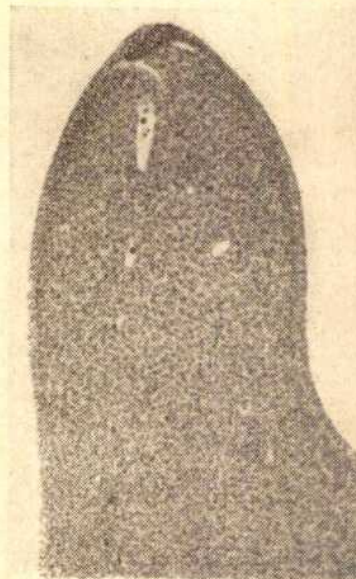


FIG. 5.—Photomicrograph of a longitudinal section of a human limb bud to show the apical ectodermal proliferation.

appeared since the withdrawal of thalidomide are at present alive and under treatment (E. P. Quibell, personal communication, 1966).

It is suggested that the formation of the deformity of phocomelia may result in one of two ways. (1) Some agent damages the proximal mesenchymal cells after they have been separated from the subapical mesenchymal cells, and that these latter, provided the damaging agent is no longer functional, may then give rise to normal distal limb elements. (2) It has been shown that mesenchymal cells destined to become thigh, if placed under the apical ridge, may form digits (Saunders *et al.*, 1957). It may be that the destructive agent damages the distal mesenchymal cells, and, by leaving the proximal mesenchymal tissue under the apical ectodermal ridge, these cells now differentiate into digits. Such a deleterious agent is thalidomide, and it has been shown (Lenz and Knapp, 1962) that there is only a limited period of development when such an agent may act to produce this effect.

It would seem that a number of teratogenic agents may exist, and that drug therapy, though bringing the subject to the forefront, is not the only cause for the development of such abnormalities.

Summary

The occurrence of phocomelia in monozygotic twins other than that resulting from thalidomide therapy is described. The exact way by which the anomalies are produced is not known, though two possible mechanisms are discussed in the light of experimental embryology and the development of the normal human limb bud.

The critical time in pregnancy for such defects to be produced varies for upper and lower limbs between narrow limits, and the rate of growth and the stage of development of one

of the twins described comparable to the other emphasize the variability of the abnormality.

I wish to thank Mr. D. M. W. Maxwell, of Windsor, for allowing me to examine these twins and for permission to report on them.

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ABO Blood Groups and Polyps of the Colon*

THOMAS C. FLEMING,† M.D.; HARVEY W. CAPLAN,‡ M.D.; GEORGE A. HYMAN,§ M.D.
F. DAVID KITCHIN,|| M.D., M.R.C.P.

Brit. med. J., 1967, 4, 526-527

Though it appears that a significant proportion of villous adenomas or papillomas of the large bowel develop malignant properties, the debate still continues on the importance of adenomatous polyps as the sources of large-bowel cancer. Evans (1966) feels that the associations between multiple cancers of the colon and adenomatous polyps, and multiple polyps and cancer of the bowel, do not necessarily indicate an orthogenetically determined polyp-carcinoma sequence. He favours the view that they represent varying degrees of genetically determined large-bowel proneness to both cancer and adenoma.

With the exception of polyposis coli, no genetic locus has been associated with cancer of the large bowel or polyp formation, though Veale (1965) has postulated an unfavourable allelic modifier of the polyposis gene which in double dose produces a few adenomas of the rectum or colon. The ABO locus which is implicated in the causation of cancer of the stomach (Aird *et al.*, 1953), multiple primary cancers (Fadhli and Dominguez, 1963; Tsudaka *et al.*, 1964), and possibly chronic lymphatic leukaemia or lymphoma and carcinoma of the colon (Hyman *et al.*, 1963), does not appear to be a factor in carcinoma of the colon.

This paper reports the ABO blood group distributions in 373 patients with polyps of the colon or rectum and an association between group O and papillary adenoma of the colon.

Materials and Methods

Case records of all patients seen at Columbia-Presbyterian Medical Center between 1948 and 1960; at Montefiore Hospital, Bronx, N.Y., between 1952 and 1959; and at the Bronx Veterans Hospital, Bronx, N.Y., between 1952 and 1959 who had the diagnosis of polyps of the colon or rectum were

checked. Only Caucasian patients whose blood types were known and whose polyps were removed and examined histologically were selected, and any family history of polyps or of carcinoma was carefully noted. For all cases from this centre the ABO blood groups were determined in the Presbyterian Hospital Blood Bank and were done on admission before transfusion. The cases totalled 317 from Columbia-Presbyterian Medical Center, 22 from Montefiore Hospital, and 34 from the Veterans Hospital. Follow-up was not complete, but 90% (335) of the patients were examined by barium meal, proctoscopy, or both to determine whether carcinoma or additional polyps had developed. During a five-year follow-up 58% (217) of the patients were seen several times. Patients were assigned to groups depending on pathological diagnosis, the number of polyps, and the family history.

For the purposes of this study adenomatous polyps are defined as being composed of a rounded, lobulated compact mass of branching glandular tubules, lined by columnar epithelium and supported by branching connective tissue. They are usually pedunculated, with the pedicle covered by normal mucosa (Grinnell and Lane, 1958). Papillary adenomas are defined as sessile growths, composed of innumerable branching villi clothed in stratified or pseudostratified columnar epithelium and usually covered by a coating of mucus (Grinnell and Lane, 1958).

Case records of all patients seen at Columbia-Presbyterian Medical Center between 1930 and 1966 with the diagnosis of polyposis of the colon, defined as 10 or more polyps, were checked. Of the 18 cases found 12 were examples of intestinal polyposis and seven had a positive family history. All patients with polyposis coli had their colon removed surgically and were found to have large numbers (from hundreds to thousands) of adenomatous polyps. The six patients with as few as 10 polyps have been included in the multiple polyposis group because it is thought by some (Veale, 1965; McConnell, 1966) that these patients may have inherited a weakly expressed polyposis gene.

As most of the patients were treated at the Columbia-Presbyterian Medical Centre the control group was chosen from this hospital's blood bank records. Non-profit Caucasian donors at the Presbyterian Hospital Blood Bank for the year 1960 were decided to be the most appropriate control, since the few Negroes with polyps were excluded from the study. In spite of careful selection there was a higher incidence of group B and a lower incidence of group A in the Presbyterian Hospital series than in other control groups (see Table I). This

* This work from the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Medical Service of Columbia-Presbyterian Medical Center and the Francis Delafield Hospital, New York City, New York, 10032, was supported in part by the United States Public Health Service Research Grant CA-02332 from the National Cancer Institute, and the Hyman Goldburg Memorial Fund.

† Surgical Intern, Bernalillo County Indian Hospital, Albuquerque, New Mexico.

‡ At present at University Hospitals, Cleveland, Ohio.

§ Assistant Clinical Professor in Medicine, Columbia University College of Physicians and Surgeons; Haematologist and Blood Bank Director, Francis Delafield Hospital; Assistant Physician in Medicine, Columbia-Presbyterian Medical Center, New York, N.Y.

|| Associate in Medicine and Human Genetics, Columbia University College of Physicians and Surgeons.

finding may be the expression of bias inherent in a non-profit donor group which is composed of friends and relations replacing blood used in the treatment of one of their family as well as public-spirited blood donors. Nevertheless, when this control group is compared, O to Not-O, with the pooled control groups from other regions in the U.S.A. the heterogeneity test gives $\chi^2=0.114$; $0.80>P>0.70$, and so the smaller control group has been used for the comparisons.

TABLE I.—ABO Blood Groups in Control Caucasian Populations

Group	A	B	O	AB	Total
Caucasian non-profit donors at Presbyterian Hospital in 1960 (group chosen as overall control)	928 36.8%	344 13.6%	1,122 44.4%	131 5.2%	2,525
Caucasians, Columbus, Ohio*	2,535 43.19%	539 9.19%	2,585 44.04%	210 3.58%	5,896
Caucasians, Detroit*	2,359 41.0%	683 11.9%	2,396 41.8%	299 5.2%	5,728
Caucasians, Massachusetts*	9,263 39.7%	2,465 10.6%	10,810 46.3%	794 3.4%	23,332
Caucasians, Rochester, N.Y.*	9,937 41.8%	2,394 10.1%	10,562 44.4%	894 3.8%	23,787
Caucasians, region unspecified*	8,200 41%	2,000 10%	9,000 45%	800 4%	20,000
Ranges of control populations	36.8–43.2%	9.2–13.6%	41.8–46.3%	3.4–5.2%	
Average	41.3%	10.3%	44.5%	3.8%	

* Fadhli and Dominguez (1963).

Results

The results (Table II) and the statistical analysis (Table III) are summarized below.

TABLE II.—ABO Blood Groups of Patients with Polyps

	A		B		AB		O		Total
	No.	%	No.	%	No.	%	No.	%	
A. All polyps ..	137	37	48	13	17	5	171	46	373
(1) Adenomatous polyps only ..	128	39	43	13	16	5	139	43	326
B. (2) One adenomatous polyp ..	76	38	25	13	9	5	87	44	197
(3) Two or more adenomatous polyps ..	52	40	18	14	7	5	52	40	129
C. Papillary adenomas only ..	2	10	3	14	0	0	16	76	21
D. Both adenomatous and papillary polyps in same patient ..	7	29	2	8	1	4	16	62	26
E. All patients with papillary adenoma (C+D) ..	9	19	5	11	1	2	32	68	47
F. Polyposis coli ..	6	33	1	6	0	0	11	61	18

TABLE III.—Statistical Analysis

Comparison O/Not-O	χ^2	Degree of Freedom	Significance
A. All polyps/control ..	0.261	1	0.70 > P > 0.60
B. Adenomatous/control polyps ..	0.378	1	0.60 > P > 0.50
C. Papillary adenomatous/control ..	8.496	1	0.005 > P > 0.001
D. Papillary/control adenomatous polyps ..	3.046	1	0.10 > P > 0.05
E. Groups C and D/control ..	10.432	1	0.005 > P > 0.001
F. Polyposis coli/control ..	2.012	1	0.20 > P > 0.10

A. Three hundred and seventy-three patients had one or more polyps, and there was no statistical difference in the distribution of blood groups between these and the controls.

B. Three hundred and twenty-six patients had one or more adenomatous polyps, and there was no statistical difference in the distribution of blood groups between these and the controls.

C. Twenty-one patients had one or more papillary adenomas, and 16 (76%) of these were blood group O. This increase was statistically significant ($P>0.001$) when compared with the control group.

D. Twenty-six patients had both papillary adenomas and adenomatous polyps, and 16 (62%) of these were type O. This finding was not statistically significant.

D

E. Groups C and D can be combined (heterogeneity test C+D gives $\chi^2=0.57$, $0.50>P>0.40$) to make a group of 47 patients, all of whom had at least one papillary adenoma. Thirty-two (68%) of these patients were group O, and this finding was significant ($P<0.005$). If the combined control group from other regions in the U.S.A. is used for comparison $\chi^2=10.958$, $P<0.001$.

F. Eighteen patients had multiple polyposis, and 11 (61%) of these were type O, but this increase was not statistically significant.

G. Only 16 of 373 patients with polyps had a family history of colonic carcinoma or polyps of the colon. Two of these had multiple polyposis and 13 had one or more adenomatous polyps.

Discussion

Analysis of the data indicates that the ABO blood group distributions in patients with polyps of the colon are not significantly different from control populations except in the subdivision of papillary adenomas.

The data suggest that papillary adenomas can be distinguished from adenomatous polyps, familial and non-familial, since the ABO locus is involved in the papillary adenoma group. Furthermore, this finding indicates that papillary adenomas have a different cause from adenomatous polyps in that the ABO locus is one of the polygenic factors conditioning the susceptibility to the disease.

The limitation of a study of this type is well recognized, particularly in view of the small number of patients and difficulty in selecting a proper control group because of the racial differences in blood type in the heterogeneous population of New York City. We hope that this study will stimulate further investigations of the ABO blood groups in patients with papillary adenomas and adenomatous polyps of the colon in other populations.

Summary

The ABO blood groups have been determined in 373 patients with polyps of the colon, divided into adenomatous polyps and familial and non-familial and papillary adenomas. In the two subdivisions of the adenomatous polyps the blood group distributions did not differ from the control group, but a significant excess of blood group O was found in the patients with papillary adenomas. This finding indicates that papillary adenomas have a different cause from adenomatous polyps and supports the separation, on histological and clinical grounds, of the two kinds of growths.

We wish to thank the following colleagues in Columbia University College of Physicians and Surgeons for their invaluable assistance in the preparation of the manuscript: Dr. Nathan Lane and Dr. Rafael Lattes, Department of Surgical Pathology; and the staff of the Department of Statistics, Columbia University School of Public Health. We also wish to thank the Record Departments of the Montefiore and Bronx Veterans Hospitals for their assistance during the performance of the studies.

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Preliminary Communications

Influence of Glucose and Insulin Administration on the Achilles Tendon Reflex Time

Brit. med. J., 1967, 4, 528-529

The Achilles tendon reflexogram or photomotogram has long been used in the diagnosis and follow-up of thyroid disorders. While an extensive literature exists on this subject, only a few investigations have been carried out concerning the relations between the Achilles tendon reflex time and carbohydrate metabolism. First, it was observed that Achilles tendon areflexia may occur in diabetic patients (Ellenberg, 1961; Krosnick, 1964). Subsequently it was reported that the reflex time is prolonged in diabetes (Beardwood and Schumacher, 1964; Kissel *et al.*, 1966). In our experience, too, the reflex time is generally prolonged in diabetic children, but the degree of prolongation is related neither to the severity or duration of the disease nor to the adequacy of treatment, and it may change from day to day. As pointed out by Beardwood and Schumacher (1964), neuropathy as an explanation for this phenomenon seems therefore unlikely. In an effort to elucidate a possible relation between carbohydrate metabolism and the Achilles tendon reflex time we have carried out the studies presented in this preliminary communication.

METHODS

Five adult subjects in good health (two males, three females), aged 24 to 43 years, were studied. None had a history of thyroid dysfunction or diabetes mellitus.

In each subject an intravenous glucose-tolerance test (15 g. glucose per sq. m. surface area) and, with an interval of several days, an intravenous insulin-tolerance test (4 units insulin (Actrapid Novo) per sq. m. surface area) were performed after an overnight fast. Blood glucose concentration in capillary blood was determined by the colorimetric glucose oxidase assay (reagents C. F. Boehringer GmbH Mannheim, Germany) at 0,

15, 30, 45, 60, 90, and 120 minutes after injection. At each of these times Achilles tendon reflexes from the same leg were recorded with a Burdick photomotograph. Thirty or more reflexes were recorded at each time. All photomotograms were measured by the same person without knowledge of the time of the tolerance test when they were recorded. The values expressed in milliseconds represent the mean time between the hammer tap and one-half relaxation from 30 to 40 technically satisfactory recordings. The standard deviations at any time of the glucose- or insulin-tolerance test ranged from 9 to 16 msec. The normal range for adults is 260 to 380 msec.

In one subject the insulin-tolerance test was repeated, but immediately before the injection of insulin an adrenergic β -receptor antagonist (propranolol, 0.15 mg./kg. body weight) was given intravenously (Abramson *et al.*, 1966). Blood glucose concentrations and half relaxation time were then determined in the same way as in the other experiments.

RESULTS

The results are summarized in Figs. 1, 2, and 3. In all subjects the mean half relaxation time increased during the glucose-tolerance test (Fig. 1). The longest mean half relaxation time was reached between 45 and 120 minutes after glucose administration, thus considerably later than the peak glucose concentration, which was always observed 15 minutes after glucose administration. The increase ranged from 12 to 18% of the mean half relaxation time at 0 minutes.

In all subjects the mean half relaxation time decreased during the insulin-tolerance test (Fig. 2). In contrast to the delay of the maximum half relaxation time during the glucose-tolerance test, the minimum half relaxation time was found here at the same time as or only 15 minutes after the minimal blood glucose concentration. The decrease ranged from 15 to 24% of the value at 0 minutes.

When insulin and propranolol were given combined the half relaxation time failed to decrease (Fig. 3). On the contrary, a continuous increase of the half relaxation time to 476 msec. at 120 minutes, even higher than that seen during the glucose-

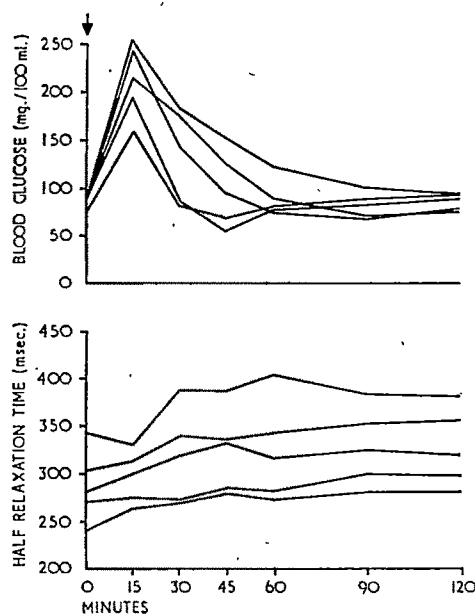


FIG. 1

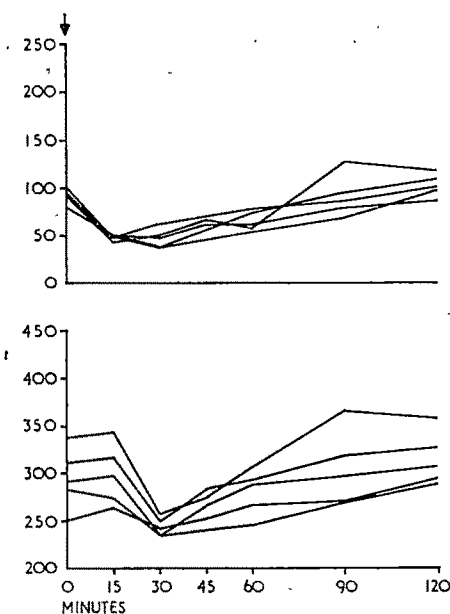


FIG. 2

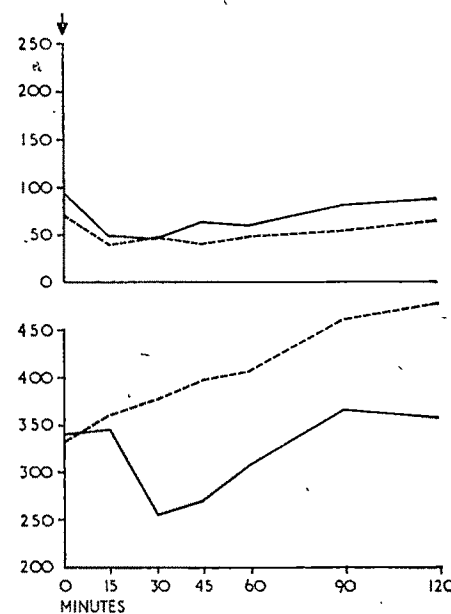


FIG. 3

FIG. 1.—Blood glucose and Achilles tendon reflex time during intravenous glucose-tolerance test in five adult subjects. FIG. 2.—Blood glucose and Achilles tendon reflex time during intravenous insulin-tolerance test in five adult subjects. FIG. 3.—Blood glucose and Achilles tendon reflex time during two intravenous insulin-tolerance tests in the same subject. — Insulin alone. ---- Insulin and propranolol.

tolerance test, was observed in spite of a markedly prolonged hypoglycaemia.

COMMENT

In all five subjects studied the mean half relaxation time increased after intravenous glucose administration and decreased after intravenous insulin administration. The increase during the glucose-tolerance test was slow and lagged considerably behind the peak of blood glucose concentration, while the decrease during the insulin-tolerance test was fast and coincided with the drop in blood glucose. This difference in the time relation between blood glucose concentration and half relaxation time in the two tests makes a direct effect of blood glucose on the half relaxation time unlikely. There seems more likely to be an indirect effect, mediated perhaps through a carbohydrate-regulating hormone like adrenaline, growth hormone, or cortisol. The absence of a decrease of the half relaxation time after simultaneous administration of insulin and propranolol suggests that the changes of blood glucose influence the half relaxation time by intermediary of the adrenaline system.

Whether the changes of the Achilles tendon reflexogram in thyroid disorders and in diabetes mellitus are related to the adrenaline system requires further investigation.

SUMMARY

In five normal subjects the Achilles tendon reflex time was prolonged by intravenous glucose and shortened by intravenous insulin administration. The effect of insulin was abolished when it was given after the application of propranolol.

M. ZACHMANN, M.D.,
Paediatric Department, University of Zurich, Kinderspital, 8032 Zurich, Switzerland.

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Medical Memoranda

Foot-and-mouth Disease in Man

Brit. med. J., 1967, 4, 529-530

Though there are numerous reports in the literature of foot-and-mouth disease in man, the total number of possible cases is still very small in relation to the frequent exposure of farmers and others to the disease in parts of the world where infection is widespread in the livestock population (Platt, 1958). In many of the reported cases the criteria on which diagnosis was based were rather less than adequate, but Pilz and Garbe (1965) described a number of cases in which the diagnosis was more completely substantiated. The virus was recovered from vesicular lesions at high titre, and significant antibody titres were developed against the strain of virus isolated from the lesions. Material from suspected cases of foot-and-mouth disease in man has been submitted to the Animal Virus Research Institute at Pirbright on several occasions, but in none of these have we been successful in isolating virus or demonstrating specific antibodies. There is, however, little doubt that the patient whose case is described below became infected with foot-and-mouth disease virus.

CASE REPORT

The patient, a man aged 35, lived on a farm with his brother, but had only indirect contact with the livestock. An outbreak of foot-and-mouth disease developed on this farm on 22 July 1966, and one of the affected animals was a cow which supplied milk used in the farmhouse. The animals were slaughtered on 24 July, and though the patient watched this operation he took no part in it.

On 28 July he complained of a slight sore throat, which became worse on the 29th. On the 30th he had a temperature of 99° F. (37.2° C.), an inflamed throat, and a few blisters on the palms and dorsa of both hands. On 31 July his temperature was normal, but the blisters on his hands had increased in number. There were two further blisters between his toes and five or six weals on the side and front of his tongue. The blisters on the backs of his hands were about 2 mm. in diameter, while those on the palmar surface were between 5 mm. and 2 cm. in diameter. The weals on the tongue were solid swellings similar in size to the blisters on the palms. There were no swellings on the fauces, soft palate, cheeks, or gums. The patient described his lesions as uncomfortable and tingling, while the tongue was hot, tingling, and sore.

Epithelium was collected from one of the blisters on the back of the hand and transferred to a container with glycerin-phosphate

buffer. Two drops of fluid from another blister were added to this medium. Foot-and-mouth disease virus of type O was recovered from this material.

These lesions had regressed by 7 August, but further crops of blisters developed on the hands on 8 and 11 August and again in December. No virus was recovered from these lesions either at the Animal Virus Research Institute or at the Pathology Department of the Newcastle General Hospital. A series of blood samples were collected for antibody assay. As there was a possibility that the patient might still be a carrier of virus, throat swabs were collected at intervals and tested at both laboratories for the presence of virus. All were negative.

The patient was examined in March 1967 and again in April at the skin clinic of the Royal Victoria Hospital in Newcastle upon Tyne. The clinical syndrome was believed to be that of erythrasma and tinea pedis with a recurrent erythema multiforme. The second report stated that the hand lesions were suggestive of healing pompholyx, while some superficial erosions of the hard palate were thought to be aphthous ulcers.

LABORATORY EXAMINATION

Virus Isolation.—A suspension of epithelium collected on 31 July 1966 was inoculated into roller tube cultures of bovine thyroid cells (Snowdon, 1966). After 48 hours cytopathic change was seen and the culture fluid gave a positive reaction in the complement-fixation test with foot-and-mouth disease type O antiserum. Five days later a fresh suspension of the same epithelium was titrated in the same culture system. The epithelium was shown to contain $10^{6.4}$ TCD₅₀ virus per gramme. Further epithelial samples collected on 8 and 11 August were examined, but no virus was detected. Throat swabs collected on 4 August, 21 October, and 4, 10, and 18 November also gave no evidence of virus.

Serology.—Antibody titres obtained with foot-and-mouth disease antigens are shown in the Table. Sera were collected from five veterinary officers who had been in contact with infected cattle in Northumberland and from 12 members of the staff of the Animal Virus Research Institute, all of whom had come into contact with

Antibody Titres Obtained with Foot-and-mouth Disease Antigens

Serum Samples (Days After Infection)	Neutralizing Titre. Virus Type			C.F. Titre (Overnight Fixation)
	O	A	C	
5	1/178	<1/8	<1/8	≤16
30	1/708	<1/8	<1/8	36
40	1/355	<1/8	<1/8	54
120	1/256	<1/8	<1/8	24
154	1/80	<1/8	<1/8	Not tested

the virus of foot-and-mouth disease in the course of their normal work. All samples, tested in parallel with the serum from the patient, were negative (titre less than 1/8) except for one serum from a member of staff which showed a neutralizing titre of 1/22 against virus of type O.

DISCUSSION

It would appear that the patient had in fact contracted an infection by the virus of foot-and-mouth disease. The lesions observed, the high titre of virus recovered from the epithelium, and the rise in antibody titre all indicate the strong probability that he became infected with foot-and-mouth disease between 24 and 31 July 1966. The high initial antibody titre was probably due to the fact that the serum was collected at least five days after the illness was first noted by the patient. The decline in antibody titre at 120 and 154 days from the beginning of the illness agrees well with the observations of Pilz and Garbe (1965).

The absence of any antibody rise in association with the recrudescence of epithelial lesions indicates that these episodes are unlikely to have anything to do with foot-and-mouth disease. But the fact that the cause of the skin condition observed in these episodes, and possibly even in the first, remains undiagnosed suggests that epithelial damage of this nature might have raised the patient's susceptibility to the foot-and-mouth disease virus. His contact with infection was less than that of many people working with infected animals in Northumberland at that time, and it is known that epithelial

damage does increase the tendency to the development of lesions in experimental animals, possibly by increasing the phagocytosis of virus by epithelial cells.

The clinical signs shown in the initial illness accord with the appearance of foot-and-mouth disease in susceptible species, though the patient may also have been suffering from a skin condition of unknown origin. No spread to other humans appears to have occurred in this case, and, as the patient did not come into contact with animals either before or after his illness, there is no evidence of spread in this direction. There is, however, a clear case for restriction of movement of a suspected case in an agricultural area and for the treatment of the condition in isolation. Virus was recovered from only one of the samples—that obtained from the patient three days after the initial clinical signs. Throat swabs collected 7, 84, 98, and 106 days after infection were negative, as were epithelial samples taken at 11 and 14 days. It is therefore likely that the disease in man is relatively short-lived and that the period of infectivity is quite restricted.

R. ARMSTRONG, M.B., B.S.,
General Practitioner, Rothbury, Northumberland.

J. DAVIE, B.Sc., M.R.C.V.S.,

R. S. HEDGER, M.R.C.V.S.,
Principal Scientific Officers, Animal Virus Research
Institute, Pirbright, Surrey.

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Recurrent Tetanus

Brit. med. J., 1967, 4, 530

The incidence of tetanus reaches endemic proportions in Ceylon. A minimum of one case a week is admitted to any large hospital in the island. However, there is no record of a recurrence or of relapse. The following report is of a patient who had two attacks of unmistakable tetanus within three months of each other.

CASE REPORT

An 8-year-old Sinhalese girl was admitted to hospital on 23 February 1965 with a history of difficulty in opening her mouth and repeated "convulsions" of one day's duration. She also complained of pain in the abdominal wall and severe headache. There was a history of an injury to the left lower limb, nearly a month previously, for which she was treated in the outpatient department. Immunization against tetanus had not been carried out at the time.

On examination she was found to have trismus, risus sardonicus, and rigidity of all four limbs. No spasms were observed. She was afebrile. She had been treated with pethidine 25 mg. intramuscularly on admission, and chlorpromazine 25 mg. by mouth twice a day. Crystalline penicillin 300,000 units twice daily was given by intramuscular injection. Antitetanus serum was given in an initial dose of 100,000 units intravenously, followed by 100,000 units intramuscularly. The latter was repeated daily for six days.

The patient was well enough to be discharged from hospital in 23 days from the date of admission. No active immunization had been carried out at the time. She was quite well after discharge and attended school until 30 May 1965.

On 3 June she was readmitted to hospital with trismus of four days' duration, and "convulsions" for one day. On examination she had severe trismus and a well-marked risus sardonicus. Neck stiffness was very conspicuous. No spasms were observed. She was treated with pethidine 50 mg. and chlorpromazine 50 mg. intra-

muscularly six-hourly. This dosage was progressively reduced and "tailed off."

Crystalline penicillin 500,000 units intramuscularly twice daily was started, but had to be stopped on the third day, as she complained of severe itching of the body and developed an urticarial rash in both axillae. Oral tetracycline 250 mg. six-hourly was substituted. Calcium gluconate 5 ml. intravenously was given daily. An intradermal test for sensitivity to antitetanus serum was strongly positive. A weal 4.2 by 2.2 cm. developed after the diluted serum (0.1 ml.) was introduced into an area of 1 sq. cm. Thus we were unwilling to administer serum even in fractional doses. The hospital had run out of toxoid at the time, so this could not be given.

Recovery was uneventful. No spasms were noted at any time. The patient was discharged on 27 June, and was quite well except for some residual trismus. It should be noted that there was no fresh trauma to cause or provoke this second attack of tetanus.

COMMENT

Standard textbooks of surgery make no mention of cases of recurrent or relapsing tetanus. However, it is stated that there is no immunity conferred on a patient after an attack of tetanus. This must be so, because there are no fewer than eight antigenic strains of *Clostridium tetani* and also because neither the bacillus nor its spores are said to enter the blood stream or be carried to distant sites. Any immunity, active or passive, will be to the exotoxin, which is actively antigenic.

This case illustrates the necessity for active immunization against tetanus after an attack of the disease. This could be done with adsorbed toxoid, three 1-ml. doses at intervals of three to six weeks. A booster dose of 1 ml. of toxoid after an injury likely to produce tetanus would suffice, and is recommended.

S. Y. D. C. WICKRAMASINGHE, M.S., F.R.C.S.,
Consultant Surgeon.

MALINIE FERNANDO, M.B., B.S.,
House-surgeon.

General Hospital, Kandy, Ceylon.

Hip Arthroplasty in a Haemophiliac and Subsequent Prophylactic Therapy with Cryoprecipitate

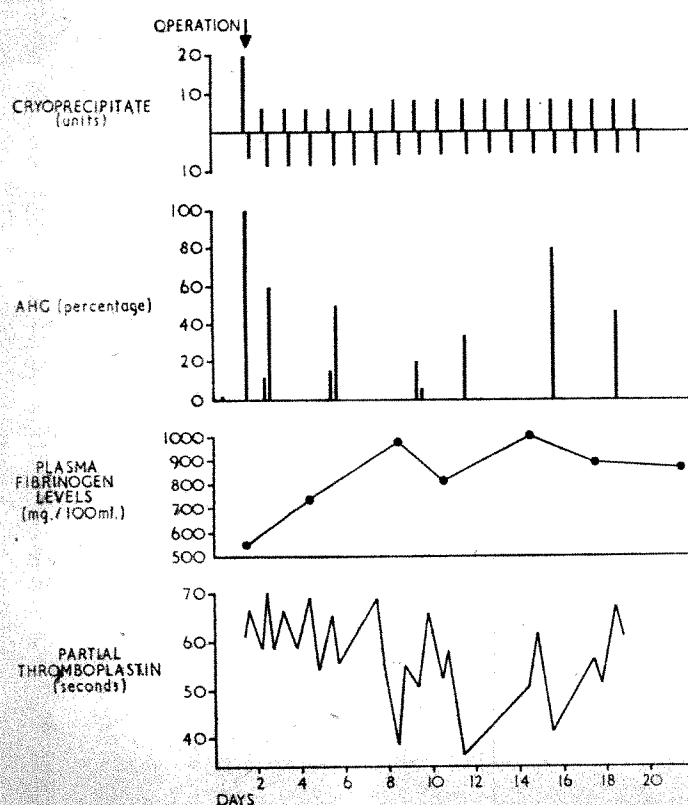
Brit. med. J., 1967, 4, 531-532

Operations on haemophiliacs are becoming increasingly common, and with the provision of antihaemophilic globulin concentrates much safer. Reports of the use of cryoprecipitate in controlling haemophilic bleeding suggest that this is a most effective form of replacement therapy (Pool and Shannon, 1965; Bennett *et al.*, 1967; Brown *et al.*, 1967). The purpose of this paper is to report the performance of a successful hip arthroplasty in a young severe haemophiliac who sustained a fracture of the left femoral neck which failed to unite. This operation is believed to be the first of its kind performed on a haemophiliac, and may provide grounds for optimism in the treatment of other patients in a similar situation. Furthermore, it has been possible to organize successful prophylactic therapy.

CASE REPORT

A 21-year-old haemophiliac had sustained repeated haemorrhagic episodes since he was 3 years old. There was no family history of haemophilia, but repeated antihaemophilic globulin assays (Hardisty and Ingram, 1965) had shown concentrations of less than 1% in his plasma. In the previous three years he had had repeated haemorrhages, many of which had been into joints, and these episodes had necessitated his admission to hospital nine times.

In October 1966 he fell and sustained an acute haemarthrosis of his left hip, and x-ray examination showed a transverse fracture of the left femoral neck. The acute episode subsided after transfusion of 6 units of cryoprecipitate and the hip fracture was treated by traction, which was maintained for 16 weeks. X-ray films after this time showed that union had not taken place.



Treatment and progress during and after operation.

The decision to insert a prosthesis in such a young man was made with difficulty, but it was judged the best treatment because his left hip was one of his few normal joints and it was felt necessary to make this painless, stable, and mobile.

Supplies of cryoprecipitate were arranged through the co-operation of the North London Blood Transfusion Centre, and were prepared according to a modification of the method of Pool and Shannon (1965) (Bennett *et al.*, 1967).

An initial loading dose of 20 units was administered, resulting in an antihaemophilic globulin level of 120% and a cephalin kaolin clotting-time of 56 seconds. The left hip was exposed through the posterior approach. The capsule was opened and adhesions on the joint were marked. There was a loose pseudarthrosis with no suggestion of union. The head of the femur was removed, the neck trimmed, the medullary cavity reamed, and a Thompson prosthesis inserted and fixed with Surgical Simplex P. The hip was reduced and the wound closed in layers. The operation lasted one hour; there was no undue haemorrhage, and no blood transfusion was required.

Four hours after the operation antihaemophilic globulin levels had fallen to 40% and further replacement was required. Subsequent replacements of antihaemophilic globulin were given at 12-hourly intervals, the dose varying according to the antihaemophilic globulin levels obtained, but 9 units twice daily produced satisfactory levels (see Chart), and this dosage was continued for eight weeks. The incision healed uneventfully, and after two weeks the patient was mobilized. Intensive physiotherapy was required, as there had been considerable muscle-wasting from immobilization, and the administration of cryoprecipitate was continued.

In view of the history of frequent severe bleeding over the three previous years it was decided to attempt to continue replacement therapy on a diminished scale by teaching the patient to give himself 6 units of cryoprecipitate on alternate days, on the assumption that this might result in his haemophilic state behaving as a mild rather than as a severe one. He soon learnt to administer his own intravenous injections and was able to continue this regimen, storing a week's supply of cryoprecipitate at home in a deep freeze. Antihaemophilic globulin levels of 15-20% were obtained immediately after the injection of 6 units of cryoprecipitate, the level falling to 1% in 48 hours before the next injection (see Table). On this regimen there has been no further bleeding, and the patient is

Antihæmophilic Globulin Levels after 6 Units of Cryoprecipitate

Time in hours	0	0.5	4	24	48
AHG levels (% of normal)	<1	14	8	2.5	<1

ambulant. On one occasion he had a severe fall and sustained only limited bruising; on another occasion he developed a mild haemarthrosis in his right knee after a severe jolt in a motor accident. Both these incidents resulted in much less incapacity than had been expected. Repeated antihaemophilic globulin assays on a number of occasions produced similar loading concentrations, and no clotting inhibitor or γ -globulin antibodies were detected. Treatment has continued for six months with these satisfactory results.

COMMENT

The control of bleeding in haemophilia by the administration of antihaemophilic globulin concentrates is a well-accepted procedure and various operations have been carried out under this cover. Cryoprecipitate appears to be an effective answer to haemophilia control by providing a high-potency source of human antihaemophilic globulin in small volumes of material, yet resulting in the unused red cells and plasma being retained for transfusion purposes.

In the case presented here bleeding has been controlled and a major hip operation performed under cover of this material. The results have been as good as had been hoped, and the patient has been mobilized without further bleeding. It has further been possible to teach him to administer his own cryoprecipitate intravenously, and from the intermittent administra-

tion of a relatively small dose on alternate days it would appear that the course of his disease has been reduced from one causing major to one causing minimal incapacity. How long it will be possible to continue replacement therapy in this way remains to be seen, but it may offer a useful means of tiding severe haemophiliacs over serious exacerbations of their disease. The risk of homologous serum jaundice would appear to be appreciable, but our patient had had so many previous administrations of plasma that it was thought likely that he had developed immunity. An additional risk of the production of antibody to antihaemophilic globulin or other globulins must be borne in mind. Those patients who possess trace amounts of antihaemophilic globulin and who presumably do not suffer from a complete gene deletion would seem unlikely to develop antihaemophilic globulin antibodies, and so far no γ -globulin antibodies have been detected in our patient. If prolonged treatment

of haemophilia in this way is practicable, more adequate provision of cryoprecipitate on a national scale will be required.

A. BELLINGHAM, M.B., B.S., M.R.C.P.

D. FLETCHER, M.B., D.PHYS.MED.

E. O'G. KIRWAN, M.B., B.CHIR., F.R.C.S.

T. A. J. PRANKERD, M.D., F.R.C.P.

University College Hospital, London W.C.1.

T. CLEGHORN, M.D., B.S.C., F.C.PATH.

North London Blood Transfusion Centre, Edgware, Middlesex.

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Delayed Perforation of Large Bowel Due to Unusual Ingested Foreign Body

Brit. med. J., 1967, 4, 532

A blunt ingested foreign body usually does not give rise to any trouble once it has negotiated the ileocaecal junction. In the present case, obstruction and later perforation of the colon resulted from massive impaction of cloth fabric.

CASE REPORT

A 29-year-old woman was admitted as an emergency case because of a five-day history of lower abdominal colicky pain, vomiting, and constipation. Early laparotomy seemed indicated because of a firm tender mass in the pouch of Douglas which was thought to be a twisted ovarian cyst.

Operative Findings.—Some clear serous fluid was found in the peritoneal cavity, but the ovaries were normal. The whole of the large bowel was loaded down to almost the rectosigmoid junction. The rectum and the distal few inches of the sigmoid colon were empty and appeared normal to inspection and palpation. The distension was maximal in the pelvic colon, which was congested, thickened, and oedematous. It was angry-looking and the appearance was not unlike that of Crohn's disease. However, the mesentery and its lymph nodes were not involved. There was an area of necrosis measuring about 3 mm. in diameter in the wall of the pelvic colon, situated between the mesenteric border and the anterior taenia coli. This was of paper-like thickness, was light green in colour, and was covered with purulent exudate. The adjacent appendices epiploicae were also involved by this acute inflammatory process. There was no evidence of any diverticulosis or diverticu-

litis. As perforation seemed imminent, the loop of pelvic colon was exteriorized after milking down its contents.

The diagnosis of this strange lesion was made on the fourth postoperative day, when the milked-down contents were passed per rectum. These consisted of several portions of cloth fabric, mostly derived from vests, stockings, and pyjamas (see illustration). On the ninth postoperative day the exteriorized pelvic colon was opened as the patient had become acutely obstructed. After this many yards of fabric, mainly in lengths of about 15 cm., were removed from the colon.

On the thirteenth postoperative day she developed faecal peritonitis after perforation of the descending colon due to impacted fabric, and a transverse colostomy was performed. Her convalescence was stormy and prolonged, but eventually she left hospital after closure of the two colostomies.

COMMENT

Only two cases of perforation of the large bowel due to blunt foreign bodies have been reported in the medical literature. In the case reported by Williamson (1952) it was the result of a gall-stone impaction, while in Goatcher's (1953) case the cause was similar to the present one.

Ward-McQuaid (1950) studied the various types of ingested foodstuffs which could cause intestinal obstruction but rarely perforation and found that the terminal ileum was the commonest site of impaction.

The above case becomes interesting from various points of view: (1) On routine examination of the patient one would not have thought of any mental retardation. She was happily married and had two children. However, she was later seen by a psychiatrist, who found her to be mentally deficient. (2) The pathology of impending perforation has not been described previously; as in Goatcher's case, it was missed by prolonging the conservative treatment. The appearance can easily be confused with Crohn's disease, particularly if the impaction should take place in the terminal ileum. (3) Though the patient presented as a case of intestinal obstruction, a delayed perforation and faecal peritonitis could not be avoided as in Goatcher's case. To guard against such a complication should such a case be discovered at laparotomy it is advisable to perform a colostomy and milk out all the impacted material.

I wish to thank Mr. J. M. Moore for his guidance in the management of this case and useful suggestions in the preparation of the paper.

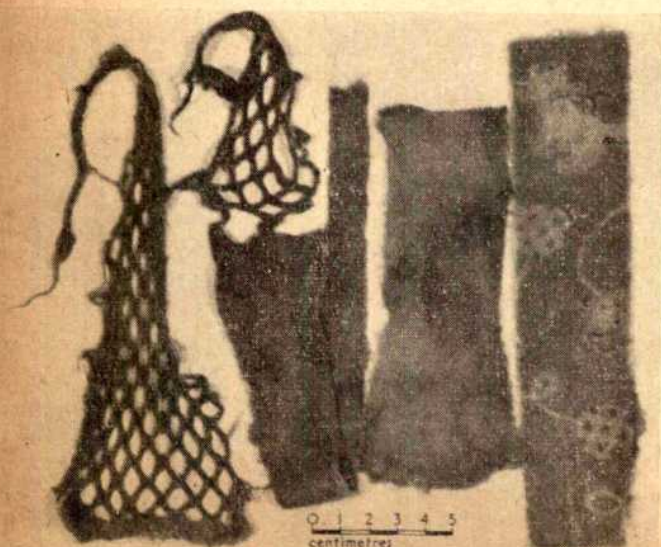
D. D. GAUR,* M.S., F.R.C.S.,
Ex-Registrar in General Surgery.

Ballochmyle Hospital,
Mauchline, Ayrshire.

* Now Consultant Surgeon, Bombay Hospital, 12 Marine Lines, Bombay 1.

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Photograph showing some of the ingested material.

Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Carcinoma of the Stomach

J. L. DAWSON,* M.S., F.R.C.S.

Carcinoma of the stomach is a common disease, but despite all efforts at early diagnosis and the application of radical methods of treatment the overall five-year survival rate is low—probably somewhere between 5% and 10%.

Pathogenesis

The association between blood group A and cancer of the stomach is found throughout the world and represents a weak but significant genetic link. Occasionally a strong family history of carcinoma is encountered.

The incidence varies in different parts of the world, e.g., high in Japan, low in the United States. It varies in different parts of the same country; it is, for example, high in North Wales compared with the rest of the United Kingdom. These variations have been variously attributed to trace elements in the water or methods of food preparation and eating; and it is interesting to note that the Japanese migrants to the United States show a fall in incidence compared with the rate in Japan, which suggests that the environmental factors are probably the most important. This is further confirmed by the fact that the incidence of the disease is actually showing a decline in the past 30 years in the United States.

Predisposing Pathological Conditions

Pernicious Anaemia.—There is a greatly increased incidence of gastric carcinoma in this disease, about twenty times the expected. The carcinoma most frequently develops in the body of the stomach—where the mucosal atrophy is—whereas in the population at large carcinoma most often originates in the pyloric antrum.

Atrophic Gastritis and Achlorhydria.—This condition almost certainly predisposes to the development of carcinoma. It is much more commonly found in association with carcinoma than with gastric ulcer or duodenal ulcer; the carcinoma is usually surrounded by atrophic mucosa, often with areas of intestinal metaplasia, which is frequent in atrophic gastritis. Atrophic gastritis is most often found in the antrum—the commonest site for carcinoma. Gastric polyps, although rare, show intestinal metaplasia and may be the origin of carcinoma.¹

Benign Gastric Ulcer.—Malignant change in a gastric ulcer almost certainly does occur. Applying strict pathological criteria for the diagnosis of ulcer cancer the incidence is probably about 10% in those stomachs resected. Much more often an error in clinical diagnosis is made—the carcinoma is wrongly regarded as a benign ulcer.

Pathology

Approximately a half of all gastric carcinomata occur at the pyloric end of the stomach. They have a variable macroscopic appearance (Borrmann): (1) *Polypoid*—growing into the lumen surrounded by atrophic mucosa. (2) *Ulcerating*—which penetrates deeply and has a raised edge well differentiated from the surrounding mucosa. (3) *Ulcerating and infiltrating*—the edge of the ulcer merges into the surrounding mucosa with obvious infiltration. (4) *Infiltrating*—in which no clear transition from normal to abnormal is seen macroscopically. The whole stomach may be involved. If ulceration develops it may be shallow or deep. It is this variety which gives rise to linitis plastica. Multiple centres of origin are often seen.

Histological appearances of carcinoma of the stomach may be graded according to the degree of cell differentiation from 1-4 (Broders).

Spread occurs by direct extension through the stomach wall and often involves adjacent viscera. Lymphatic spread is frequently present and involves the regional nodes along the lesser curvature, in the greater omentum, the hilum of the spleen, the subpyloric and suprapancreatic glands. The site of the tumour usually determines the nodes first involved. Blood spread and transcoelomic spread are also frequent.

Superficial Cancer

In this variety the carcinoma is found to involve only the mucosa of the stomach and does not penetrate in the muscularis mucosa, though spread to the regional lymph nodes may have occurred. This type of growth may be impossible to feel from outside the stomach²; it is usually well differentiated. Whether many stomach cancers begin in this way or whether it represents a form in which host resistance is high is not yet settled. The latter possibility seems likely, for even with nodal involvement the five-year survival rate is very high³ after resection (75%).

Symptoms

The oft-quoted clinical syndrome of epigastric pain, anorexia, and loss of weight associated with an epigastric mass represents advanced disease. Diagnosis at this stage will not usually benefit the patient very much apart from palliation of symptoms.

Several investigators have found that the average delay between the onset of symptoms and definitive treatment varies from six months to a year.⁴ The patient does not usually seek advice until symptoms have been present for at least six months. The first symptoms noted are firstly a slight diminution of appetite with a distaste for some foods and a relish for others,

* Consultant Surgeon, King's College Hospital, London, and Bromley Hospital, Kent.

and secondly vague epigastric discomfort—usually a feeling of fullness after meals, sometimes associated with belching. The patient often adjusts his diet with temporary relief of symptoms for weeks or even months.

Lesions close to the pylorus or cardia will produce obstructive symptoms (vomiting or dysphagia) comparatively early. Occasionally haematemesis and melaena or perforation will be the presenting symptom. Unexplained iron deficiency anaemia due to occult bleeding will sometimes lead to the discovery of a completely symptomless tumour. Rarely diarrhoea will be the presenting symptom, usually in the linitis plastica type of lesion. All too often, however, it is the manifestations of metastatic disease which cause the patient to seek advice: ascites, gross loss of weight, jaundice, and loss of strength.

Clinical Examination and Investigation

Physical examination is directed towards detection of anaemia, palpable supraclavicular nodes, and evidence of loss of weight. Examination of the abdomen may reveal a palpable mass, an enlarged liver, or the presence of ascites. Pelvic deposits may be palpable on rectal examination.

Barium studies are the most useful special investigations and they achieve a high degree of accuracy in good hands. The signs vary with the site and type of cancer—for example, deep ulceration, filling defect, areas of mucosal irregularity, or rigidity of the stomach wall. An x-ray film of the chest should be done to exclude metastatic disease.

Most gastric carcinomata are easily seen at gastroscopy and the diagnosis is not in doubt. Sometimes it is not possible to distinguish between a benign and malignant ulcer. If the lesion shows no evidence of healing when re-examined after the patient has rested in bed for 14 to 21 days then it should be regarded as malignant and explored.

Gastroscope examination has become available in the past few years.⁵ The instrument is flexible, so that the discomfort for the patient is comparable with gastroscopy using the fibroscope. The gastroscope has a great advantage over the gastro-scope in that it provides a permanent record of the appearances of the gastric mucosa for comparison with later examinations. It is also much easier to learn the technique and interpretation of appearances with a permanent record available. The accuracy of the methods varies from one reported series to another, but in Japan, where the method originated, the gastroscope has been found with experience to be slightly more accurate than even barium studies. It should be of special value in diagnosing superficial carcinoma of the stomach.

Achlorhydria is frequently found with carcinoma (excluding those patients with pernicious anaemia) but some 25% of patients will have normal gastric secretion, so that studies of secretion are not of much value in the diagnosis of a particular patient. Patients found to be achlorhydric may be screened as a high risk group, as it has been estimated that the risk of gastric cancer is 4.5 times higher than normal.¹

Gastric cytology (including tetracycline staining) and the use of radioactive phosphorus have also been employed, but they are time-consuming and are not widely used. Sometimes cytology will lead to a correct diagnosis of carcinoma when the other methods have not.⁶

Treatment

The only treatment producing a significant number of long-term survivors is excision of the tumour and adjacent stomach. In a large series reported from the Mayo Clinic it has been noted that in the past decade the proportions of patients who were explored, resected, and the number surviving five years have all risen. No proper controlled series is available, but these results have been attributed to the increased use of radical

surgery. Most of the patients treated at the Mayo Clinic come from afar, so that some selection may be exercised by the referring doctor. It is therefore not possible to say definitely whether these improved figures are real or apparent.

In the light of present knowledge radical surgery should be undertaken if the tumour is macroscopically limited to the stomach. The growth, with 5 cm. of macroscopically normal stomach either side, should be resected together with the regional lymph nodes.⁶

For lesions in the distal part of the stomach these criteria are satisfied by a radical lower partial gastrectomy, done through the abdomen. The distal stomach and the first part of the duodenum are removed together with the greater omentum, the lesser omentum, the subpyloric nodes, and the nodes along the hepatic artery and coeliac axis. The left gastric artery is divided flush at the coeliac axis. If the posterior wall of the stomach is involved then the suprapancreatic nodes and the peritoneum of the lesser sac are removed. Continuity is restored by an antecolic gastrojejunal anastomosis.

For lesions of the proximal stomach a thoraco-abdominal approach is required, and, except for tumours limited to the cardia, a total gastrectomy is done, taking the spleen and suprapancreatic and coeliac nodes. If the tumour is on the posterior wall of the stomach, the tail and part of the body of the pancreas is often removed to achieve an *en bloc* resection.

For tumours limited to the cardia a radical upper partial gastrectomy may be done, retaining the distal half of the stomach, the lesser curve being closed and the oesophagus anastomosed to the greater curve side of the cut end of the stomach. The lymph nodes of the coeliac axis and suprapancreatic region are taken, together with the tissues around the hiatus, the spleen, and the adjacent parts of the greater omentum.

If the carcinoma is found to have spread beyond the limits of complete removal, then a more limited palliative resection should be done if the tumour is mobile, because resection usually produces better palliation than bypass procedures. If the tumour is irremovable and the patient has severe obstructive symptoms at either the distal or proximal end of the stomach, then gastroenterostomy or end-in-side jejuno-oesophagostomy will afford the best symptomatic relief.

In recent years systemic or regional chemotherapy has been used and may produce temporary remission of symptoms, although in most recorded series this is usually short-lived, a matter of a few weeks only.⁷

Prognosis

The outlook for the patient depends upon the length of the history, the extent of the lesion (including nodal involvement), and the degree of cell differentiation. Somewhat paradoxically it has been found that the longer the history the better the prognosis—this is probably best explained by the suggestion that the patient who takes many months before his symptoms progress to significance after first appearing has a much more slowly growing tumour than the patient whose symptoms demand investigation only a short period after first appearing.

The proliferative type of tumour usually carries the most favourable prognosis, while the linitis plastica type of lesion is almost never associated with five years' survival. The well-differentiated tumours carry a better prognosis than the anaplastic.

Infiltration of the nodes found on examination of the specimen removed at radical operation is usually an accurate guide to prognosis. Of those patients found to have involvement of the subpyloric glands only 6% survive five years; while if only the lesser curve nodes are involved 65% survive for five years.⁸

The prognosis of superficial carcinoma of the stomach is altogether different—95% survival in those without nodal involvement and 75% for those with nodal involvement.³

Prophylaxis

For the vast majority of patients it is difficult to see how the prognosis can be improved. The average delay between onset of symptoms and seeking advice is six months, so that the biology of the tumour usually determines the outcome.

Screening of high risk groups—for example, those with pernicious anaemia, will make little difference to the overall figures because only 5% of gastric carcinomas occur in these patients.

There is some evidence that earlier diagnosis would improve the outlook. When a large group of patients with pernicious anaemia was screened, 38 cancers were found; in 22 without symptoms only 6 had nodal metastases at surgery. On the other hand, of the remainder with mild to moderate symptoms elicited on questioning (the patients had not sought advice) 13 out of 15 had nodal deposits.⁹ In patients with pernicious anaemia, six-monthly x-ray examinations have been recom-

mended. Against the credit of picking up a cancer in less than 5% of patients must be set the introspection and neurosis engendered in the patient, the irradiation hazard, and the considerable demands on the time of a skilled radiologist.

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TODAY'S DRUGS

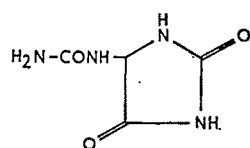
With the help of expert contributors we publish below notes on a selection of drugs in current use.

Allantoin

This drug is marketed by Stafford-Miller Limited under the name of Alphosyl. Two preparations are available—a cream containing 5% of a refined alcoholic extract of crude coal tar and 2% allantoin in a vanishing cream base, or a greaseless, stainless lotion. It is a recent addition to the range of agents used in the treatment of psoriasis.

Chemistry and Pharmacology

The chemical structure of allantoin is:



5 Ureidohydantoin or glyoxyldureide

It has been shown that plant extracts containing large amounts of allantoin produced healing of intractable ulcers, as did pure solutions of allantoin. Similarly, the successful use of maggots in the treatment of chronic ulcers and non-healing wounds is also apparently due to allantoin present in the excretions of the maggots. Though it might seem that this action would not have any direct application in the treatment of psoriasis, allantoin has been shown to possess a keratin-dispersing activity, which may explain its beneficial activity in psoriasis.

Clinical Use

Trials in the United States of America have shown^{1,2} that allantoin appears of value in the management of psoriasis. From 70% to 88% of patients were helped, and 50% or more had their lesions cleared completely by the treatment. Clearing tended to be slow and treatment had to be main-

tained for relatively long periods of time, while any recurrence had to be treated immediately. Nevertheless, these studies were not well controlled, even after allowance has been made for the difficulties in conducting satisfactory clinical trials of treatment in psoriasis.

It is also suggested that allantoin is of value in the treatment of chronic scaling dermatoses other than psoriasis, but not enough has been written about its use in such conditions to enable any assessment to be made.

Advantages

Allantoin has not been reported as causing any skin reactions and phototoxicity has not been observed. The preparations are acceptable to the patients. The cream can be applied under polyethylene occlusion with increased effect.

It seems that allantoin may well be of value in the management of psoriasis. It certainly avoids the hazards of anti-metabolites and local and systemic corticosteroids, and it does not have the disadvantages of staining, burning, and discoloration that occur with other topical preparations.

Presentation and Cost

Alphosyl is available as a 5% refined alcoholic extract of coal tar and 2% allantoin in a cream and lotion.

The basic N.H.S. price of 60 g. of cream is 9s. 2d. and of 8 fluid oz. lotion 17s. 7d.

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B.M.J. Publications

The following are available from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1. The prices include postage.

<i>Is There an Alternative?</i>	Price 7s. 6d.
<i>Treatment of Common Skin Diseases</i>	Price 10s.
<i>Obstetrics in General Practice</i>	Price 32s. 6d.
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<i>Charles Hastings and Worcester</i>	Price 3s. 6d.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Killed-measles-virus Vaccine

Q.—In view of a report¹ that some children who had been immunized with killed-measles-virus vaccine developed a severe atypical form of the disease when exposed to natural infection, and of the opinion that the administration of killed vaccine alters the host in some unknown way, would it be wise for the time to refrain from using killed-measles-virus vaccine?

A.—In the studies reported by Fulginiti and Kempe,¹ in which an "atypical measles" developed in children five to six years after giving killed measles vaccine, two groups were involved. In one three doses of killed vaccine were given (KKK), while in the other two doses of killed vaccine preceded a single dose of live vaccine (KKL). In Britain either live vaccine alone has been used—that has not given rise to this atypical measles—or a single dose of killed vaccine followed by the live vaccine, which was not a schedule studied by Fulginiti and Kempe.

In the Medical Research Council trials a few of the children in each of the vaccinated groups have had measles, but none has had this atypical measles. It is perhaps significant, however, that so far the observation period has been only three years, whereas the cases in America occurred five to six years after primary immunization.

It is generally believed that the killed vaccine in the schedules KKK or KKL has sensitized the vaccinees rather than immunizing them, and it is known that immunity has fallen within a year. In view of the fact that the immunity to both the KL and the L alone schedules used in Britain seem to be holding up for at least three years, it is hopeful that satisfactory immunity has been conferred and that cases of atypical measles will not be seen. There has been no evidence from the M.R.C. trials, therefore, that a KL schedule for those demanding reaction-free immunization should be stopped.

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Scriver's Test for Phenylketonuria

Q.—What is Scriver's test for phenylketonuria? How do the results of this test compare with the Phenistix test?

A.—The term "Scriver's test" is somewhat misleading. In 1964 Scriver, Davies, and Cullen¹ described a simple method for screening for amino-acid disorders. This is a semi-quantitative technique of one-dimensional chromatography applied to the plasma, for which blood is taken by heel-prick and run into heparinized capillary tubes. The tubes are then sealed with Plasticine. They can be sent through the post in suitable containers. The method can be easily adapted for mass screening.

The advantages compared to the Phenistix test are that: (1) it is easier to obtain a small

sample of blood from an infant than a fresh specimen of urine; (2) other disorders of amino-acid metabolism as well as phenylketonuria can be detected; (3) it can be used as a rough method of control during the dietary treatment of phenylketonuria; and (4) a standardized method can be applied to all specimens.

Some of the shortcomings of the Phenistix test have been recently described by Stephenson and McBean,² and Woolf³ has briefly reviewed the present situation.

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Thalidomide in Leprosy

Q.—Has thalidomide proved effective in the treatment of leprosy?

A.—Patients with lepromatous-type leprosy frequently develop serious reactions—variably referred to as lepra reactions, lepromatous exacerbations, or erythema nodosum leprosum (E.N.L.)—during the course of anti-leprosy treatment. These reactions are commonly manifested by outbreaks of subcutaneous nodules; pain in bones, joints, and nerves; and fever. They may be fatal. When these reactions occur under field conditions chemotherapy is usually stopped, and the more severe reactions can be controlled only by prolonged treatment with corticosteroids, resulting in the usual toxic side-effects.

There is now good evidence that thalidomide can control lepra reactions of this type as effectively as corticosteroids. This finding arose from a chance observation by Sheskin,¹ in Israel, while using thalidomide as a sedative for patients with lepra reactions. His first observation was based on six patients,¹ his second on 13 patients in Israel,² and more recently on those in an extensive double-blind trial carried out in Venezuela.³ The trial comprised 173 treatments, in which thalidomide was used in 85 and a placebo in 88. In the thalidomide-treated cases there was amelioration in 92% and no change in 8%; no deterioration was observed. In the placebo-treated cases amelioration was observed in 27%, no change in 50%, and a deterioration in 23%. Similar satisfactory results have been obtained by Cazort and his colleagues⁴ in 24 patients treated with thalidomide in Thailand.

Treatment has been initiated with 100 mg. thalidomide thrice daily, and the reactions have shown improvement within 48 hours. In some of Sheskin's cases treatment has been maintained successfully for 10 months and the dose of thalidomide reduced to 100 mg. a day. In the majority of patients thalidomide has enabled the patients to be weaned of corticosteroids. The complications have been dryness of the mouth, constipation, and various skin eruptions, but none were severe enough to necessitate withdrawal of treatment. Even with prolonged treatment the compli-

cations were considered to be less serious than those produced by corticosteroids. Because of the teratogenic action of thalidomide the drug was used only in male patients or female patients beyond child-bearing age.

Therefore, despite the promising results obtained with thalidomide in the control of lepra reactions, and particularly as an alternative to corticosteroids, its use can be envisaged only at centres where the patients are under rigorous supervision. There is now good evidence that thalidomide has an immunosuppressant action in animals, as demonstrated in the skin homograft reaction.⁵ However, the observation that it depresses reactional phases in patients with leprosy provides the first direct evidence that thalidomide can be also an immunosuppressive in man.

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⁶ Turk, J. L., Hellmann, K., and Duke, D. I., *Lancet*, 1966, 1, 1134.

Notes and Comments

Medical Equipment for Explorers.—Dr. L. M. KELLY (Board of Trade, London S.E.1) writes: This question ("Any Questions?" 7 October, p. 43) concerning the kind of medical equipment which might be taken by laymen for a three-month voyage in a sailing-boat also raised the question of a suitable medical book. I should like to draw attention to the latest edition of the *Ship Captain's Medical Guide*.¹ This medical guide was devised for use on board ships which do not carry a doctor and is written especially for use by laymen. It might be considered of value to explorers, to those on expeditions in remote areas, or indeed to any isolated community where no doctor is at hand.

REFERENCE

- ¹ *Ship Captain's Medical Guide*, 1967. H.M.S.O., London.

Oral Diuretics and Hyperuricaemia.—Professor W. I. CRANSTON (Department of Medicine, St. Thomas's Hospital, London S.E.1) writes: In answer to this question ("Any Questions?" 28 October, p. 221) it is stated that triamterene does not cause elevation of uric acid. I do not believe this to be true. The evidence for this belief is given in a paper by myself and colleagues.¹ There is also indirect evidence in a paper by Heath and Freis.² I do not think this is of any particular importance with regard to the question which was raised, and I mention it only in the interests of accuracy.

OUR EXPERT replies: I am grateful to Professor Cranston for drawing my attention to the fact that there is evidence that triamterene, like the other oral diuretics, probably does cause a rise in serum uric acid. It would appear from the two references he gives that the degree of hyperuricaemia with triamterene is less than that produced by equivalent doses of other oral diuretics. As he says, the matter is relatively unimportant in relation to the question which was asked.

REFERENCES

- ¹ Cranston, W. I., Semmence, A. M., Richardson, D. W., and Barnett, C. F., *Amer. Heart J.*, 1965, 70, 455.
² Heath, W. C., and Freis, E. D., *J. Amer. med. Ass.*, 1963, 188, 119.

Book Reviews

Being a Good G.P.

The Doctor-Patient Relationship. By Kevin Browne, M.B., B.S., D.Obst.R.C.O.G., D.C.H., and Paul Freeling, M.B., B.S. (Pp. 73+vii. 10s. 6d.) Edinburgh and London: E. & S. Livingstone. 1967.

A characteristic of many books and articles written for general practitioners is the tendency of their authors to equate the function and requirements of general practitioners with those of hospital junior doctors. This is a basic misconception which the authors of *The Doctor-Patient Relationship* avoid. Their thesis is that the role of the general practitioner is unique and that particular training and skills are necessary for him to fulfil satisfactorily his primary role of "first contact doctor."

They consider it important for the general practitioner to learn to use as a diagnostic and therapeutic agent the emotional responses evoked in him by the attitude and bearing of his patients. This emotional response between the doctor and his patient is in their opinion much less important, diagnostically and therapeutically, for the specialist than for the general practitioner. Their purpose is to show some of the ways in which an understanding of the emotional transaction occur-

ring between a doctor and his patient can be used therapeutically. While acknowledging the importance of experience, they suggest that the necessary basic insight is best obtained by a period of formal training, and mention briefly two contrasting training schemes. One scheme they mention is the general practitioner seminars at the Tavistock Clinic, and one wonders to what extent these seminars may have helped to formulate some of the concepts expressed in their book.

Browne and Freeling write clearly and well. Their skill in handling the emotional problems of their patients is evident from the many case reports with which they illustrate their comments. Their book contains much that is interesting and admirable, but little that is fundamentally new. Nevertheless, most practitioners could learn from it, and I must record success with two patients after using one of their techniques. They describe various ways in which a doctor's emotional response—be it anger, depression, sexuality,

anxiety, or sympathy—when properly recognized and understood can be used to help the patient. The important role of relatives and colleagues in precipitating or affecting an illness is indicated. The need for the doctor to be constantly alert is underlined and the habit of some patients to report their main anxieties as they disappear through the surgery door is noted. The small extent to which they record using psychotropic drugs is noteworthy, especially, I felt, as I might have treated some of their depressed patients with a thymoleptic drug.

This book was originally published as a series of thirteen articles in *The Practitioner*. The chapters are short and divided into subsections that are almost complete entities in themselves. The contents and structure are such that it can be browsed through at leisure. New entrants will find it a useful introduction to an important aspect of general practice. Older practitioners may well feel that they have learnt from experience much of what is implicit in it; if not, they now have an excellent opportunity to learn from the experience of others.

W. DEWI REES.

Proteins and Related Subjects

Protides of the Biological Fluids. Proceedings of the 14th Colloquium, Bruges, 1966. Edited by H. Peeters. (Pp. 734+xiii; illustrated. £12.) London: Elsevier. 1967.

A notable annual event in biochemistry is the meeting on proteins and related subjects in Bruges, steered by Professor H. Peeters, who has now edited the proceedings of the 1966 colloquium. Printed in small but readable type on some 700 pages, there are more than 100 contributions. The authors' index consists of almost twice as many names, and the subject index lists some 500 items. It is clear that it is not possible to do such a book full justice in a review. In addition there must have been in the course of this meeting many informal exchanges which must have added to the delight and inspiration of this colloquium, and which could not find their way into print.

The volume is introduced by an academic lecture given by Professor E. F. Lüscher, of Berne, on the biochemical properties and biological function of fibrinogen. Although Professor Lüscher himself describes his contribution as a "brief account," it is in fact an exhaustive survey of the subject, discussing the known properties of the fibrinogen molecule and its biological functions and the areas where future research is required. This lecture alone is supported by 139 references.

There are four main sections. The first deals with metal-binding proteins, and the subsection concerned with the structure and function of these compounds includes such attractive features as pictures of molecular

structures and a complete table of metallo-protein enzymes, their function and distribution. The metals include magnesium, manganese, cobalt, zinc, iron, copper, and even molybdenum, and the enzymes amount now to more than 40. One subsection is entirely devoted to the iron binding of transferrin, lactoferrin, and ferredoxin, and other subsections to the copper binding of ceruloplasmin, and to proteins binding zinc, manganese, and vanadium, respectively.

The second major section deals with protein levels and protein turnover. Methods are described such as the use of computers to analyse the metabolism of tissue proteins. Regulation factors are discussed such as the relation between synthesis, metabolism, and serum concentration of plasma proteins, and the synthesis of proteins in cultures of human lymphocytes. One subsection is concerned with individual plasma proteins such as albumin, gammaglobulin, haptoglobin, and lipoprotein.

The third section is devoted to the determination of protein structure by physical methods, and, among others, includes a lucid account of the optical rotatory dispersion of α helical and β structures in relation to protein conformation. There is also a contribution in which the application of this technique to the investigation of Bence Jones proteins is discussed in detail. The fourth section includes numerous papers on separation techniques, improvements of chromatography by recycling to cause zone sharpening, new light on D.E.A.E. cellulose and D.E.A.E. Sephadex, variations in immuno-electrophoresis, and gel infiltration. Gel filtration can now also be used with considerable accuracy for the determination of molecular weight. A

fifth section includes various papers such as a contribution on the isoenzymes of catalase amongst the soluble non-haemoglobin proteins of red cells.

As usual for the proceedings of the Bruges conferences, this volume will be a rich source of up-to-date information for a wide circle of research workers interested in proteins of biological fluids.

H. LEHMANN.

Cancer Methodology

Methods of Cancer Research. Vol. 1. Edited by Harris Busch. (Pp. 612+xvi; illustrated. £11 4s.) New York and London: Academic Press. 1967.

This is the first of four volumes intended "for young individuals entering the field of cancer research." In fact many graduate students and postdoctoral fellows may be working for a long time on cancer problems without the intention of dedicating their scientific lives to cancer research. They may therefore hesitate to embark on equipping themselves with a comprehensive knowledge of techniques applicable to the field. Later, when they feel committed to cancer research, they may well have only limited time for wide and general reading. The present series may therefore be doing itself less than justice by restricting its appeal to workers in the cancer field. In any case many of the chapters are of interest in related biological and medical areas.

The first volume consists of ten review articles, each of them between 20 and 100 pages. Some of them might just as well have

appeared in the *Advances in Cancer Research* series produced by the same publishers. The volume begins with a chapter by Etienne de Harven, on methods in electromicroscopic cytology. Like others in the book, this contribution is lucid and informative; nevertheless, the serious student of electronmicroscopy would need to consult longer textbooks. This is more obvious in the case of M. B. Shimkin's chapter on epidemiology, which is merely a brief statement of the problem rather than a description of methods. A happier balance is achieved by J. H. and E. K. Weisburger in their chapter on tests for chemical carcinogens. Here much useful information of a practical nature is given in a sufficiently broadly based way to maintain the interest of the general reader. It is a pity that the chapter by T. S. Hsu and F. E. Arrighi was limited to karyological methods and did not extend over the whole field of cytogenetics. Also it is surprising that in a book on cancer methodology there are no illustrations of tumour karyotypes. Instead there appear the seemingly irrelevant pictures of the karyotypes of a male bobcat and of a male ocelot. A more serious omission is of any reference to the quantitative assessment of chromosome size and D.N.A. content by microspectrophotometry or of chromosome mass by interference microscopy.

The standards of writing, of presentation, and of editing are high, but the series falls between two stools; the chapters are too short for textbook purposes and too long for background reading. In any case the series is prohibitively expensive (at £11 4s. 0d. for just the first volume). Without doubt the set of four volumes will become a valuable source of reference in libraries at research institutes, but it is difficult to believe that it will find its way on to the bookshelves of more than a few individual students or young cancer workers.

F. J. C. ROE.
D. T. HUGHES.

What is Known about Candidosis

Symposium on Candida Infections. Edited by H. I. Winner, M.D., F.C.Path., and Rosalinde Hurley, M.D., M.C.Path. (Pp. 249+xii; illustrated. 35s.) Edinburgh and London: E. & S. Livingstone, 1966.

Following the introduction of drugs with an immunosuppressive action such as the corticosteroids and antibiotics with a wide spectrum of activity, fungi were given opportunities to cause clinical infection previously denied them. *Candida albicans* has been the most successful in taking advantage of the new situation, and it is now responsible for a group of pathological conditions known as "candidosis." This, the editors explain, is preferable to the alternative "candidiadis," used in America, on the grounds of priority, brevity, and euphony, and its wide usage in this and other countries. Even so, infections of any severity are still very unusual, and few clinicians have had much experience of them, or clinical pathologists of the organism itself. There was therefore every justification for bringing together twenty experts in their respective fields to take part in a symposium on *Candida*. This volume is an account of the proceedings.

The papers in Part I deal with the pathological potentialities of *Candida*, its isolation, recognition, and antigenic analysis. In Part II there are papers on the efficiency of chemotherapeutic agents, the allergic manifestations that may occur, the experimental production of infections, and the part played by the organisms in animal disease. Part III, which makes up half the book, gives a series of descriptions, often in considerable detail, of the various forms of infection that may be encountered. This naturally includes very full descriptions of candidosis of the mouth, vagina, and urethra, and the special manifestations of the disease in children. The more unusual manifestations, such as candidal infection of the skin, nails, hair, and external ear, infection of the lungs and invasion of the blood by the organism, are also given their due weight. The book ends with a chapter on treatment.

Taken together, these papers throw a flood of light on the subject, and there can be little that is known to which reference is not made somewhere in its 250 pages. It is lavishly illustrated, there is a bibliography at the end of each chapter, and the index is adequate. All connected with its production are to be congratulated.

RONALD HARE.

Immature Babies and How they Grow up

Children of Very Low Birth Weight. By Alison McDonald. (Pp. 126. 25s.) London: Spastics Society (in association with William Heinemann), 1967.

This book reports the results of a follow-up study of more than a thousand children with a birth weight of 1,800 g. or less, born between 1951 and 1953, originally collected by the Medical Research Council for a study of the relationship of retrolental fibroplasia to oxygen therapy. A very high proportion of the children were traced and 1,066 were available for examination. The survey was undertaken in order to identify more clearly the causes of cerebral palsy. The children were between 6 and 8 years of age and were old enough for a satisfactory neurological and intelligence assessment to be made. They were collected from 14 cities in different parts of Great Britain. Of the children who weighed less than 1,360 g. at birth 33% had a congenital defect, and from this weight up to 1,800 g. 24% had a congenital defect.

The author divides the factors causing low birth weight into two broad groups—those leading to early delivery and those depressing foetal growth (the "small for dates" babies—S.F.D.). Apart from retrolental fibroplasia the greatest hazards following early delivery were spastic diplegia and deafness, while the S.F.D. children tended to suffer from cerebral palsy other than spastic diplegia, from cataracts, fits, and mental retardation. Dr. McDonald concludes that the damage resulting in spastic diplegia and deafness occurred postnatally, particularly in association with cyanotic attacks, and the strong correlation found with gestational age suggested that immaturity was a factor of primary importance.

The S.F.D. children tended to have signs of cerebral disease—presumably consequent upon prenatal brain damage. The author

draws several other important conclusions from a study of these two aetiological groups. She supports the hypothesis that the periventricular lesions described by Banker and Larroche may well prove to be the cause of spastic diplegia. She analyses the statistical evidence concerning cerebral palsy, intelligence, eye defects, deafness, and fits in considerable detail.

In regard to intelligence, Dr. McDonald concludes that when children with severe neurological or sensory defects were excluded the I.Q. did not differ appreciably from that of the general population—the mean was 102.4 (Terman-Merrill revision of the Stanford-Binet test). The lack of correlation between the I.Q. and factors leading to oxygen deprivation around the time of birth suggested that, although cerebral anoxia may lead to death or neurological disorders in small premature babies, it does not affect intelligence.

This is a careful and accurate piece of work which well justifies its selection as the first monograph in a new series of "Research Monographs." Immature babies survive in increasing numbers and we are too ignorant of the aetiological and pathogenetic factors concerned with their abnormalities. Biochemical factors are now being more closely examined, and Dr. McDonald asks for more detailed post-mortem studies by collaborating premature baby units. She hints that the fear of damage by excessive oxygen therapy may have limited its use, with a resulting high incidence of spastic diplegia. There is no suggestion in any of her conclusions that the last word has been written; her work provides a stimulus to further inquiry.

DOUGLAS HUBBLE.

Normal and Abnormal Sexuality

Sexual Problems. Diagnosis and Treatment in Medical Practice. Edited by Charles William Wahl, M.D. (Pp. 300+xxix. 63s.) London: Collier-Macmillan, 1967.

This book originated in a postgraduate course on sexual problems in medical practice held in the University of California. It consists of 22 articles by 18 contributors and is addressed mainly to non-psychiatrists. In the United States, as in this country, the average medical practitioner is insufficiently informed about sexual matters. The book aims at remedying this deficiency.

Although the majority of the contributors are psychoanalytically oriented there is no undue emphasis on theory nor do they recommend psychoanalysis for all cases of sexual disorder. There are articles on taking a sexual history, on physical symptoms that may reveal sexual conflict, on sexual problems in gynaecological practice, on the psychological effects of abortion, on impotence, on promiscuity as a symptom of anxiety, the intersexed patient, and several other subjects. Inevitably, there is much overlapping. The presentation is neither systematic nor comprehensive, but it is lucidly written, and should help to introduce general practitioners and other doctors into the problems of normal and abnormal sexuality.

E. STENGEL.

Significance of the Systolic Murmur

The Innocent Murmur. A Problem in Clinical Practice. Edited by Cesar A. Caceres, M.D., and Lowell W. Perry, M.D. (Pp. 300+xvi; illustrated. 97s. 6d.) London: J. & A. Churchill. 1967.

This monograph, with 23 eminent American cardiologists as contributors, deals with the history of innocent murmurs, mechanism of sound production, and principles of phonocardiography, as well as discussing the aetiology and significance of the systolic murmur.

Much of the text is taken up by a verbatim discussion between cardiologists, and is presented in the form of reports on panel discussions or clinicopathological meetings. This may appeal to some readers, but it takes a long time to sort the wheat from the chaff and at the end one is not always clear about the outcome of many pages of talk. It is unfortunate that the phonocardiograms, so vital to augment the text, are of such a poor quality and are not printed on art paper.

The cardiologist will find profit in reading through the views of his American colleagues on this most important subject. The misinterpretation of innocent systolic murmurs has led to much unwarranted cardiac invalidism in the past, and authors are to be congratulated on bringing together the views of all the leading authorities in this one volume. There is an excellent collection of references.

J. P. SHILLINGFORD.

Hierarchy and Culture

Caste and Race. Comparative Approaches. Edited by Anthony de Reuck and Julie Knight. (Pp. 348+xi. 60s.) London: J. & A. Churchill. 1967.

This is another symposium in the Ciba series for the promotion of understanding and knowledge on an international basis by bringing together persons prominent in their

respective professions for free exchange of views and ideas. A previous contribution *Man and Africa* is an outstanding example and remains on my bookshelf as a significant reference on Africa for a practising public health physician. The present volume follows the same format of a series of carefully prepared papers, each followed by open discussion.

It is not a book for the busy general physician to relax with; it is an intellectual contribution to a current and persisting anachronism to Western civilization's concept of an egalitarian society. Sociologists, however, like anthropologists and historians, follow the event, and by analysing past social experience hope to give the world a greater understanding of the present. The present volume attempts to do this by making a comparative study of social segregation as it occurs around the world, whether it be due to traditionally derived cultural customs or ethnic groupings. Both may be ascribed to an accident of birth; which thus determines man's status in society. Its effect upon modern outlook will depend upon how far its contents can be translated into easily assimilable terms. Those most in need of its understanding analysis are least likely to read it in its present form.

The symposium is in difficulties from its very inception in its attempts to define and distinguish caste, class, and slavery; but this is an excellent opening chapter. Perhaps the most concise and embracing definition of caste occurs some three chapters later: "a caste system occurs where a society is made up of birth ascribed groups which are hierarchically ordered and culturally distinct. The hierarchy entails differential evaluation, rewards, and associations" (page 48). Or, more simple (page 58), "Caste is people, and especially people interacting in characteristic ways and thinking in characteristic ways." Later on a moment of truth? (page 81): "They do not want equality—they want superiority; lower castes want to move up the ladder rather than to eliminate the ladder." Degrees of slavery are observed from chattel slaves with involuntary servility

to bond slaves with voluntary servility. The rights and privileges of slavery are noted (an article in *Life* magazine of 6 October 1967 entitled "Dead Hand of the Ottomans" graphically portrays this). The term "unfreedom" is coined.

Perhaps class is the most difficult to define and the most clearly understood. The haves and the have-nots; the professional status syndrome where profession supplants economics; and the "degenerate culture group view." This latter is described as an essentially practical class concept defined in terms of speech, standards of living, and interests displayed. That is, people tend to group themselves according to the similarity of their ways of living. The common fundamental facets of race and caste discrimination are later defined as "Besides endogamy and status stratification, the concept of pollution in sexual relations, commensality and residence, and belief in the inheritance of biopsychological qualities along racial or ethnic lines, are common properties of the two sets of relationships" (p. 98).

A review of this length cannot do justice to such a symposium. From discussions on definitions, philosophical and comparative sociology, chapters are devoted to discussions of the problems of discrimination on a geographic basis. Much of the tone of the book is set by the realization that the very words race, caste, slavery themselves carry implicit overtones of prejudice. Curiously enough, the word tribalism is neither mentioned nor defined. Africa receives scant attention, though there is brief mention on pages 109 and 110 of East Africa, and again reference is made to the difficulties of assimilation experienced by Francophone negroes in France—the psycho-dynamics of acculturation in relation to Francophone Africa. Perhaps there are lessons for the physician in the phrase "Each social class has a kind of sub-culture of its own within the wider whole." And, maybe, we as physicians would do well to consider our own subculture classes in terms of status hierarchy.

N. R. E. FENDALL.

Books Received

Review is not precluded by notice here of books recently received.

Ärztliche Aufklärungspflicht und Schweigepflicht. Proceedings of a Symposium. Edited by Helmut Kraatz and Hans Szewczyk. (Pp. 178. 17s. 4d.) Jena: Gustav Fischer. 1967.

Gynäkologie und Geburtshilfe. Vol. 2. Schwangerschaft und Geburt. Edited by O. Käser *et al.* (Pp. 1193+xxi; illustrated. DM. 298.) Stuttgart: Georg Thieme. 1967.

Laboratory Evaluation of Hemostasis. Medical Technology—1. By Marjorie S. Sirridge, M.D. (Pp. 163+xi; illustrated. 56s.) London: Henry Kimpton. 1967.

System of Ophthalmology. Vol. 10. Diseases of the Retina. Edited by Sir Stewart Duke-Elder, G.C.V.O., F.R.S., and John H. Dobree. (Pp. 878+xv; illustrated. £10.) London: Henry Kimpton. 1967.

Harley Street. By Reginald Pound. (Pp. 198 +x; illustrated. 36s.) London: Michael Joseph. 1967.

Electrotherapeutic Sleep and Electro-Anaesthesia. Proceedings of First International Symposium, Graz, Austria, 1966. Edited by F. M. Wageneder and St. Schuy. (Pp. 357; illustrated. £6 17s. 6d.) Amsterdam: Excerpta Medica Foundation. 1967.

Medicine for Mountaineering. Edited by James A. Wilkerson, M.D. (Pp. 309+xx; illustrated. \$7.50.) Washington: The Mountaineers. 1967.

The Management and Nursing of Burns. By J. Ellsworth Laing, M.B., F.R.C.S., and Joyce Harvey, S.R.N., S.C.M. (Pp. 116; illustrated. 17s. 6d. Paper 10s. 6d.) London: English Universities Press. 1967.

A Practical Guide to the Care of the Injured. By P. S. London, M.B.E., M.B., B.S.(Lond.), F.R.C.S.(Eng.). (Pp. 777+xii; illustrated. £7 10s.) Edinburgh and London: E. & S. Livingstone. 1967.

Principles of Pathology for Dental Students. By J. B. Walter, T.D., M.D., M.R.C.P., F.C. Path., Margaret C. Hamilton, F.D.S.R.C.S. (Eng.), M. S. Israel, M.B., M.R.C.P., D.C.P., M.C.Path. (Pp. 437+x; illustrated. 60s.) London: J. & A. Churchill. 1967.

A Short Textbook of Orthopaedics and Traumatology. By J. N. Aston, M.B., F.R.C.S. (Pp. 307; illustrated. 40s. Paper 27s. 6d.) London: English Universities Press. 1967.

Lymphatics and Lymph Circulation. Physiology and Pathology. 2nd edition. By Istvan Rusznyak, Mihály Földi, and György Szabo. (Pp. 971; illustrated. £8 8s.) Oxford: Pergamon. 1967.

Pemphigus: Occupational Dermatoses due to Chemical Sensitization. Edited by E. Liebner and E. Florian. (Pp. 711; illustrated. £6 10s.) Budapest: Hungarian Academy of Sciences. 1965.

Gastric Secretion. Mechanisms and Control. Proceedings of Symposium held at Edmonton, Canada, 1965. Edited by T. K. Shnitka, J. A. L. Gilbert, and R. C. Harrison. (Pp. 501 +xvii; illustrated. £7.) Oxford: Pergamon. 1967.

Innovation and the Balance of Payments. The Experience in the Pharmaceutical Industry. Symposium. Edited by George Teeling-Smith. (Pp. 99+xvii. 21s.) London: Office of Health Economics. 1967.

Middle Articles

MEDICAL HISTORY

The Worshipful Society of Apothecaries of London—1617–1967

W. S. C. COPEMAN, C.B.E., M.D., F.R.C.P.

[WITH SPECIAL PLATE BETWEEN PAGES 540 AND 541]

Brit. med. J., 1967, 4, 540–541

The Ancient City Companies and Guilds were formed in mediaeval times as "friendly societies" for mutual help among members of certain trades and crafts, and for the relief of their distressed colleagues. Since Elizabethan times the Grocers' Company had imported spices and drugs from the newly discovered countries to the far east and west, and had compounded medicines from these. Those members of that company who performed this useful function were known as apothecaries. As early as 1525, however, we hear of the Apothecarial Grocers petitioning for a corporation of their own, as their art was a separate one and should not be subordinated to fallible tradesmen like grocers who favoured only the mercenary part of their trade. Their wish was not then granted, but it became obvious that secession was imminent, as a new profession, pharmacy, involving special training and study, was evolving.

The Charter

In 1616 the Royal Apothecary, Gideon De Laune, with the co-operation of Sir Theodore de Mayerne, the Court Physician, again petitioned King James I for a charter such as had been granted a century previously to the physicians. Lord Chancellor Francis Bacon approved, and the King agreed, saying, "Grocers are but merchants, the business of an apothecary is a Mystery, wherefore I think it fitting that they be a Corporation of themselves." This, however, greatly displeased the powerful city fathers and the College of Physicians, which was then in the city; so in conjunction they placed every obstacle in the path of the new company and succeeded in delaying its charter until 6 December 1617, on which day it finally passed the Great Seal. Thus the apothecaries were free at last, but with little money and no headquarters. They possessed boundless confidence in their future, however, and their written records have survived unbroken from that day, enabling us to reconstruct their unique story.

The new company, or society, now regarded its main function as being to improve the quality of all drugs sold to His Majesty's subjects, and also to supervise and improve the qualifications of the vendors. Their charter gave them the right to search apothecaries' shops within a seven-mile radius of Cornhill, and to destroy all materials found which they considered below standard. With incautious naiveté, which they would regret for two centuries, they agreed "to put their dependence upon the liberal-minded College of Physicians," whose prescriptions they dispensed and who they felt sure would be more sympathetic to their aims than the mercenary grocers.

With the death of their protector King James, however, the College at once claimed before the Privy Council the right to control "those lowly dispensers of drugs and boluses." But the newly incorporated apothecaries had stout hearts and nursed ambitions of their own; they boldly opposed the claims of the College—and won—but not before the physicians had obtained a draft Order in Council which ordained that "No Apothecary was to sell any poyson drugges or medicines" except on their prescription. The indignant apothecaries suggested with some justice that if to prevent danger they might not sell drugs, then cutlers should be forbidden to sell knives and the gun-makers pistols. This argument impressed the Attorney-General, and the matter was dropped.

Evolution of the General Practitioner

London in 1617 was still a mediaeval city in appearance, confined within walls, with dark narrow streets bordered by rickety half-timbered homes in which the merchants lived above their businesses. The chief highway was the river, and the whole was dominated by the towering Gothic pile of St. Paul's. Its chief playwright was William Shakespeare. The apothecaries mostly congregated around "sweet-smelling" Bucklebury, where they stored and retailed their drugs and other medicaments.

At the time the medical profession consisted of physicians, who were learned, unpractical, scarce, and expensive; surgeons, who were unlettered craftsmen of lowly status; and quacks—some very picturesque characters, but undoubtedly dangerous. Until the dissolution of the monasteries the monks had also occupied an important role in the care of the sick poor. There were no general practitioners or family doctors.

It seems inevitable that apothecaries should have often included a little free advice with the package of drugs, and so in time the indigent sick came to look upon the apothecaries as their general medical advisers and attendants. Indeed, this position seems to have been forced upon them both by the large numbers of sufferers "unable or unwilling to fee a physician" who sought their aid, as well as the exodus of most physicians from the city during the frequent epidemics of the plague. They recognized that they had no right to claim a fee for such advice, but found adequate remuneration through their charges for dispensing the remedies. At a later stage, particularly in country districts, the apothecary would leave his shop and visit such clients at their homes, so becoming in fact their general medical attendant.

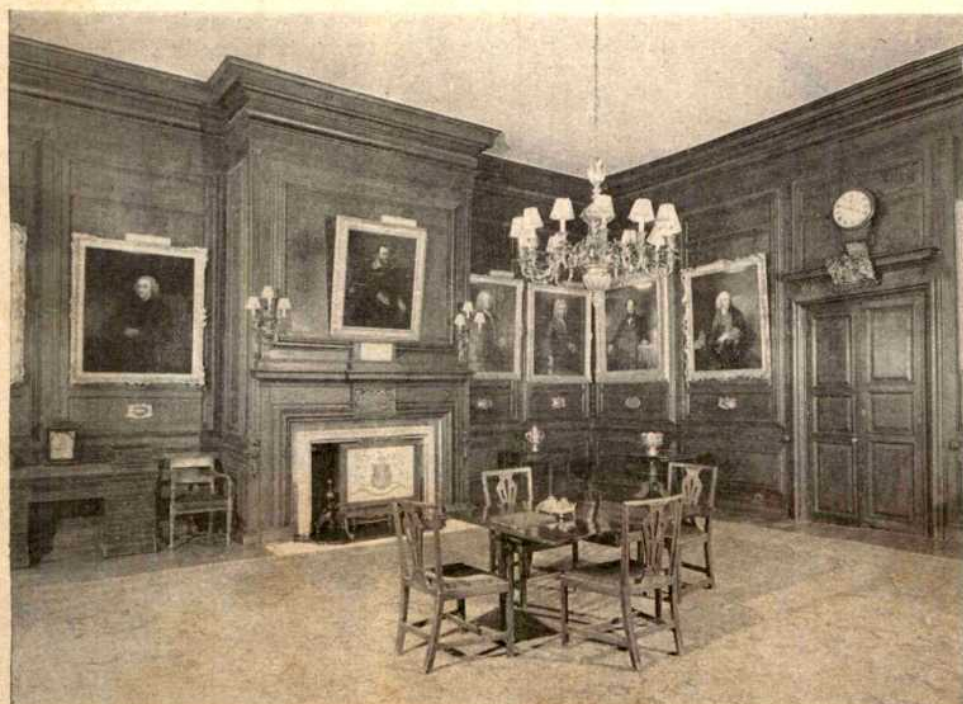
Such behaviour infringed the College of Physicians' legal monopoly of medical practice within the city and for seven

THE WORSHIPFUL SOCIETY OF APOTHECARIES

W. S. C. Copeman

The Great Hall. This is now the oldest surviving hall in the City of London. The 24-branch candelabrum was presented by Sir Benjamin Rawling, who was Master of the Society in 1736. The great chest was given to the Society in 1668 by Sir William Clarke.

The Entry to the Hall, in Black Friars Lane. This was built in 1786, and opens into a paved court.



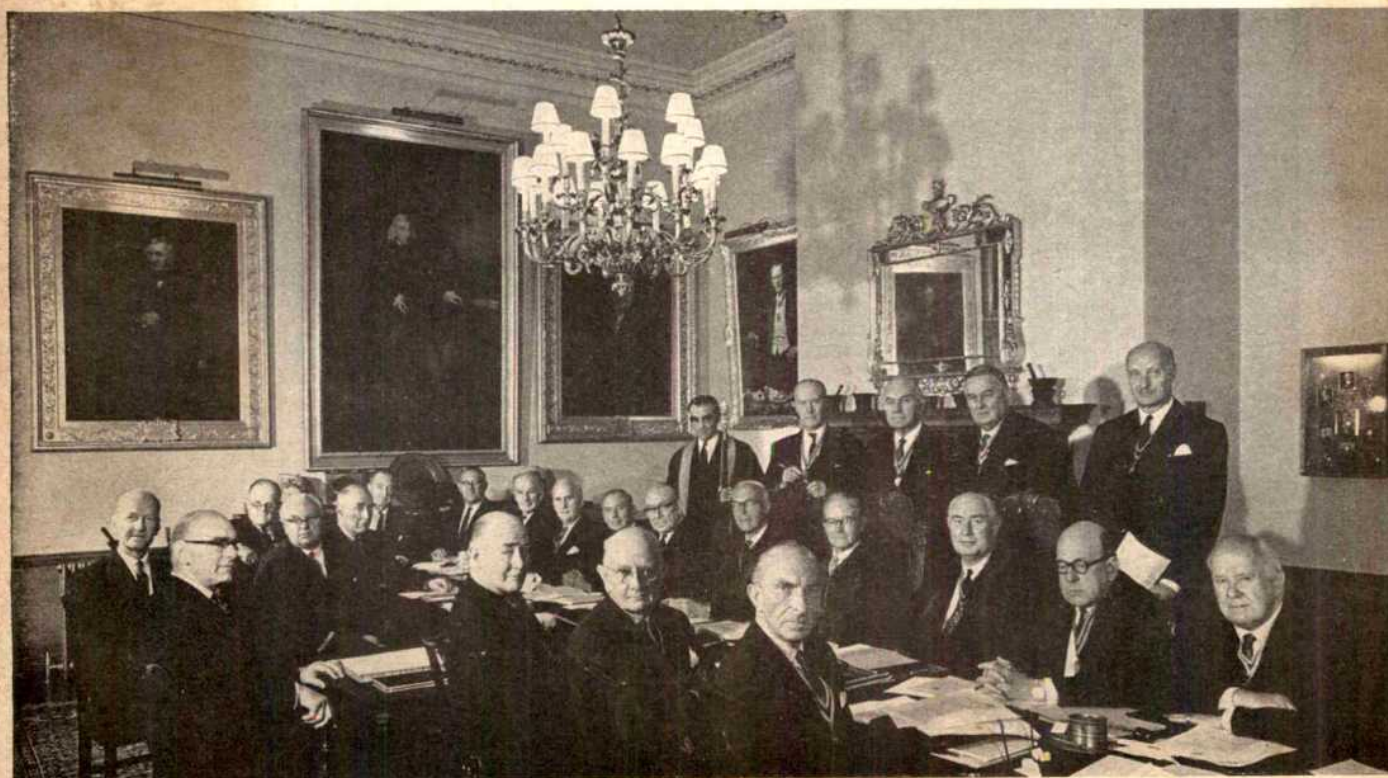
The Court Room. This was completely panelled in oak in 1672 and it contains portraits of previous officers of the Society, among them of Gideon De Laune — the reputed founder of the Society—and of John Hunter, by Reynolds.

W. S. C. COPEMAN: THE WORSHIPFUL SOCIETY OF APOTHECARIES

The Parlour. This contains a pine mantel by William Kent, by which a wartime bomb fell but failed to explode.



The Court in Session. Members of Court (from left to right) Mr. Ian M. Jackson, Mr. Ernest Busby (clerk), Sir Ronald Bodley Scott, Dr. R. Donald Teare, Dr. E. Grey-Turner, Dr. G. B. Mitchell-Heggs, Sir Brian Windeyer, Sir Arthur Porritt, Mr. Alistair L. Gunn, Sir John Richardson, Dr. Redvers N. Ironside, Dr. Peter Bishop, The Bedel, Dr. Hugh M. Sinclair (Senior Warden), Dr. Macdonald Critchley, Mr. T. Keith Lyle (foreground), Mr. Harold C. Edwards (Master), Dr. R. R. Trail, Mr. Henry R. Thompson (Junior Warden), Mr. A. M. A. Moore, Sir Charles Dodds, Dr. W. S. C. Copeman, and Sir Cecil Wakeley.



miles around, and was punishable by imprisonment on the orders of its president in any prison other than the Tower of London, and confiscation of their stock. Thus the issue between the College and the company crystallized into the latter's right to practise (without direct fee) as well as dispense.

The dispute continued with increasing acrimony throughout the years of the Civil War, during which the city influence of the apothecaries increased as the College followed the King to Oxford. Both bodies lost their premises during the Great Fire of London, but the apothecaries, being on the spot, were able to rebuild theirs in its present form on the site of the old Black Friars' Monastery. As they increased in status and wealth they added to their possessions a State barge with 18 lusty watermen, and in 1673, as London expanded and it became more difficult to find the wild herbs and roots which were their stock-in-trade, they acquired a physic garden of four and a half acres on the river bank at Chelsea from Lord Cheyne, where these could be grown and the instruction of their apprentices carried out. In the early eighteenth century the company's finances declined, and but for the generosity of Sir Hans Sloane the garden would have had to be sold. Many of those whose names feature on the roll of fame for botany and medicine received their training in this garden, which still stands where it did and is a focal point of modern botanical and agricultural research under the auspices of London University.

The Rose Case

In 1704 the final clash between the College and the apothecaries took place. William Rose, a liveryman of the company, was sued as a test case by the College for treating a patient without the intermediary of a physician, and the case was decided against him in the Queen's Bench Division. The House of Lords, however, reversed this decision on appeal, holding that despite the existing law it was contrary to custom and against the public interest to prevent the giving of advice and treatment by members of the Apothecaries' Company. Thus the age-long monopoly of the College was broken. Henceforward the apprentice who had satisfied his examiners at Apothecaries' Hall and taken up the Freedom of the City was free to practise, without fear of prosecution, as well as compound his medicines, although he had another century to wait before he was allowed to charge for his advice as well as his remedies. It was in this way that the British dispensing doctor arose, as did the public's continuing expectation of a routine bottle of medicine when they visit their general practitioner. It was not until the Medical Act of 1858, which established the General Medical Council, that the practice of charging a fee for advice or visiting only was finally legalized and the modern family doctor emerged.

Some apothecaries did not aspire to become medical practitioners, however, and such men continued in pharmaceutical business, some of which prospered greatly and grew into firms whose names are today household words. Others broke away and in 1841 formed the Pharmaceutical Society. Still others answered the call of science and followed the academic path.

Reform

Following the political unrest engendered throughout Europe by the French Revolution the desire for "reform" spread rapidly, and the medical fraternity became involved. The chief need was thought to be for the institution of more systematic and practical teaching which would culminate in a standardized examination system. These matters were long debated in Parliament but found little support from the two Royal Colleges.

It was therefore a surprise to the Society of Apothecaries, who had been forward in this field, when the choice fell upon them to carry through these reforms. By the great Apothecaries' Act of 1815 the Society suddenly found itself in control of all general medical practice throughout England and Wales, and in the recent words of Sir Zachary Cope: "There are few in this generation who realize what an important part the Society of Apothecaries has taken in the development of medical education in this country, and in creating that type of modern practice which is a cause for legitimate pride."

The lives of Englishmen have always been ruled more by custom than logic, and the medical profession, as Underwood has pointed out, has developed in a way unlike anywhere else in Europe. For a city mercantile company to have been entrusted by the State with the control of a learned profession, as were the apothecaries by the Act of 1815, might seem inconceivable. The task was, however, willingly undertaken, and, possibly somewhat to their own surprise, brilliantly carried through. Thus the erstwhile apprentices of a city trade-guild rose from the humble status of mere minor shopkeepers and developed in the course of three centuries to that professional status which had always been their ambition, and by the end of the Victorian era they could show clear title to rank as members of a learned and respected profession, as they do today.

Present and Future

The Society maintains the mediaeval domestic hierarchy common to all city companies. The apprentice becomes in due course a yeoman (or journeyman), and later, if approved, a liveryman, and so entitled to the Freedom of the City and all those privileges which accompany such status. The governing body is the Court, which consists of 24 senior members, headed by the master and his two wardens.

A monthly examination is held for candidates for the Society's medical qualifying diploma (L.M.S.S.A.); and postgraduate diplomas are also awarded in midwifery, industrial health, and medical jurisprudence. Its certificate in dispensing is also eagerly sought by hospital and commercial technicians. The study of history is fostered by the Faculty of the History of Medicine and Pharmacy, which like the parent Society has a number of endowed lectureships, including that named after Gideon De Laune, its founder.

The continuing interest of the Society in medical education—a subject in which it pioneered—was recognized by the recent request for two memoranda by the Royal Commission on Medical Education, which is at present sitting.

As to the future, the Society looks forward confident that it will continue to play an important part in the continuing development of all branches of our profession. It is thus perhaps fitting to end this brief epitome of the Society's long and eventful period of evolution with the pious aspiration of its members as expressed in the Master's Toast given after every meal: "The Worshipful Society of Apothecaries of London, May it flourish, root and branch, giving help and health to all—till Time ceases."

The illustrations are taken from the *History of the Worshipful Society of Apothecaries*, by Dr. W. S. C. Copeman, by kind permission of the Pergamon Press. This book was published on 30 November, price 63s.

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GENERAL PRACTICE OBSERVED

An Appointment System Service for General Practitioners:
Its Growth and Present Usage

BRUCE CARDEW, L.M.S.S.A.

Brit. med. J., 1967, 4, 542-543

"An appointment system has completely altered our lives; it has brought order out of chaos and we can never cease to wonder how we endured our old ways so long."

This paper provides an analysis of the use to which a particular appointment system service given to N.H.S. general practitioners has been put during the past seven years. The launching of the service was undertaken not with the idea that it would provide subsequent material for research but solely to help general practitioners. Nevertheless, this retrospective approach does provide information which will, I believe, be of interest to those concerned with the changing pattern of general practice in this country.

History

In 1959, when I was editor of the *Medical World*, it was thought desirable by my colleagues that guidance should be offered to general practitioners who wished to introduce an appointment system into their practices. Since little information had been published on the subject, we had to look to the experience gained by individual practitioners who had themselves run appointment systems over a period of years. Seven doctors were approached to form a committee to pool their experience and draft a handbook of advice. It was later agreed to make a short discussion film, "Appointment Systems in General Practice," based on the recommendations in the handbook.* The cost of making the film and printing the handbook was generously borne by Messrs. Lloyd-Hamoll Ltd., who decided also to provide any interested general practitioners with an appointment diary and a continuing supply of sheets. This service is referred to in the article as the A.S. Service.

At first the demand for the A.S. Service was small. It grew gradually until a fresh impetus was given by the introduction of the new method of payment for general practitioners under which a substantial part of the cost of employing receptionists

TABLE I.—Approximate Number of G.P.s Using the A.S. Service at End of Each Year

1961	1962	1963	1964	1965	1966	1967 Oct.
250	700	1,500	2,300	3,200	4,500	7,840

was met by direct repayment. Since the presence of a receptionist is a virtual sine qua non in the introduction of an appointment system the recent increased demand is readily explained. The rate of growth of the A.S. Service is shown in Table I.

Evaluation of the A.S. Service

Late in 1966, when it became clear that a large number of practices were already using the service and that the demand

was likely to increase, I felt that the time had come to reappraise the advice offered in the handbook in the light of the practical experience gained by thousands of doctors who had used the recommended system. A questionnaire was sent to all continuing users asking for suggestions for modification, however minor.

The response rate was 85%, and the forms were sent to the Gallup Poll for analysis. The publication here of the results would not be of general interest, but I can say that 87% expressed positive or tacit approval of the existing system. The suggestions for modification mostly related to the time allowed on the appointment sheets for seeing a patient. Some wanted a longer period, others a shorter one. No group represented more than 1% of the total number questioned. The conclusion which emerged was that the A.S. Service met to a very large extent the requirements of the various types of practice in which it was used. I have no doubt, however, that some doctors, having used the service and having for some reason found that it was unsatisfactory, abandoned it and introduced some variation more to their liking. These doctors would not have received our questionnaire, and their views would not be revealed in our records.

How Many Practices Run An Appointment System?

In Table II are set out the number of doctors in each English county and in Scotland, Wales, and Northern Ireland using the A.S. Service. In the left-hand column is included for comparison the number of N.H.S. general practitioners practising mainly in the area concerned. These numbers are not identical with those shown on local executive council lists, because doctors often practise in several adjacent areas and their names appear on two or more lists. The users of the A.S. Service are divided into those providing a full appointment system to their patients and those providing a partial system. This is clearly an arbitrary distinction and needs explanation. It was decided to call any system "full" where over 80% of surgery consultation periods were available for seeing patients by appointment. Where the percentage was less than 80% doctors were asked to estimate the percentage of patients seen by appointment. An analysis of their replies is set out in Table III. Many expressed their intention of extending the use of the system as soon as circumstances permitted.

Table II also gives the relevant percentage figures of use of the A.S. Service in each county and region.

Discussion

Table I shows that there has been a large increase in the number of appointment systems introduced by N.H.S. general practitioners in recent years. The figures given here relate solely to one particular service and should not be equated with the total use of appointment systems in the country. Unfortunately there are no official sources of information available to complete the picture. Evidently there must be many

* A *Medical World* film distributed by the B.M.A. film library and by Sound Services Ltd.

practices running appointment systems of their own design which are not taken into account in this article.

Using the figures given in Table II as minimum ones and allowing for some hundred additional practices using other systems, one can say with certainty that *a third of all N.H.S. practices are offering a complete appointment system to their patients*. This means, in effect, that at least 17 million patients can now see their family doctors by appointment.

TABLE II.—General Practitioners Using the Appointment System Service as at 31 August 1967

Standard Region	No. of N.H.S. G.P.s	Doctors Using Full Appt. Syst.		Doctors Using Partial Appt. Syst.	Total Users	% of Total Users to N.H.S. G.P.s
		No.	%			
1 and 2. Northern:						
Cumberland ..	129	70	54	5	75	58
Durham ..	525	248	47	14	262	50
Northumberland ..	327	155	47	20	175	54
Westmorland ..	31	12	39	2	14	45
Yorkshire (whole) ..	1,828	411	22	59	470	26
	2,840	896	32	100	996	35
3. North-Western:						
Cheshire ..	587	174	30	25	199	34
Derbyshire (whole) ..	250	73	29	7	80	32
Lancashire ..	1,967	458	23	63	521	27
	2,804	705	25	95	800	28
4. North Midland*:						
Leicestershire ..	242	80	33	7	87	36
Lincolnshire (whole) ..	304	65	21	7	72	24
Northamptonshire ..	150	59	39	1	60	40
Notts ..	339	187	55	18	205	60
Rutland ..	10	—	—	—	—	0
	1,045	391	37	33	424	38
5. Midland:						
Hereford ..	49	27	55	4	31	63
Shropshire ..	115	43	37	1	44	38
Staffordshire ..	566	196	35	20	216	38
Warwick ..	786	258	33	32	290	37
Worcestershire ..	196	100	51	—	100	51
	1,712	624	36	57	681	39
6. Eastern:						
Beds ..	144	75	52	1	76	53
Cambs† ..	112	38	34	3	41	37
Essex (whole) ..	660	259	39	24	283	43
Herts (whole) ..	364	133	38	26	159	44
Huntingdon ..	25	8	32	5	13	52
Norfolk ..	238	61	26	18	79	33
Suffolk ..	195	82	42	15	97	50
	1,738	656	38	92	748	43
7. London and S.E.‡:						
Kent ..	704	260	38	31	291	41
London (whole) ..	2,198	384	17	52	436	20
Middlesex ..	458	54	12	12	66	14
Surrey ..	653	242	38	19	261	40
Sussex (whole) ..	510	148	29	17	165	32
	4,523	1,088	24	131	1,219	27
8. Southern§:						
Berks ..	234	105	45	1	106	45
Bucks ..	197	83	42	4	87	44
Hants ..	623	285	46	23	308	49
Oxon ..	149	73	49	6	79	53
	1,203	546	45	34	580	48
9. South-western:						
Cornwall ..	169	25	15	4	29	17
Devon ..	391	100	26	6	106	27
Dorset (whole) ..	163	38	23	—	38	23
Gloucs ..	452	158	35	17	175	39
Somerset ..	239	96	40	17	113	47
Wilts ..	159	58	38	5	63	40
	1,573	475	30	49	524	34
England Total..	17,438	5,381	31	591	5,972	34
Wales (whole) ..	1,129	253	22	38	291	26
Scotland (whole) ..	2,502	730	29	88	818	33
N. Ireland ..	714	158	22	22	180	25
Channel Islands ..	139	12	9	—	12	9
Grand total (U.K.) ..	21,922	6,534	30	739	7,273	33

* Excluding part of Derbyshire included in Region 3. Peterborough is included in Northants.

† Including Isle of Ely.

‡ Excluding parts of Essex and Herts already in Region 6.

§ Excluding part of Dorset and the Isle of Wight included in Region 9.

The recent striking increase in the introduction of appointment systems (2,000 additional doctors have adopted the A.S. Service during the last nine months) suggests that within a few years the great majority of general practitioners will see all patients by appointment.

The geographical distribution of the use of appointment systems is shown in Table II, and raises questions of interest. Why should Cumberland and Westmorland show a high rate of usage, whereas Cornwall, Devon, and Dorset show a low rate? Why are the figures for London and Middlesex disproportionately low, whereas those for the adjacent counties of Surrey, Essex, and Herts are above the average? At first sight one might assume that factors associated with urban and rural practices could explain the differences, but an analysis of the figures by county does not bear out such an assumption. Fortuitous circumstances may explain some of the differences. If one or more go-ahead practitioners in an area introduce an

TABLE III.—Percentage of Patients Seen by Appointment in Practices Running a Partial Appointment System

	5-10%	11-25%	26-45%	46-65%	65-79%	Total
No. of doctors ..	69	165	193	114	57	598*
% of total ..	12	28	32	19	9	100

* This figure is not the same as that shown in Table II because some doctors did not reply to the question.

appointment system the tendency may well be for others to follow suit. In other areas no such stimulus may be present. One thing is quite certain—appointment systems can be successfully run in the slums of the great towns, in rich residential areas, and in remote country regions.

This article makes no attempt to describe the system recommended by the Appointment System Committee. Neither does it seek to evaluate the benefits of an appointment system to doctors or patients. This task has been undertaken by the Unit of Biometry of Oxford University in their report, *Appointment Systems in General Practice*, recently published by the Nuffield Provincial Hospitals Trust. I commend this report to anyone interested in the organization of general practice. Nevertheless, I must also mention the many hundreds of letters of appreciation sent by users of the A.S. Service. One of the recurring phrases which appear in these letters is reproduced at the head of this article.

My personal view is that an appointment system, after a few months, almost invariably improves the doctor-patient relationship, helps partners to work more closely together, and establishes a framework of orderly practice in which other new developments may take place.

Summary

The problems of appointment systems in general practice were considered by a committee of the *Medical World*, and a system was devised which formed the subject of a handbook.

A service based on the recommendations in the handbook was offered to N.H.S. general practitioners free of charge by Messrs. Lloyd-Hamoll Ltd. The growth of the service and the extent of its present usage are described. Some of the associated problems are discussed.

I wish to thank Drs. J. T. Baldwin (Penicuik), Dr. D. Dean (Birmingham), Dr. A. Elliott (Ilford), Dr. C. K. Elliott (Wisbech), Dr. H. C. Faulkner (London), Dr. H. N. Levitt (London), and Dr. A. S. Playfair (Cambridge), who designed the original handbook on which the appointment system service was based. I believe that the widespread use of the service and the fact that it has not required modification over a period of seven years is clear evidence of the soundness of the advice they offered. The profession owes them a debt of gratitude.

An Appointment System in a Practice with Immigrant Patients

STUART CARNE,* M.B., M.R.C.G.P., D.C.H.

Brit. med. J., 1967, 4, 544-546

In the group practice of which I am a partner patients have been seen by appointment for over six years. We adopted an appointment system when the two previously separate parts of the practice joined on 1 January 1962. It was essential to do something of this nature because of the shortage of space in the waiting-room. The premises now used by the group were those originally occupied by a single-handed general practitioner with a list of 1,600 patients. The space available was barely adequate for his needs. We were able to convert two rooms into extra consulting-rooms, so that at any one time three doctors can now consult, but there was no one room bigger than that used as the waiting-room. Unless we had two waiting-spaces, which would have been difficult to administer, we had no alternative but to restrict the number of patients waiting to be seen at any one time. In that the waiting-room, which has seats for only 12 people, has rarely been full to capacity, and patients no longer have to wait in the street outside; and in spite of there being three doctors, each seeing up to 12 patients an hour; and notwithstanding the fact that some patients (children always) come accompanied by at least one relative, the appointment system has worked.

I have described elsewhere the mechanics of our system of arranging appointments (Carne, 1963). We in our group believe that patients should, whenever possible, have choice of doctor. Even more important, we believe that one doctor should normally treat every member of each family. Most important of all, we aim to arrange our bookings so that each illness episode is dealt with by the same G.P. To assist the receptionists (we need two working full-time on a shift system plus a full-time secretary) we have colour-coded our appointment cards, and we colour-code the family medical record envelopes where one member of the group deals with their personal problems.

A high proportion of the patients in the practice are immigrants (Carne, 1967). Some of the social difficulties, with particular reference to the poverty of their housing, have been described elsewhere (Carne, 1962). It was therefore thought worth while to study the utilization of an appointment system by such patients.

Method

From time to time we have attached to the practice pupils from West London College who are taking the medical secretary's course with the view of obtaining the diploma of the Association of Medical Secretaries. They come in turn for a week of practical experience. For one session during their week the girls from the 1966-7 course were asked to keep a note of the time of arrival, the time of the appointment, and the time the patient actually went into the doctor's consulting-room. One record card was kept for each consultation. As most patients had booked an appointment, and as the medical record envelopes for these patients together with the relevant sheet from the appointment book was available the day before the session, the girls were able to set up most of their study cards in advance. On each card they also put the code number we use for the practice, which enables us to identify the patient's

age, sex, and race.¹ At the end of the study the age, sex, and race groups were sorted by hand. It was then an easy task to determine how early or how late a patient arrived in relation to the time of his appointment (arrival time : appointment time) and how long each patient had to wait (arrival time : time of actual consultation).

Findings

Altogether there were records of 950 patients who had made appointments and were seen. In addition, there were 100 patients who had made appointments and failed to attend. There were also 98 patients who had not made an appointment but wished to see the doctor at the time they visited the surgery. It was (and still is) our practice to offer such patients an appointment either later at that consulting session or at another session. If the patients express a preference to be seen then and there they are invited to wait until there is a gap. If in the opinion of the receptionist they look ill or she thinks it unwise to keep them waiting—for example, some mothers still bring children with a rash to the surgery rather than call for a visit (Carne, 1967)—she will send them through to a doctor ahead of waiting patients who have an appointment. In the rare event of an emergency—for example, a child carried in from a street accident outside—she will even “buzz” one doctor on the intercom and ask him to clear his surgery at once. We rely very heavily on our receptionists for the success of the appointment system.

Arrival and Waiting Times

In Table I are given the waiting and arrival times for all the patients who attended by appointment, and the proportion for the different age, sex, and race groups.

There is hardly any difference in the waiting or arrival time between men and women.

Of all the patients who were seen by appointment 13.8% walked straight through to their doctor on arrival; the doctor was waiting for them. This is because we have always aimed to avoid overbooking. We believe that in general practice there cannot be a predetermined end to an ordinary consulting session. If 85 instead of the usual 75 patients need to be seen (or think they need to be seen) at one session then that session will take that much longer. What is possible is to anticipate difficulties. For example, reappointments are kept to a minimum on Monday mornings; none at all are made for the individual doctor at any session if he wishes to finish early—for example, to go to the theatre. The effect of this is to even out some of the humps of an ordinary practice load, but not all. Because we do this, and because so many appointments are missed, there are gaps into which extra patients can be fitted and there are many times when the doctor has to wait for his

¹ The code used is simple: the last two numbers of the year of birth; 0 and 1 for male and female respectively; and 0-6 to describe the various race groups—for example, 46.1.3 refers to a patient born in 1946, female, and West Indian.

* General Practitioner, London W.12.

TABLE I.—Waiting and Arrival Times (Expressed as Percentages)

	All Patients	Sex		Race*				Age				
		Male	Female	English	Irish	West Indian	West African	0-4	5-14	15-44	45-64	65+
Waiting time:												
Over 25 min.	1.8	0	1.6	1.6	6.1	0	0	6.1	0	2.2	0	5.3
16-25 " " " " " "	8.9	10.2	8.0	10.4	6.1	2.9	12	9.1	5.3	6.7	10.1	10.5
6-15 " " " " " "	41.7	44.9	39.5	38.3	44.9	38.3	42	27.3	39.5	50.7	40.7	26.3
1-5 " " " " " "	33.7	29.1	36.5	39.0	24.5	38.3	33	33.3	39.5	29.1	37.9	42.1
0 " " " " " "	13.8	15.8	12.5	10.9	18.4	20.6	12	24.2	15.8	11.9	11.4	15.8
No. of consultations . .	950	481	469	481	227	117	24	115	86	493	172	84
Arrival time:												
Over 25 min. early . .	2.5	3.1	2.2	1.9	4.1	3.0	0	6.1	0	2.2	1.3	5.3
16-25 " " " " " "	7.1	6.3	7.6	4.8	6.1	9.1	4	3.0	5.3	5.9	4.6	15.8
6-15 " " " " " "	25.0	26.0	24.6	24.6	20.4	24.2	21	21.2	18.4	21.6	25.2	28.9
0-5 " " " " " "	37.6	40.9	35.0	40.6	36.7	27.2	17	39.4	36.8	38.8	45.6	34.2
1-4 " " " " " "	9.2	10.2	8.6	7.2	16.3	0	21	9.1	2.6	9.0	11.4	5.3
5-14 " " " " " "	13.2	9.4	15.7	17.4	12.2	15.1	25	18.2	26.3	15.7	6.3	2.6
15-24 " " " " " "	4.3	2.4	5.4	2.9	4.1	18.2	12	3.0	10.5	3.7	1.3	2.6
25 or more min. late . .	0.9	1.6	0.6	0.5	0	3.0	0	0	0	2.2	1.3	5.3

* Excluding 101 patients who did not come into the four groups listed.

next patient. We have discussed this among ourselves. We would rather have these gaps than revert to the pressures of a crowded waiting-room.

There is little difference between the English and Irish patients so far as waiting and arrival times are concerned; the English are a little bit better at arriving promptly. The West Indian patients, however, are not as good timekeepers. A larger proportion come much too early or come late for their appointment. On the other hand, for reasons discussed later, they tend to spend less time in the waiting-room. There were only 24 booked consultations with West African patients recorded for this study, and this number is too small for any valid conclusions to be drawn. If the sample is in any way representative the West Africans are the worst timekeepers of all.

Though there are differences in the waiting times of the patients of varying ages, none of these differences are significant. More children tend to arrive late than adults. The best timekeepers of all are the elderly. Only 20% of the 45-64's come late and only 15% of the over 65's. On the other hand, it should be noted that there are very few immigrants in these two older age groups (Carne, 1967).

The mean waiting time for all the patients is six to eight minutes. As we book two patients every 10 minutes, and are therefore expecting one to wait five minutes, this is about as optimal a degree of efficiency as we can hope for, though we would like to see the extremes reduced so far as is possible.

Fewer of our patients are punctual than the patients described by Bevan and Draper (1967) for the 10 practices they studied. Our practice has had an appointment system five years longer than any of those described in that study. On the other hand, far fewer of our patients wait more than 30 minutes, so that perhaps we have had time to get ourselves better organized. The waiting time is less than that found by Fry *et al.* (1963).

What are the patient's best chances of reducing his waiting time? Table II shows the waiting time in relation to the arrival time, from which it can be seen that the optimal time of arrival appears to be 15 to 24 minutes late; 4.3% of all the patients chose such a time of arrival. It is certain that if the other patients also arrived as late the system would collapse. In

TABLE II.—Time Spent Waiting by Patients in Relation to Time They Arrived Before or After the Scheduled Times of Appointment (Expressed as a Percentage)

Waiting Time	Arrival Time (minutes)							
	Early				Late			
	Over 25	16-25	6-15	0-5	1-4	5-14	15-24	Over 25
Over 25 min	25	8.7	1.2	0.8	0	0	0	0
16-25 " "	25	4.3	14.6	9.0	3.3	4.7	0	0
6-15 " "	37.5	43.5	37.8	40.7	46.7	48.8	28.6	100
1-5 " "	12.5	21.7	39.0	33.3	36.7	32.6	42.9	0
0 " "	0	21.7	7.3	16.3	13.3	14.0	28.9	0

fact 72.2% of the patients arrived early for their appointment, 2.5% coming 25 minutes or more too early. Bevan and Draper (1967) reckon that patients who arrive between five minutes early and four minutes late are punctual. If we extend this licence to our patients then 81.4% came on time or early.

TABLE III.—Patients Seen Without an Appointment (Expressed as Percentages of the Total Consultations Booked and Unbooked)

Total	Sex	Race*	Age Group
98 (9.4%)	Male 47 (8.9%) Female 51 (9.8%)	English 45 (8.6%) Irish 20 (8.1%) West Indian 15 (11.4%) West African 9 (27.3%)	0-4 21 (15.4%) 5-14 5 (3.4%) 15-44 50 (9.4%) 45-64 17 (9.0%) 65+ 5 (5.5%)

* Excluding nine patients who did not come into the four groups listed.

Unkept Appointments

It is interesting that the number of patients who did not keep a booked appointment is almost the same as the number who came to the surgery without an appointment (Tables III and IV), and that by and large the age and race distribution of these two groups is identical. Our senior receptionist is of the opinion that in the main it is the same patients who miss booked appointments who, when they do come, do so without at first booking. The worst offenders are children under school age and "workers" (those aged 15-44). West Indian and West African patients also seem to find it as difficult to keep appointments as they do to arrive on time. Many explanations could be offered for these differences; each explanation might be valid.

TABLE IV.—Patients Who Did Not Keep Their Appointment (Expressed as Percentages of Those Who Booked an Appointment, Whether or Not They Kept Their Appointment)

Total	Sex	Race*	Age Group
100 (9.5%)	Male 42 (8.0%) Female 58 (11.0%)	English 48 (9.1%) Irish 19 (7.7%) West Indian 20 (14.6%) West African 5 (27.3%)	0-4 22 (16.1%) 5-14 3 (3.4%) 15-44 52 (9.5%) 45-64 16 (8.5%) 65+ 7 (7.7%)

* Excluding eight patients who did not come into the four groups listed.

We also asked 240 of our patients whether or not they wanted us to continue to work an appointment system: 84.2% said they wanted us to continue; 7.7% said they would prefer us not to make appointments; 8.1% said they did not mind what we did. These proportions are remarkably similar to those found by my brother in his practice (Carne and Dell, 1965), and by others (Fry *et al.*, 1963; Dean *et al.*, 1965; Stevenson, 1966).

The sample was not selected for age, sex, or race. It was merely a selection of patients living in the area. Those who did not like making appointments to see their doctor have had

five years to change to another practice where patients can wait their turn during fixed surgery hours.

Conclusion

Several studies, already referred to, have shown that it is possible to organize an appointment system within a National Health Service general practice even where the average time for a consultation is only five minutes. In this study we have shown that the system also works well in a practice with a large proportion of immigrant patients.

The West Indian and West African immigrants are not as good timekeepers as the English and Irish patients, but their lack of punctuality is not sufficiently great to upset the smooth running of the surgery sessions.

It is our belief that the ability to see patients by appointment has been a major benefit to both patients and us. In addition to the advantages referred to by other authors (summarized by

Bevan and Draper, 1967) we are of the opinion that the making of an appointment gives "status" to the consultation. It is the aim of a supermarket to encourage "impulse buying." It is debatable whether "impulse consulting" is in the interest of anyone, notwithstanding the patients who find it difficult to tell the doctor all their problems first time.

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CONFERENCES AND MEETINGS

Medicine, Science, and Humanity—Annual Meeting of R.C.G.P.

[FROM A SPECIAL CORRESPONDENT]

The Fifteenth Annual General Meeting of the Royal College of General Practitioners was held in London on 18 November. The Chairman of the Council, Dr. H. N. LEVITT, said that in the year in which the College had been granted the Royal Prefix it was for the first time financially solvent. Fifteen years ago it had set out to convince other doctors, especially those in hospital and in the universities, that the general practitioner had a significant role in the future of medicine. Its views were now accepted, and general practice was recognized as a discipline in its own right. The College's next task was to establish a form of education which would raise the quality and realize the potentialities of general practice.

James Mackenzie Lecture

Giving the James Mackenzie lecture, "Lucerna Pedibus Meis," Dr. RONALD GIBSON (Winchester) emphasized two facts. Firstly, today—as in Mackenzie's time—what mattered most was the family unit. Secondly, throughout the ages the medical profession had a responsibility to society, which was becoming increasingly important today as the influence of the Church and authority declined. He asked whether anything was more likely to disturb family relationships and destroy attempts at collective responsibility than paying adolescents as much as their parents might earn. Fortunately most adolescents emerged unscathed and became useful members of society.

Where had society been found wanting? People had not yet accepted that the failings and shortcomings of the adolescent were those of society as a whole. If people were content to perpetuate this second-rate society they were too insecure and too unstable to benefit fully from a Welfare State. The family was the medium on which the Welfare State could grow and adolescents could thrive, and the State should have a supporting and secondary role.

Problems of Today

On 19 November the College held a symposium on "Combined Operations—Medicine, Science, and Humanity." Opening the symposium, Professor Sir EDWARD WAYNE (Glasgow) said that though we had eliminated the infectious diseases we had other problems to face: the care of an ageing population; the implications of such advances as artificial insemination; and the impact of automation. Scientific advances made the ability to deal sympathetically with human beings more important than ever before.

Professor JOHN ANDERSON (London) spoke about the changing relationship between medicine and society. The medical relationship, traditionally based on a personal contract between patient and doctor, was changing. Individual health was linked to community health, and doctors had a duty to the community as well as to their patients. Doctors' basic premises needed rethinking in this context; the demand for medical care was unlimited and they must learn to reorganize their limited resources to meet it. Computers, by helping people to think logically, could help doctors to deal with the psychological and social pressures of society.

Medical education needed new attitudes if it was to produce doctors who remained students of medicine in a rapidly changing field. The domination of the basic science departments in medical schools must give way to the teaching of community care if future doctors were to combine basic clinical skills with ability to communicate with patients and retain flexible attitudes of mind. In King's College Hospital they were trying to establish general-practitioner teaching for medical students, but were hampered by lack of money. They encouraged students who could find a general practitioner willing to take them to spend a fortnight in general practice during their undergraduate course.

Research in General Practice

Professor Sir MAX ROSENHEIM, P.R.C.P. (London), speaking of the importance of research in general practice, said that it was needed not only to stimulate and improve morale but to cultivate the inquiring minds which good medical schools were producing. The Royal College of General Practitioners had played a very large part in encouraging research which was both operational—organization of general practice, functions of group practices and health centres, the work of the general practitioner—and true medical research, exemplified by the work of Pickles in epidemiology. Both kinds of research needed now a combined operation in which hospitals, local authorities, social workers, statisticians, and doctors all took part, in order to get significant results. More research was needed into psychiatric disorders in the community, and he cited the work of general practitioners such as C. A. H. Watts on depression, Max Clyne on school absenteeism, and Anthony Ryle on neurosis in ordinary families as forerunners. Clinical trials of new drugs were also needed in general practice, and they must be controlled by teams which included clinical pharmacologists and sociologists, if their findings were to be valid. Medical schools now acknowledged their responsibilities to the community. Educationally their task was to produce a general-purpose doctor, who after qualification would be vocationally trained for general practice as for other branches of medicine.

Professor WILFRID CARD (Glasgow), speaking on "Clinical Medicine in the Computer Age," said that the Hippocratic method was coming to an end; the private world of the individual doctor would be replaced by the public world of science. We needed a calculus of medicine, for, whereas the concept of disease was a useful fiction, a patient with signs and symptoms was the reality. A computer if fed the right data could make a diagnosis more accurately and

much more quickly than the most experienced specialist, but computers could not replace doctors because they were dependent on them to elicit the data from the patients. No computer could rival a human being in acuity of auditory and visual perception, and its effectiveness was particularly limited in certain specialties—for example, psychiatry. A computer could increase a doctor's reasoning power and his productivity but would not impair the doctor-patient relationship. The family doctor of the future could become a general medical consultant prompted by a hospital computer.

Medical Education

In the discussion Dr. P. S. BYRNE described the changes in medical education in some provincial medical schools as a breath of fresh air from red brick. In Manchester the general-practitioner teaching unit was the meeting-point of undergraduate, vocational, and in-service education. Dr. D. CROMBIE said that the first essential in medicine was to assess undifferentiated situations. Only a doctor could do that, and since the patient's fears, phobias, and past experience had to be taken into account a personal doctor could do it best. The computer was his tool.

Dr. JOHN FRY thought that research in general practice was being done on a shoe-string in an amateur and incoordinated way. It needed time, money, and team work with experts in other fields. This should be supplied by some agency, such as the Royal College of General Practitioners, the Medical Research Council, or academic departments of general practice in universities.

Dr. W. SIDEL, from the Department of Social Medicine in the Massachusetts General Hospital, said that a computer forced doctors to reorganize their thinking. He stressed the importance of gathering the data to feed it with and of knowing what kinds of data are important.

Medical Ethics

The Hon. Sir ROGER ORMROD, a High Court Judge who is also a doctor, spoke on medical ethics. The Western world was changing from the Christian to the humanistic ethic, and our attitudes to abortion, euthanasia, resuscitation of the aged, and transplantation of organs could no longer be determined by Christian dogma. Social and legal considerations played a part—as, for example, when an epileptic patient insisted on driving a motor vehicle: his doctor must choose between his duty as a doctor and as a citizen and could abdicate that duty to nobody. Renal dialysis posed other ethical problems. The number of kidney machines had to be rationed by available resources in money and personnel, and the responsibility of deciding which patients got them had to be borne by doctors alone; it could not be delegated to lay bodies.

Dr. P. W. BOTHWELL (Birmingham) spoke on "Social Responsibility as a Continuing Concept of Medical Care." Humanity would be best served by dealing medically with people before they got ill, but money and medical facilities were so limited that they had to be given to the already sick. Human beings were interdependent, yet each person wanted to survive and each patient to get better at the expense of the community. The development of spare-part surgery could absorb the whole budget of the N.H.S. if it were allowed to. Research was needed into which diseases could be prevented and how, but, since preventive medicine does not attract publicity or votes, it was difficult to persuade Governments to allocate a greater proportion of the Health Service budget to it.

Professor Sir DENIS HILL (London) discussed future trends. The gap between demand and supply of medical facilities would increase as a better-educated and older population expected more from the complex procedures which increasing specialization would bring. A reorganization of the profession was needed. The most important func-

tion of a doctor was to provide continuing and personal care to his patient and it had to be preserved. Undergraduate education, dominated by clinical scientists working within the framework of physical sciences, must give greater prominence to the teaching of the psychological and social sciences. The aims of medicine differed from the aims of science. The way that patients behave and feel was a dimension of medical aetiology, and a doctor must acquire skill in communicating with patients to elicit the facts about illness. An increasing amount of pure research could be done by non-medical scientists.

Medical education should aim to produce a basic doctor. The future general practitioner would be formed by a vocational training course tailored to his needs as a specialist in community medicine, and he would continue his education throughout his career. The divisive effect of the tripartite N.H.S. would diminish and general practitioners would become increasingly associated with hospitals, not as users of general practitioners' beds and pathological services but as part of a hospital-centred community-orientated health service. The family doctor would continue to look after his patient in hospital, though he would entrust the techniques of diagnosis and treatment to specialists. The mutual esteem and collaboration between general practitioner and consultant which existed before the National Health Service would be re-established. There was no place for medical practice in isolation. People were best served by a complex of general and specialist practice and this was already coming about. Automation would increase productivity and computers would help with diagnosis, but the understanding of the personality of the patient, his history and reactions, demanded human qualities, understanding, and tact. Academic departments of psychiatry and general practice were needed in all teaching centres to establish the importance of medicine as the study of man and disease rather than disease in man.

Applied Microbiology : Global Impacts

[FROM A SPECIAL CORRESPONDENT]

Applied microbiology can make an enormous contribution to the welfare and economy of developing nations. To focus attention on this contribution the second Conference on Global Impacts of Applied Microbiology was recently held at Addis Ababa. The main conference themes were the contribution of micro-organisms to the production of food by fermentation not only of sugars but of petroleum products, including methane; economic aspects of the control of tropical disease; international assistance programmes and training in microbiology; and water microbiology.

Regarding methane fermentation the conference concluded that the potential food production from this source was enormous, but that it would not be technically practicable for a decade. Nevertheless, an increase in basic research into these technical difficulties might shorten this period. The production of protein by yeast fermentation of sugar (particularly waste sugar) had, however, very great unrealized capacity at present. In the

Philippines, for example, 1,323,817,000 litres of coconut milk were said annually to be poured into rivers and streams. This occurred when copra and oil were made from coconuts, and the milk was unwanted even though such a quantity contained 25,000 tons of sugar. Moreover, its disposal into rivers and streams created a hygiene problem. In other regions where sugar was produced from cane much waste also occurred. In India, for example, it was calculated that waste sugar could annually produce 1,000,000 tons of yeast of 50% protein content. It was pointed out that the technique of continuous fermentation, in which the substrate was kept at a constant composition, had great potential for increasing the yield and constancy of the product in this field.

Economic Aspects

The economic aspects of microbiology also received attention. Biological surveillance was being established, particularly by the

World Health Organization in developing countries, and was enabling more effective and more economic health schemes to be put into operation. Such biological surveillance entailed, for example, the collection of sera for immunological assessment from persons of representative age groups over a period. Thus it had been shown that only specific age groups were likely to benefit by inoculation against various diseases—hence effort should be focused on these groups and not on the entire population.

The economic impact of many tropical diseases were discussed, particularly onchocerciasis and schistosomiasis, and for most control would, it was considered, cost considerably less than the losses brought about by the disease. The magnitude of the funds available for health control schemes, however, was agreed to bear no relation to the need for such schemes, and hence priorities had to be assigned among those that were feasible. The application of systems analysis and cybernetics in this field was becoming urgent.

Correspondence

Letters to the Editor should not exceed 500 words.

Pseudomonas Infection in Hospital

SIR,—I was glad to read the report by Dr. J. E. Tinne and colleagues (11 November, p. 313) and your leading article (same issue, p. 309) on this very serious problem. Somebody once said that the *Pseudomonas* is the nearest thing to spontaneous generation, and how right that is. The ever-present danger of *Ps. aeruginosa* cross-infection is most typically exemplified by the situation arising in cases of burns. In my experience hardly any burn case with over 30% of body surface affected and staying in hospital long enough will escape colonization or infection by *Ps. aeruginosa*.

I was pleased to see that the authors regard airborne *Pseudomonas* infection as relatively uncommon, as this accords with my findings. In the last six years, performing weekly slit-sampling of the air in the burns unit, only twice did we isolate a *Pseudomonas* from the air. Furthermore, eight plates were exposed for 24 hours round the clock, changing them every few hours, in a small cubicle occupied by a patient heavily infected with *Pseudomonas*. Not a single *Ps. aeruginosa* colony was found. *Pseudomonas* does not jump, it crawls; and it can be found first of all where there is moisture.

This brings me to the role of the drainage and plumbing system—that is, sinks, wash-basins, and traps. Your leading article is perhaps too cautious in saying that the evidence of infection from sinks and drains, etc., is not clearly established. In fact traps and wash-basins undoubtedly are a reservoir and can and do become a source of cross-infection. On a number of occasions patients' raw areas were colonized or infected by strains isolated from the traps of the wash-basins previous to the patient's admission. The strains belonged to rare pyocyanea groups (pyocin, serological, and phage-typing), and in one case the strain was a Rubrum type, which increased the chance of positive identification. A patient became infected with this strain after the ward had been closed, washed, and fumigated two weeks prior to his admission, and a thorough bacteriological check revealed the presence of the strain only in the wash-basin trap. Once the *Pseudomonas* is established in the trap it is extremely difficult to eliminate. Having had to cope with the *Pseudomonas* problem for many years, and having tried everything in the book and a great deal which is not, I am afraid I do not share the authors' faith in any particular type of disinfectant. After all, most disinfectants in 10% concentration are capable of killing *Pseudomonas* under suitable conditions given sufficient concentration and time, but if the killing time is longer than the drying-out or evaporation time of the disinfectant applied to the surface the whole exercise is pointless.¹

We have compared a number of disinfectants under conditions simulating ward procedures and

the differences in effectiveness of the most commonly used disinfectants, including the one mentioned by the authors, were only marginal. It is not so much the type of disinfectant which matters but the way it is used. There is still not much which can beat thorough cleaning, washing, and removal of plain dirt. It might also be worth while to recall the usual sequence of events leading to prolonged contamination of the drainage system. Perhaps the most common thing falling into a wash-basin is hair, which on reaching the trap curls up and stays there. After some time a hair "cushion" is formed and desquamated epithelium and all sorts of organic debris fill the interstices. *Pseudomonas*, which can grow and multiply at relatively lower temperature, thus enjoys excellent breeding conditions. Being a motile organism it wriggles its way upwards into the basin, finding en route an excellent hiding-place under the strainer, which is inaccessible to cleaning from below and flushing from above and which cannot be sterilized. Strains of *Ps. aeruginosa*, which could have come only from the trap, were frequently isolated from wash-basins. One must also consider the organisms in the numerous crevices on and around the plughole, shed by the contaminated hands of a previous user. Washing under running water does not eliminate the danger of contamination. This was also shown experimentally by seeding the trap and plughole area with a fluorescent dye and *Serratia marcescens*. Both the dye and the organism could be recovered from the hands, obviously due to back-splash. Taking the above into consideration, we have tried to modify the design of the wash-basins. Better access for cleaning, and flushing is provided by having the plughole area sloping and the strainer removable (therefore sterilizable). The overflow has of course been eliminated. Some wash-basins of this modified design were recently installed in the new maternity wing at this hospital.

Further, two potentially dangerous sources of cross-infection, thermometers¹ and flowers, should be mentioned. When contaminated, as is often the case, active dissemination occurs when the thermometer is shaken or the flowers removed and handled. I would like to make another point regarding the common fallacy perpetuated over the years, that *Pseudomonas* is sensitive to drying. In fact, on the floor of the ward, suspended in blood or exudate, as is usually the case, it will survive for 72 hours. Under experimental conditions in a fan-ventilated oven, temperatures of 65° C. for many hours and up to 95° C. for shorter periods of time failed to kill a broth suspension of *Pseudomonas* dried on to lino or a P.V.C. tile.

I am well aware that much of what I have said applies primarily to susceptible patient population at risk, but there are still quite a few misconceptions regarding *Pseudomonas* to which attention needs to be drawn.—I am, etc.,

Queen Mary's Hospital,
Rochampton,
London S.W.15.

J. KOHN.

REFERENCES

- ¹ Kohn, J., in *Research in Burns*, Trans. 2nd Int. Cong., 1966, p. 486-500, edited by A. B. Wallace and A. W. Wilkinson. Edinburgh.

SIR,—We read with great interest the report by Dr. J. E. Tinne and others (11 November, p. 313), regarding an outbreak of *Pseudomonas* sp. cross-infection in a cardiac surgery unit. They mentioned, among other things, the problem of *Pseudomonas* sp. contaminating the ventilator, in particular the humidifier.

At this hospital we found occasionally that the humidifier of the Engström ventilator was contaminated in this way, especially when a patient was treated with the ventilator for a prolonged period. In order to overcome this problem the humidifier is now cleaned and heat-disinfected after each application. It is then filled with a sterile solution of 0.1% chlorhexidine (Hibitane) in water. The necessary refills during actual use are made with sterile water. We checked the results of this method in 57 cases by taking cultures from the humidifier after each usage. In no case did any growth occur.

We disinfect the Engström ventilator by passing ultrasonically nebulized 70% ethyl alcohol through the respirator in a closed system for two hours.

The efficacy of this disinfection is tested by placing filter paper discs impregnated with staphylococci, *E. coli*, and *Pseudomonas* sp. in the circuit of the ventilator before disinfection and culturing from them afterwards. This method has given excellent results and will be the subject of a report in the near future.—We are, etc.,

KRISTINA GÜLLERS.
ANNA-STINA MALMBORG.
OLOF NORLANDER.
BERTIL NYSTRÖM.
NILS PETERSON.

Department of Anaesthesia,
Thoracic Clinics, and Clinical
Bacteriological Laboratory,
Karolinska Hospital,
Stockholm, Sweden.

SIR,—With reference to the recent paper by Dr. J. C. Tinne and others (11 November, p. 313), this is most valuable in emphasizing the importance in apparatus of reservoirs of water that are difficult to drain and easily infected.

In the intensive care of the newborn baby we have come across two unexpected examples of this, which gave rise to potentially dangerous situations. The first was in the water reservoir of the incubators used for premature infants, and the second in apparatus which sucked out the pharynx immediately after birth. Both were exacerbated by faults in the design of the machinery. In the incubators the water could not be drained completely, as the plug was not at the bottom of the tank; the manufacturers have since remedied this defect. Cleaning of the suction apparatus was rendered difficult by the poor quality of the glass of the catch bottles, which it was thus not possible to sterilize by heat, and the presence of what appeared to be an unnecessary number of rubber washers behind which small amounts of moisture accumulate. *Pseudomonas*

aeruginosa has been found repeatedly in these situations.—We are, etc.,

R. E. REWELL.

W. E. TULLOCH.

Liverpool Maternity Hospital,
Liverpool 7.

Respiratory Infection in Early Childhood

SIR,—It is encouraging to see that Dr. P. S. Gardner and his colleagues (11 November, p. 316) and your leader-writer (p. 307) are now advocating the use of blood gas and acid-base measurements in the management of the child with severe respiratory infection. However, it is of little use demonstrating the presence of a major degree of respiratory acidosis unless the facilities for treatment are readily available, and this means intermittent positive-pressure ventilation (I.P.P.V.) through a nasotracheal tube. This point does not seem to be emphasized enough in either of these articles.

I would agree that this type of therapy is easily undertaken only in a hospital with facilities for intensive care, but this should not be taken to imply that I.P.P.V. is an extremely difficult technical exercise. A number of centres in Great Britain have this well established as part of a routine service, and it may not be entirely coincidental that two centres reporting series of I.P.P.V. free of major technical troubles have been those where there has been considerable co-operation between paediatricians and paediatric anaesthetists.^{1,2}

The number of children with respiratory infections requiring I.P.P.V. is probably not great, and it is therefore important that experience gained in the operating-theatre in the management of infants with respiratory distress syndrome, apnoeic attacks, or after major surgery, and in older children with status epilepticus, meningitis, tetanus, etc., should be concentrated. This may well mean channelling admissions to larger centres, but it seems unlikely that there will be much progress in further reducing mortality in a number of diseases in children unless this is done.

Surely we have now reached a stage when a children's hospital should find prolonged I.P.P.V. no more unusual or difficult than caring for the more severely ill child with, say, pyloric stenosis or intussusception.—I am, etc.,

Royal Aberdeen Hospital
for Sick Children,
Aberdeen.

H. G. PLEDGER.

REFERENCES

- ¹ Reid, D. H. S., and Tunstall, M. E., *Anaesthesia*, 1966, 21, 72.
- ² Rees, G. J., Stead, A. L., Bush, G. H., and Jones, R. S., *Brit. med. J.*, 1966, 2, 1611.

Brand Names of Drugs

SIR,—We have read with some concern your editorial attitude (7 October, p. 1) towards the Sainsbury Committee's recommendations that brand names should be abolished for new medicines. In our view too much emphasis has been put on the theoretical advantages of this proposal, while too little weight has been given to the economic and practical considerations.

Firstly, on the economic side, let us assume that a company has developed a useful new product but is required to market it under an

officially approved name. If it were patentable (and often, for a variety of reasons, it is not) the fact that imitators could use the original name would greatly encourage them to obtain a compulsory licence, as they are able to do under section 41 of the Patents Act. Thus the lack of trade-mark protection would swiftly lead to fragmentation of the originator's market, since doctors are unlikely always to specify on their prescriptions the name of the originating company, however great its reputation. The greatly enhanced financial risks involved for the developer would be bound to constitute a severe deterrent to long-term investment in pharmaceutical research in this country. As to export markets, there are many countries where products cannot be sold under brand names unless these have first been registered in the product's country of origin. In any event, the difficulties already explained of establishing a clear lead for the developer's original product in this country would undoubtedly prejudice its export potential.

For the N.H.S., however, the savings from the abolition of brand names would be negligible. There are only a small number of cases where branded products are more expensive than similarly formulated unbranded medicines. It is calculated that savings, if such branded products were eliminated from N.H.S. prescribing, would be something of the order of 0.5% of cost of the pharmaceutical services.

Nor would the abolition of brand names significantly reduce the numbers of differently named preparations on the market. Out of the 2,150 or so branded prescription medicines listed in *Medindex* at the beginning of 1967 there were some 1,780 different formulations each based on different chemical entities. That is, abolishing brand names could reduce the number of differently named preparations only by less than a fifth. Brand duplication is very much the exception, but the fact that it can occur provides for the possibility of competition leading to superior formulations.

In practical terms it is possible that the difficulties of prescribing and dispensing in the absence of brand names have been treated too lightly because there has been too little distinction drawn between the terminology for the chemical *ingredients* and that for the *preparations* which are formulated from one or more such ingredients. For the former, the approved name is unambiguous. For the latter, difficulties would arise from the absence of brand names in at least three ways: firstly, in describing special formulations, such as delayed release capsules, aerosols, or specially flavoured mixtures acceptable to children; secondly, and more particularly, in the case of small but significant variations between such formulations—for example, with capsules designed to release their medicament at different rates; and, thirdly, in identifying specially formulated presentations which were only subtle improvements over the "official" preparations. In theory each could be described in a phrase describing the formulations, coupled with the approved name and that of the manufacturer. In practice this would probably add to the confusion, rather than decrease it. Many of us must have recollections of this type of nomenclature from our time in the Services.

Finally, we do not accept that legislative controls, relying on severe penalties for

improperly formulated medicines, provide the best way of ensuring uniformly high standards of pharmaceutical quality. We believe that the manufacturers' pride in their own products, when marketed under their own brand names, provides a much stronger incentive.

General practitioners are busy men, and the use of brand names can be convenient as well as logical in their prescribing. We believe that the medical profession should give very careful consideration before supporting proposals to abolish brand names for medicines.—I am, etc.,

E. B. TEESDALE,

Director,
Association of the British
Pharmaceutical Industry.

London W.1.

Abortion and Conscience

SIR,—Dr. Myre Sim in his letter on abortion and conscience (4 November, p. 297) complains that doctors have no reliable evidence to guide them in their interpretation of the various clauses of the new Abortion Act.

The World Health Organization¹ defines health as follows: "Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity." This definition is surely relevant when one is considering whether or not to advise termination of pregnancy.

Dr. Sim quite rightly feels that the doctor who advises a termination of pregnancy should have a clear conscience that the dangers threatening the pregnant woman are real. Should he not feel that the doctor who advises against termination of pregnancy also has a clear conscience that no dangers threaten the patient? It is ironical that his letter should appear but a few pages after an article (p. 271) describing 48 days' intensive hospital treatment of a woman who died from complications of a self-induced abortion.—I am, etc.,

Aland, Finland.

PETER DARBY.

REFERENCE

- ¹ Constitution of the World Health Organization, *Chron. Wld Hlth Org.*, 1947, 1, 29.

Institutional Care of the Mentally Subnormal

SIR,—Professor T. McKeown and Dr. I. Leck (2 September, p. 573) have drawn attention yet again to the shortage of facilities generally for the subnormal. These studies have much to commend them, and their accuracy, especially in relation to the needs of adult patients, is not in doubt. However, should their findings be applied to the needs of patients under 16 years of age any future planning based on them can only have disastrous results. Whatever the authors themselves may have intended, their results will certainly be quoted and used by those intent on reducing costs, and therefore some of their omissions should be mentioned. My remarks here refer only to children.

The singular lack of hospital accommodation at the time of their survey for children in Birmingham is mentioned, and it is suggested that this shortage is overcome by it being "a relatively compact area in which

paediatric and psychiatric centres do a considerable amount of investigation which might elsewhere be done in hospitals for the subnormal." Unfortunately, none of these statements is in keeping with the facts. Apart from its "compact" nature not being obvious to me, "centres" in Birmingham have been unable to carry out all the investigations necessary, while in other parts of the country hospitals for the subnormal are generally not equipped to carry them out either.

In the light of the unqualified statement that only seven of the 1,652 patients in hospital were thought to need "medical investigation or treatment of any kind necessitating hospital admission," the expenditure of £2m. on Lea Castle Hospital must appear to be the best blatant outrage to the taxpayer since the cancellation of "Blue Streak." Even more ridiculous, however, is the fact that 560 of its 660 places are already occupied, over 200 by children, more than half of whom come from Birmingham and who were in fact awaiting admission at the time of McKeown and Leck's survey but were obviously overlooked. The number of children awaiting admission to hospitals for the subnormal in Birmingham at the time of McKeown and Leck's survey was I believe over 100, and at present four requests per month for the permanent care of severely handicapped children are received from that half of the city served by this hospital alone.

The establishment of a "multi-disciplinary assessment centre" in this hospital (a report on this is in preparation) and the demand for this indicates the lack of an assessment service for these children in the city of Birmingham in the past. Requests have been received from paediatricians, E.N.T. departments, the school medical service, and general practitioners, so that these children would not appear on the waiting-lists of hospitals for the subnormal. McKeown and Leck's survey could therefore not have encountered this particular group even if it had reviewed the waiting-lists for this or any other hospital for subnormal children. The provision of this service in this hospital has become necessary because previous attempts at assessment had failed at one or other of the existing paediatric, psychiatric, or school clinics. Our experience suggests that Pilkington's 10%¹ is far more realistic than that of McKeown and Leck.

The behaviour of a number of these children is such that the ophthalmological, audiological, and even x-ray studies often require to be carried out in sleep or under general anaesthetic, while adequate psychological assessment can be achieved only by continuous observation over a minimum period of two weeks. Our experience has shown that many of these children cannot be tolerated for more than a few hours in general paediatric wards, and many who have already been returned to schools and training centres had been previously designated "not assessable," "untreatable," or, in desperation, "impossible."

The handicaps for which assistance is most commonly requested are varying degrees of cerebral palsy, deafness, blindness, speech retardation, or combinations of these, often, but not necessarily, associated with behavioural disorders and intellectual retardation. The staff involved in these assessments have been drawn from various specialties—paediatrics, orthopaedics, ophthalmology, otology, biochemistry, psychology, and psychiatry—assisted by specialist teachers, a speech therapist, and a physiotherapist. The waiting-list for such assessments after four months is now over 25, and demand is increasing. None is accepted without one of three consultants deciding that it is impossible elsewhere. Several children are accepted following assessment for varying periods of treatment

or diagnostic teaching, for which special units have been established in the hospital. The majority, however, have so far been returned to the community with recommendations on placement and management.

The service outlined here is far from complete at present, but it would be quite unrealistic to suggest that, even in its present form, it could be carried out adequately on these children anywhere but in the context of a hospital specializing in the treatment and management of the severely handicapped child.

Despite their underestimate of the need, it should be remembered that McKeown and Leck do suggest that the provision of such facilities in hospitals for the subnormal is most desirable. From our brief experience of the demand, this is indeed fast becoming a necessity. Inevitably, however, the cost per patient in such hospitals must rise, and until the controllers of hospital finances are made aware of the need for this progress it can never be achieved. Estimates of the cost per bed in hospitals for the subnormal in the past few years have varied from £10 to £12 per week, whereas provision of the most basic service on the lines suggested above would amount to from £16 to £20 per week. Personal experience, however, has made it apparent that the treasury and finance departments of regional boards have not yet become aware of the necessity for any such increase. The Minister, in his recent directive on "the upgrading of hospitals," indicated his awareness of the need for a rise in standards, but, apart from expressing a pious hope that this might come about, makes no mention of meeting the increased cost. Until hospitals for the subnormal are given the necessary financial support, and until they cease to be looked upon as a "last resort" for the hopeless, neither these advances nor the wishful thinking of the Minister will ever materialize.

Finally, if any justification should be necessary for this expenditure on the handicapped child, it could be mentioned that at least half of these entering hospital at 5 years of age or under can expect to survive for possibly 50 or more years. At a conservative estimate this will cost £30,000 per patient. Surely it cannot require a great deal of foresight to become aware of the advantages of an increase in expenditure, which will then amount to only half the cost in a city general hospital, or one-third that of the teaching-hospital bed, and which could enable 10–15% of these children to be discharged after one or two years, in some cases with no further expense to the hospital service.—I am, etc.,

Lea Castle Hospital,
Wolverley, Worcs.

G. B. SIMON.

REFERENCES

- 1 Pilkington, T. L., in *Report of the Annual Conference of the National Association for Mental Health*, 1966, p. 50. London.
- 2 *First Report of the Joint Working Party on the Organization of Medical Work in Hospitals*, 1967. H.M.S.O.

Ventricular Aneurysm

SIR,—Your leading article (11 November, p. 312) on ventricular aneurysms prompts us to record a physical sign that we have not infrequently observed after extensive cardiac infarction, especially in women. This consists in a lifting or rocking movement of the fourth and sometimes also of the third rib which can be followed by the palpating finger from the costo-chondral junction right out to

the axilla. In a number of cases the movement is visible and we have, in one case, recorded it with a cinecamera. The sign may persist for two or three months, but can also be permanent. Although it more commonly follows anterior wall lesions, we have on at least one occasion observed it after a postero-diaphragmatic infarct.

We can offer no ready explanation for this phenomenon, which has not, to our knowledge, been described before. The fact that it is not due to localized outpouching is clearly shown on radioscopy, when the movement transmitted to the examiner's hand is visible at sites well clear of the left cardiac border.—We are, etc.,

E. MONTUSCHI.

H. E. S. PEARSON.

Whittington Hospital,
St. Mary's Wing,
London N.19.

Errors in Blood Transfusion

SIR,—Once again a transfusion catastrophe has received nationwide publicity,¹ and, in so far as it is fatal cases which are reported, we can draw no comfort from the knowledge that the incidence of incompatible transfusion is higher than this annual event would imply. I would suggest that a re-emphasis of certain facts relating to the practice of blood transfusion will not come amiss at this time. Having regard to the complexities of the subject, it might be thought surprising that more difficulty was not encountered, but there is a common theme running through most of these reported accidents. The incompatibility is in the ABO system and results not from technical incompetence but from clerical error.

I believe that a heavy responsibility rests upon the pathologist in respect of both the technical and clerical aspects of this problem. The problem of safeguarding identification of patients clearly varies from one hospital to another, but I cannot help feeling that more attention should be paid to this aspect of transfusion practice. Many hospitals have devised their own internal system; others have not, or at best have failed to enforce it.

Some years ago, at a meeting of the Association of Clinical Pathologists, I demonstrated a system which we have now operated successfully for many years at the Royal National Throat, Nose, and Ear Hospital. We use a three-part label which follows the colour coding employed by the National Blood Transfusion Service. An example is shown in the Figure. When blood is prepared the first and third part are completed and part three is detached and secured to the blood bottle. If there is no state of emergency requiring the immediate issue of the blood parts one and two are sent out on a report form indicating that the blood is available. Before the blood is issued part two has to be completed and returned to

The label in three parts:—

Part 1	Part 2	Part 3
GROUP A Rh POSITIVE	GROUP A Rh POSITIVE	GROUP A Rh POSITIVE
Name _____	Please supply X matched blood for Name _____	X matched with serum of Name _____
No. _____	No. _____	No. _____
Signature _____	Signature _____	Date _____
Attach to Form.	Return to Laboratory	Attach to bottle

the laboratory, where it is checked against part three by the person removing the blood from the blood bank refrigerator. Even if the person is colour-blind they can presumably read, and we lay great emphasis on the proper use of hospital numbers. Both medical and nursing staff receive repeated indoctrination, and all house-surgeons are interviewed at the commencement of their appointment. The system is not foolproof, especially as we suffer in part from the disadvantages of dispersal. However, it does induce a greater awareness of the dangers inherent in the commodity which we are handling, and I would be glad to supply further details to anyone who might be interested.

I am convinced that some system can be evolved to meet the requirements of any hospital, but it must be rigorously enforced. The price of safety is eternal vigilance.—I am, etc.,

Institute of Laryngology and Otolaryngology,
London W.C.1. D. A. OSBORN.

REFERENCE

¹ *Daily Telegraph*, 17 November.

Alcoholism

SIR,—I would like to reassure Dr. J. J. MacSorley (25 November, p. 487) that the National Council on Alcoholism is not solely concerned with the alcoholic addict.

The National Council's activities at the moment are directed towards the discovery of the alcoholic who refuses, through sheer fear of social censure, to consult a doctor or a religious counsellor. For centuries past alcoholism has been mankind's best hidden secret. The more alcoholics the information centres discover the more we shall be able to present to the public known scientific facts about this disease, and this will form part of wider prophylactic measures to deal with it.

Since the aetiological factors of this disease are unknown and no one form of treatment is applicable to all alcoholics, the National Council on Alcoholism entirely endorses the view that prevention is better than cure, and therefore the education of the public, indeed of our own medical colleagues, is of paramount importance.—I am, etc.,

E. LINCOLN WILLIAMS,
President,
National Council on Alcoholism.
London W.C.2.

SIR,—In the article "Clients of Alcoholism Information Centres" (11 November, p. 346) Dr. Griffith Edwards and others show that the clients of the centres differ from those alcoholics on "Skid Row."

A survey of alcoholics admitted to the Addiction Unit of this hospital confirms the findings that "Skid Row" alcoholics do not reach treatment facilities. During the period 1965-6 at the time of admission 66% of the alcoholics were living with their next of kin (wife or blood relation). A one-in-three sample of general psychiatric patients in the same hospital at the same time revealed that only 53% were living with their next of kin when admitted.

The difference between the two groups is not statistically significant, but it is of interest to note that the alcoholics admitted for treat-

ment have been those who are in the main still in close contact with their families.—I am, etc.,

Addiction Unit,
Moston Hospital,
Chester.

R. P. SWINSON.

Bottle Cuts

SIR,—Dr. M. J. McArthur is to be congratulated on his letter (21 October, p. 171) urging the introduction of polyethylene containers to take the place of glass milk bottles. I would go further and suggest banning the use of glass bottles for the supply of milk altogether. The annual toll of casualties from glass used for domestic purposes is truly lamentable and could be largely prevented. Personal suffering and loss of working hours, not to mention the permanent disabilities that may ensue, create a problem of grave concern to all. . . . The campaign for cleaner milk, with its spectacular benefits to health, was waged successfully some years ago despite opposition from certain quarters, so why not a campaign for safer containers.—I am, etc.,

Llanhamlach,
Brecon.

E. F. ADAMS.

Paraquat Poisoning

SIR,—In your correspondence column Dr. K. A. Mourin (25 November, p. 486) has referred to the report of a case of suicide in Israel by subcutaneous injection of paraquat from Dr. Ch. Almog and Dr. E. Tal (16 September, p. 721), in which the transient occurrence of a right facial paresis was observed between the second and fifth days, and has reported a case of his own in which a right lower motor neurone facial palsy developed four days after a febrile episode with sore throat and general malaise, and 10 days after a trivial exposure to paraquat, occasioned by smoking a cigarette rolled with unwashed hands.

There is no doubt that, as Dr. Mourin indeed suggests, the association with paraquat in his case is coincidental. The paresis in the Israeli case was accompanied by signs of pyramidal tract involvement (also transient), loss of abdominal reflexes, and the presence of Oppenheim's sign—conceivably due to temporary vascular disturbances or other local toxic effect following the systemic absorption of a fatal dose. Dr. Mourin's case was clearly a peripheral lesion of the facial nerve (Bell's paralysis), with the fairly common history of a preceding nasopharyngeal infection. Indeed, the description of vesicles on the right fauces suggests the possibility of a geniculate herpes zoster infection. The initial neurological symptoms observed in animal experiments with paraquat,¹ referred to by Drs. Almog and Tal, were seen only in a proportion of animals after single lethal intraperitoneal doses (30-75 mg. ion/kg.), and consisted of hyperexcitability, violent forced movements, and stiffness and incoordination of gait. In no species have lesions of peripheral nerve been produced.

The burning sensation of the tongue in Dr. Mourin's case can, however, certainly be attributed to exposure to paraquat, since it has a pronounced irritant action on mucous membranes, which is the main reason for insisting that concentrated solutions should be handled with care. In spite of extensive

field experience over the past six years, in which by now several million people must have used paraquat more than once, there have been less than half a dozen cases to suggest skin reactions in abnormally sensitive individuals, and none in which any evidence of an allergic state has been demonstrated.

One can only wish that all cases of illness thought to be associated with the use of agricultural chemicals were as fully investigated and clearly reported as Dr. Mourin's.—I am, etc.,

A. A. B. SWAN,
Director,
Industrial Hygiene Research Laboratories,
Imperial Chemical Industries Ltd.
Alderley Park,
Cheshire.

REFERENCE

¹ Clark, D. G., McElligott, T. F., and Hurst, E. W., *Brit. J. industr. Med.*, 1966, 23, 126.

Salmonella in Tortoises and Terrapins

SIR,—Dr. L. T. Newman (4 November, p. 296) was no doubt right to draw attention in his letter to the possibility of human salmonella infection arising from contact with infected tortoises. Terrapins are also imported into this country in large numbers and present a potentially greater hazard because they are aquatic.

A family of two adults and two children were recently under investigation for an infective illness, with symptoms including fever and mild diarrhoea. They had acquired a small Spanish terrapin (*Clemmys leprosa*), which was not healthy from the outset and died soon after the two children fell ill. Cultures from the gut of the terrapin yielded *Salmonella poona*. Although no salmonella was isolated from any member of the family and the two children were shown to have an adenovirus type 7 infection, nevertheless the serum of the elder child agglutinated an H suspension of *Salm. poona* to a titre of 1/40. This suggests that she may have passed through an inapparent infection. Further inquiry showed that the infected terrapin came from a batch of 5,000 imported from Tunisia. Very few of these still remained on the wholesaler's premises, but the water from the tank in which they had lived yielded *Salm. montevideo* and *Salm. anderssoni*.

American reports show that terrapins and their relatives are often infected by salmonellas, including serotypes which are regularly associated with human infection.¹ The water in which infected terrapins are kept is liable to contain salmonellas for long periods, in spite of frequent changes of water.² Terrapin owners are much more likely to acquire infection by repeated exposure to infected water than are the owners of tortoises, which are terrestrial in habit and likely in the main to contaminate only the garden.

It may not be out of place also to deplore the importation of large numbers of these small creatures, which are beautiful when seen in their natural setting but are doomed to die when imprisoned as pets in tanks. The large numbers exported annually could lead to their elimination from the countries of origin.—We are, etc.,

Public Health Laboratory,
Bath.

P. G. MANN.

Public Health Laboratory,
Watford.

B. R. EATON.

REFERENCES

¹ Williams, L. P., and Helsdon, H. L., *J. Amer. med. Ass.*, 1965, 192, 347.
² Kaufmann, A. F., Feeley, J. C., and DeWitt, W. E., *Publ. Hlth Rep. (Wash.)*, 1967, 82, 840.

Cancer Hazards

SIR,—Dr. Georgiana M. Bonser (21 October, p. 129) restates the interesting association between the teratogenic and carcinogenic action of trypan blue. In fact observations which could account for the teratogenic action of the trypan blue group of compounds (acid bisazo dyes) have recently been made,¹ and it is interesting to speculate whether the same cellular disturbances might not also be related to some aspects of the oncogenic process.

In rats trypan blue and related compounds are actively phagocytosed by macrophages and by certain extra-embryonic membranes, subsequently entering the vacuolar apparatus of the cells. They accumulate in heterolysosomes, and in this situation actively inhibit the hydrolytic enzymes found in these organelles. In the context of placental function the short-term effect would appear to be an inhibition of embryotrophic nutrition leading to congenital malformation. Investigations to see whether lysosomal enzyme inhibition is in itself associated with carcinogenesis and whether such a cellular event could account for the development of reticuloses are currently under way.—We are, etc.,

F. BECK.
J. B. LLOYD.
M. DAVIES.

Tenovus Institute for Cancer Research,
Welsh National School of
Medicine,
Cardiff.

REFERENCE

- ¹ Beck, F., Lloyd, J. B., and Griffiths, A., *Science*, 1967, 157, 1180.

M.A.O. Inhibitor Headache

SIR,—To obtain an accurate picture of the pattern of monoamine oxidase inhibitor drug headache, closer observation appears necessary to clarify the picture than is usually possible in general practice. Dr. C. A. H. Watts (28 October, p. 238) reports in his first case that he "took her blood pressure several times." He does not report over what time interval he made his readings.

In 1964 I was treating a depressed patient with Actomol (mefenazine) 5 mg. t.d.s. Six weeks after commencing treatment, instead of her daily English Cheddar-cheese sandwich, she had a sandwich of Canadian "Cheddar." At 11.30 p.m. a pounding headache mimicking a subarachnoid haemorrhage started. I saw her at midnight in very great distress but without neck rigidity. Her blood pressure was then 160/95. In view of the degree of her distress and my anxiety not to give her an unsuitable drug and thus complicate the issue further I admitted her to a general-practitioner bed, and hourly readings showed her blood pressure to be 200/104 at 1 a.m., but by 2 a.m. it was 120/98, never rising higher again, and being 110/82 by 6 a.m.

Without such general-practitioner bed facilities I would have been unaware of the rise at 1 a.m. The difference between English and Canadian cheeses was interesting, as at that stage we were warned only of blue-vein cheeses. The following day the patient remarked she had had so much benefit from Actomol she would give up cheese for life. I regret I had not heard of phentolamine (Dr. R. K. Rondel, 11 November, p. 357).—I am, etc.,

Welwyn Garden City,
Herts. E. H. J. COTTER.

Treatment of Myocardial Ischaemia

SIR,—In your leading article (4 November, p. 249) you do not mention the role of anticoagulant therapy in the treatment of angina pectoris. This is an important omission, as there is evidence that the outlook for males with angina without frank infarction is considerably improved by anticoagulant therapy.^{1,2} I believe that all such cases should receive anticoagulant therapy as soon as the diagnosis is made, provided there is no contraindication, and thereby reduce the incidence of subsequent myocardial infarction

with its mortality in hospital of about 20%. My policy for some years has been to use anticoagulant therapy on all male cases of angina provided they are breadwinners and below the age of 70. This policy has been shown to pay dividends in the form of diminished mortality. The age limit is not critical.—I am, etc.,

G. R. ROYSTON.

Barnet General Hospital,
Barnet, Herts.

REFERENCES

- ¹ Borchgrevink, C. F., in *World Medicine*, 30 July 1967.
² Royston, G. R., *Angiology*, 1967, 18, 133.

Oxygen Concentrations in Tents

SIR,—The article by Dr. H. Simpson and Dr. Doreen J. Russell (28 October, p. 201) indicates the variability in the relationship between oxygen inflow rates and the concentrations found within tents and incubators. Our own investigations^{1,2} have shown that, after a tent or incubator has been opened for nursing procedures, it can take a very long time for the oxygen concentration to rise to

by Simpson and Russell between the "ideal" levels (presumably plateau levels) and the random samples taken during routine clinical use.

Continuous recordings of the changes in oxygen concentration in tents and incubators have led us to believe that, if any particular high level is required, it is essential to monitor the oxygen percentage and regulate the inflow

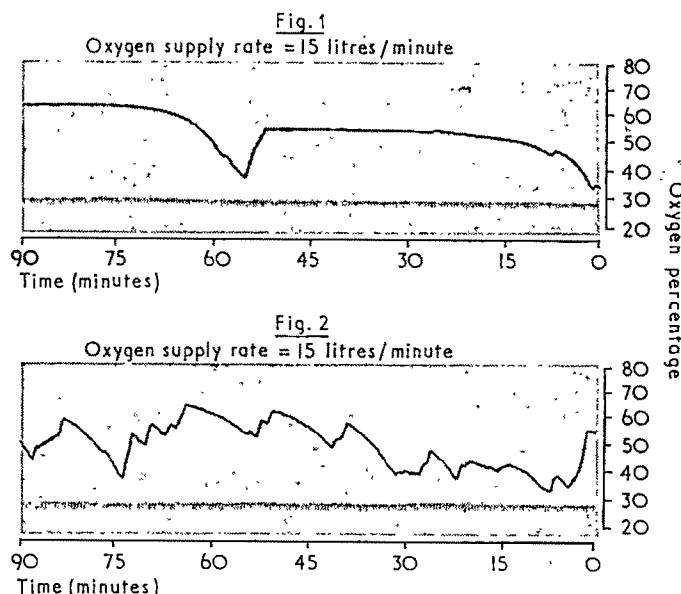


FIG. 1.—Oxygen concentrations measured within an Oxygenaire Junior Oxygen Tent. Note the gradual rise to plateau following routine nursing procedures. The two plateau levels (approximately 50% and 60%) are due to normal variations in seal. FIG. 2.—Same tent and patient as in Fig. 1. Note that frequent openings of the tent do not permit the attainment of a plateau.

a plateau, unless there has been a period of flushing. The gradual rise is illustrated in Fig. 1, although at lower inflow rates we have found this may take about one hour. If a tent or incubator is opened frequently the oxygen concentration may not attain a plateau; Fig. 2 shows a typical recording of changes in oxygen concentration during intensive nursing care. We have also found that the plateau concentration is affected by the efficiency of the sealing of a tent (as shown by the two plateau levels in Fig. 1), and by the temperature difference between the inside of an incubator and its surroundings.

In view of the influence of these factors it is impossible to predict the oxygen concentration from the inflow rate. This is well demonstrated by the wide discrepancy found

rate accordingly. Furthermore, we have found that the site of sampling is not critical and that readings taken from a central position are representative of the concentrations throughout the tent or incubator.

The authors wish to thank the Editor of the *Journal of the Royal College of Surgeons in Ireland* for permission to reproduce Figs. 1 and 2.

—We are, etc.,

G. W. BURTON.
G. WRAY.

Department of Anaesthetics,
University of Bristol,
Bristol 2.

REFERENCES

- ¹ Burton, G. W., *J. roy. Coll. Surg. Ireland*, in press.
² Burton, G. W., and Wray, G., in preparation.

Obstetric Forceps or Vacuum Extractor?

SIR,—I cannot let the condemnation of the vacuum extractor in your leading article (23 September, p. 753) pass without comment. Having used this instrument with increasing frequency in the past four years, I have come to regard it as very safe for both mother and babe. Indeed, this has been shown conclusively by many authors and latterly by Bird¹ and again by Fahmy.² This is also my interpretation of the paper in the *American Journal of Obstetrics and Gynecology* to which you refer.³

The ventouse can be used in practically every case where forceps are indicated, and provided the classic requirements for the application of forceps are fulfilled it is a very safe instrument even in the hands of the novice. For the skilled obstetrician, as you most rightly point out, it also has the advantage that a patient can be delivered safely before complete dilatation of the cervix where there is urgent need for delivery. Further, it should be remembered that a young doctor can be trained to use this instrument safely and effectively in weeks, as compared to the many months required for training in the use of forceps. This is of particular importance in a country like Australia, where the country doctor has to put his hand to everything and often to cases which would be referred to specialist care in the cities. This instrument is also favoured by obstetricians in the so-called underprivileged countries for much the same reasons.

It seems a pity that you pay so much attention to this article and, in my opinion, misinterpret it. The many publications which emphasize the safety of the ventouse to both mother and child cannot be ignored. Finally, I must disagree with your statement that the vacuum extractor has no place in the district or in a general-practitioner maternity unit. These are the very situations where the instrument stands supreme.—I am, etc.,

Perth,
Western Australia.

N. K. CROOKE.

REFERENCES

- 1 Bird, G. C., *Aust. N.Z. J. Obstet. Gynaec.*, 1966, 9, 242.
- 2 Fahmy, K., *ibid.*, 1967, 7, 114.
- 3 Schenken, J. G., and Serr, D. M., *Amer. J. Obstet. Gynec.*, 1967, 98, 32.

SIR,—It is with considerable dismay that I have just read your leading article "Obstetric Forceps or Vacuum Extractor?" (23 September, p. 753). It suggests a parochial approach to the subject in the confines of obstetrics carried out by "the trained obstetrician" in a well-developed country. However, it is almost certainly fair to state that most complicated deliveries in the world are carried out by doctors who are not specialists in obstetrics, and the lesser skill required to apply the vacuum extractor, as opposed to forceps suggests that some points in your article may merit reconsideration. Even so, enlightened obstetricians in Europe such as Chalmers,¹ Fothergill,² Willocks,³ and Snoeck⁴ are replacing forceps with the vacuum extractor. Donald's remarks on the instrument in his *Practical Obstetric Problems*⁵ are particularly relevant.

In developing countries, with exceedingly few obstetricians about, the situation is even more poignant. Apart from being easier to apply, it can be used without anaesthesia, or

by local infiltration of the vulva only, in emergencies of foetal distress (although pudendal block is probably desirable), making the delivery just as quick as with forceps, with which anaesthesia is essential.

It is the writer's impression that it is merely tradition that makes forceps the instrument of choice in delay or foetal distress in the second stage. Dalley⁶ has said, "I could deliver safely any baby with the vacuum extractor that I could deliver alive by forceps," and Lange⁷ has concluded that there is less danger for the mother and only half the perinatal mortality. These remarks must be even more relevant with the limited obstetric skill available in developing countries, where disasters with forceps have been so frequent in the past that the caesarean section rate has risen to high percentage levels, this being undesirable for several reasons, until the vacuum extractor arrived. The relative ease with which an occipito-posterior can be delivered with the vacuum extractor may surprise many obstetricians who prefer the often difficult manual rotation or Kiellands forceps. This is certainly contrary to your own comments on this point.

It is difficult for those pre-eminent in the considerable skill needed to apply forceps to turn their attention to an instrument that may appear to usurp their prowess, but there are those of us who work as general duty medical officers, but have complicated obstetrics thrust upon us, and feel that the introduction of the vacuum extractor is the greatest advance in obstetrics since the advent of ergometrine, when considering the best management for our patients.—I am, etc.,

Ministry of Health
Regional Medical Office,
Arusha, Tanzania.

D. E. BROOKE.

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- 1 Chalmers, J. A., *Brit. med. J.*, 1964, 1, 1216.
- 2 — and Fothergill, R. J., *ibid.*, 1960, 1, 1684.
- 3 Willocks, J. J., *Obstet. Gynaec. Brit. Col.*, 1962, 69, 266.
- 4 Snoeck, J., *Proc. roy. Soc. Med.*, 1960, 53, 749.
- 5 Donald, I., *Practical Obstetric Problems*, 1964, 3rd ed. London.
- 6 Dalley, G., *Lancet*, 1962, 1, 692.
- 7 Lange, P., *Dan. med. Bull.*, 1961, 8, 11.

SIR,—Those who use the vacuum extractor to drag a baby through an undilated cervix admit the procedure carries with it the serious risks of brain damage, uterine rupture, and ruined uterine supports with subsequent prolapse. These risks should never be taken.

With good antenatal care, selective booking, careful observation during the first stage of labour, anticipating—rather than awaiting—foetal distress, and deciding on termination of labour at the latest by the eighteenth hour from its onset (or before, if it is clear that labour is halted) and while the condition of the mother and baby remain good; then, if the cervix is not fully dilated, a caesarean section should be done.—I am,

Mayday Hospital,
Croydon, Surrey.

A. CLIFT.

Deaths from Tuberculosis

SIR,—One must be grateful to Dr. A. Pines (18 November, p. 416) for drawing attention to the dangers to the community from the pool of drug-resistant, positive-sputum patients at large. Certainly there are reasons enough for making all possible efforts

to deal with their tuberculosis, but Dr. Pines has enumerated some of the difficulties.

These patients are largely from a group who have failed to stay the course in hospital, will not voluntarily return on any terms, and who cannot be relied upon to take the drugs conscientiously while remaining in their homes. The public health hazard is the real issue, I believe, rather than the mortality in this select circle of sufferers, many of whom were saved from death by the advent of the standard chemotherapeutic agents; but not before extensive lung damage had been done. Surely the latter is responsible for the gloomy figures. Do we know that adequate treatment with the second-line drugs means a longer life? Did the 33% die of their tuberculosis or from secondary infection?

If these patients resist institutional care, for their manifold reasons (largely psychological), chest physicians must continue to treat each individual as a particular and personal problem in his own environment, and the special centre will have empty beds until winter infection and respiratory failure force the victim to enter on a stretcher.—I am, etc.,

Brighton Chest Clinic,
Brighton, Sussex.

F. B. MEADE.

Smallpox Revaccination

SIR,—I was interested to read Dr. T. McL. Galloway's letter (16 September, p. 740) about smallpox revaccination. I agree with his plea in favour of vaccination.

I have been involved personally in two outbreaks of smallpox. On both occasions it was most remarkable how the disease picked out those individuals among the contacts who had never previously been satisfactorily vaccinated for one reason or another. Virulent smallpox is a killer and is so awesome that the possible side-effects of vaccination are of small significance in its presence. That has been my experience. The public will not thank the medical profession for underestimating the risk of a smallpox epidemic occurring in a poorly vaccinated population.

Until a more reliable alternative to vaccination is available, we doctors, when discussing the possible side-effects of vaccination with our patients, should tell them as well of the ravages of clinical smallpox and of the problems which arise when vaccination is not performed timeously and efficiently. Incidentally in a series of half a million vaccinations in my city there has been no fatality nor permanent disability reported among those concerned.—I am, etc.,

DUNCAN L. FERGUSON.

Divisional Council of
Port Elizabeth,
South Africa.

Screening for Phenylketonuria

SIR,—Drs. J. B. P. Stephenson and M. S. McBean (2 September, p. 582) drew attention to the lack of success in detecting phenylketonuria by early screening with Phenistix. This prompted us to investigate the stability of phenylpyruvic acid on towel napkins and also cellulose disposable napkins.

Freshly voided urine was used, to which sodium phenylpyruvate 25 mg./100 ml. was added. At this level a definite positive reaction was obtained from Phenistix when

dipped into the urine. When 5 ml. of this was applied to a 3-in. × 3-in. (7.5-cm. × 7.5-cm.) doubled piece of towel, a much reduced colour was observed on testing, and after an hour several skilled observers recorded a negative or doubtful reaction. The cellulose napkin, when used in the same manner, gave a definite positive even after two hours. These findings were consistent on four separate occasions. Quantitative estimation suggested some instability on the towel napkins associated with urine of high pH, but results varied and difficulty with turbidity from traces of detergent left from washing were experienced. However, it was found that the quantity of urine taken up by a Phenistix was much less from towel-type napkins than from cellulose or by direct dipping, as shown by the increase in weight. Average of 10 tests: dipping 29.4 mg., cellulose 39.5 mg., and towel 16.5 mg.

We suggest that this reduced uptake may be responsible for a lowering of sensitivity when Phenistix is used to detect phenylpyruvic acid on towelling napkins, especially when the urine has been given time to spread over a larger area from the original point of application. Perhaps the use of cellulose napkins would increase the detection rate of phenylketonuria to an acceptable level, as they appear to provide a more favourable material for an adequate transfer of urine to Phenistix.—We are, etc.,

D. A. BAXTER.

M. E. YORK-MOORE.

Royal Eastern Counties
Hospital,
Colchester, Essex.

Mercury Perchloride in Surgery

SIR,—We were interested in the letter by Mr. D. H. Patey (28 October, p. 238) suggesting that an accurate evaluation be made of the use of mercury perchloride in eradicating malignant cells from operation wounds. Like Mr. Patey, we too had not found any evidence of this having been done, and began some experiments some nine months ago. It is too early yet to make a complete evaluation, but our preliminary results using T₂₄₁ sarcoma cells in C₅₇ mice are encouraging and are summarized below.

Wounds Seeded with Sarcoma Cells

Irrigating Solution	Saline	Hypo-chlorite	0.1% Mercury Perchloride
Number of mice used	98	82	47
Number of mice in which tumours grew	88	40	11
Percentage in which tumours grew	90	49	23

In our earlier experiments^{1,2} we found that, using carcinoma cells under similar experimental conditions, cetrimide solution was more effective than other agents tested in preventing growth of malignant cells in operation wounds. The other agents tested included nitrogen mustard solution and hypochlorite solution.

In view of the favourable early results using mercury perchloride, we are currently comparing the effects of mercury perchloride solution with other irrigating solutions, including 1% cetrimide solution, in experi-

mental wounds seeded with carcinoma, sarcoma, and melanoma cells.—We are, etc.,

GEOFFREY R. GIBSON.

FREDERICK O. STEPHENS.

Department of Surgery,
University of Sydney,
Sydney, Australia.

REFERENCES

- ¹ Stephens, F. O., and Gibson, G. R., *Cancer (Philad.)*, 1966, 19, 1286.
- ² Gibson, G. R., and Stephens, F. O., *Lancet*, 1966, 2, 678.

Oculogyric Crisis after Phenothiazines

SIR,—A nurse, aged 21, was recently admitted to this hospital with a severe oculogyric crisis following an injection of Fentazin (perphenazine) 10 mg. given for unexplained vomiting. She also complained of a choking sensation, had severe trismus, and presented a dramatic clinical picture.

In view of the fact that this appeared to be an extrapyramidal syndrome, as described in the manufacturer's literature, she was given atropine (0.6 mg.) as a potent anti-Parkinsonian drug. Pethidine (50 mg.) was also given. This was followed by a complete remission of symptoms within 10 minutes. There was a minor recurrence two hours later and she was given a second dose of atropine (0.6 mg.). After this she had no further symptoms.

Although this complication of Fentazin therapy is mentioned in the manufacturer's literature there is no reference to treatment.

This particular patient gave a history four months before of taking perphenazine tab. 4 mg. b.d. for five days without any adverse effect. This raises the possibility that the patient had been sensitized by the earlier administration of the drug, but such sensitization does not appear to have been previously described.—We are, etc.,

J. J. KIMERLING.

S. R. PATEL.

Heatherwood Hospital,
Ascot, Berks.

Safety of Dimethoate Insecticide

SIR,—The organophosphate anticholinesterase insecticide dimethoate is widely used in many countries for the systemic control of insects on food crops. At harvest some recently treated crops contain a small residue of dimethoate, from 0.05 up to 1 p.p.m. The safety of such residues to consumers of the crops is clearly an important matter.

Toxicological studies conducted before marketing showed that dimethoate intake rates as high as 0.04 mg./kg. bodyweight per day produced no detectable effect on whole-blood cholinesterase (ChE) values in rats (trial duration 6–12 months) or in human volunteers (duration one month). Individual human subjects were also given 0.13 and 0.26 mg./kg./day respectively for 21 days without detectable effect.¹ A special F.A.O./W.H.O. committee responsible for reviewing

safe levels of pesticides in food was naturally reluctant to accept data on individual subjects, and recommended the maximum allowable intake rate for dimethoate as 0.004 mg./kg./day.² This is the intake rate shown harmless to humans but reduced by a safety factor of 10. This recommendation tended to limit the permissible uses of an efficient insecticide with an excellent record of safe use in the field. Further studies were therefore desirable.

We now report extended observations on the response of humans to the daily ingestion of dimethoate, and in particular on the daily intake rate required to cause depression of whole-blood ChE values.

Thirty-six male and female adult volunteers without occupational exposure to organophosphate insecticides were arranged in groups and given repeated doses of dimethoate as indicated in the Table. Actual dosage was on five days per week, and each daily dose was therefore seven-fifths that shown in the Table. Missed doses of one or two days were made up by double doses on the day before or after. The dimethoate was administered as a flavoured aqueous solution. Venous blood samples were taken twice before and once or twice per week after dimethoate dosage started. ChE in whole blood was measured by the electrometric method of Michel³ and its depression taken as the critical first response to dimethoate. Activity in red cells and plasma were also determined separately. The study was under close medical supervision, and inquiry was also made for any effects other than ChE depression, though none was detected.

The Table summarizes the experimental plan and results of the study. ChE values are expressed in "cholinesterase units" (ΔpH/hr. × 100). Groups D and E were made up of previously discontinued Groups A and B, and were included to confirm at higher dosage levels the response seen in Group C.

The results show that no significant change occurred in Groups A and B. ChE values in Group C began to show a slow downward trend by day 20, and this continued to the end of the test at 57 days. Groups D and E showed the same effects at an earlier stage, and a somewhat faster rate. The rate and extent of red cell ChE depressions closely paralleled those of whole-blood ChE in Groups C and D. No localized gastrointestinal or other clinical effects occurred in any group.

From this study we concluded that dimethoate ingestion by humans at the rate of 0.4 mg./kg./day or above will cause a slow decrease in whole-blood ChE activity, but that at 0.2 mg./kg./day and below such an effect is most unlikely to occur. (Eight subjects were studied at a mean intake rate of 0.2 mg./kg./day. Their range of ChE activity before ingestion was 108–148 units (mean ± 2 standard deviations) and after 39 days was 102–146 units.)

It is therefore suggested that the experimentally adduced "no-effect level" for dimethoate ingestion by small groups of humans may now safely be taken as 0.2 mg./kg./day, which when reduced by a safety factor of 10 would imply an acceptable daily intake rate

Group	No. in Group	Daily Dose mg. Dimethoate	Duration of Test (days)	Mean Whole Blood ChE		Mean Weight (kg.)	Daily Intake Rate (mg./kg./day)
				Before	At End		
A	12	5	28	114	110	74	0.068
B	9	15	39	128	124	75	0.202
C	8	30	57	121	92	71	0.434
D	6	45	45	113	74	77	0.587
E	6	60	14	121	96	60	1.02

of 0.02 mg./kg./day. This is equivalent to the daily consumption by 60-kg. humans of 1 kg. of foodstuff containing 1.2 p.p.m. dimethoate residue. It bears a safety factor of at least 10 before the slightest effect on blood ChE activity would occur, and (from animal studies) a safety factor of about 400 before the first signs of clinical toxicity would arise. The full details of this study will be reported elsewhere. It is hoped that the findings may extend the permissible usage of an important and safe insecticide.

Grateful acknowledgement is made to the 36 volunteers concerned and to Soc. Montecatini (Milan) for providing the necessary materials.

—We are, etc.,

E. F. EDSON.
K. H. JONES.
W. A. WATSON.

Chesterford Park Research
Station (Research Centre of
Pisons Pest Control Ltd.),
Saffron Walden, Essex.

REFERENCES

- ¹ Sanderson, D. M., and Edson, E. F., *Brit. J. industr. Med.*, 1964, 21, 52.
- ² F.A.O./W.H.O. Joint Report, 1965, *Evaluation of the Toxicity of Pesticide Residue in Food*, Rome.
- ³ Aldridge, W. N., and Davies, D. R., *Brit. med. J.*, 1952, 1, 945.

Injury from High-speed Drills

SIR,—A serious ophthalmological hazard exists to dental practitioners from the new high-speed drills used for cavity preparation in teeth. Particles of filling or other dental debris may be projected at great speed into the orbital region of the operator, and cause damage to the eye.

In a recent case a fragment of tooth substance, propelled in this way, caused a severe corneal abrasion, which prevented the dental surgeon from working for a considerable period of time.

The necessity to wear some form of eye protection, such as goggles or spectacles, while using these drills cannot be too strongly stressed.—I am, etc.,

N. E. A. RENNER.

Eastman Dental Hospital,
London W.C.1.

Psychotropic Drugs

SIR,—As the co-author of the first British paper on phenelzine¹ I should like to comment on the views of Dr. P. Leyburn and his colleagues (18 November, p. 417).

In designing that first trial I was deeply concerned about the dangers of prescribing a placebo for depressed patients, since suicide is a possible outcome of imperfectly treated depressed patients. That risk was taken in the trial described but was not taken in any subsequent trial. The M.R.C. trial² expected a large number of investigators to take a similar risk, and this is one reason why I did not take part in the M.R.C. trial. In the design of any further trial one would hope that the M.R.C. would take the advice of people like Dr. P. J. Dally (28 October, p. 233) who are engaged in active clinical psychiatry. The previous trial was concerned with a type of patient who is found only in the pages of the older history books on psychiatry.

One of the hidden advances that monoamine oxidase inhibitor drugs and tricyclic compounds have given us has been the dis-

covery of hitherto unsuspected varieties of depression. The important task now is to marry symptomatology up with treatment. No single antidepressant drug is a specific cure for all varieties of depression.

It is time that clinicians ceased to be afraid of the dangers of these drugs. I have not seen one death from them in eight years of use, but I have seen several deaths from suicide in that period. Yet the deaths from suicide appear to be fewer than they were before these treatments were available. It would be of value for investigators to use the suicide rate as an index of success or failure in treatment.

In conclusion, it is important to remember that the elimination of suicide in depression is the main goal of all types of treatment. The suicide rate is still comparable to the death rate from road accidents, but the research and publicity directed towards its elimination compare very unfavourably with the efforts of the Ministry of Transport in dealing with its particular problem.—I am, etc.,

Cane Hill Hospital, JOHN T. HUTCHINSON.
Coulston, Surrey.

REFERENCES

- ¹ Hutchinson, J. T., and Smedberg, D., *J. ment. Sci.*, 1960, 106, 704.
- ² Report to the M.R.C. on Treatment of Depressive Illness, *Brit. med. J.*, 1965, 1, 881.

Surgery in Pulmonary Tuberculosis

SIR,—Your leading article "Surgery in Pulmonary Tuberculosis" (21 October, p. 127) defined six groups of patients who still require surgical treatment to complete their recovery. The fourth group contained "a few patients with 'healed cavities' which have become secondarily infected with aspergillus fungus. . . ."

The British Tuberculosis Association (B.T.A.) investigation, to be published shortly, into the incidence of aspergillus infection in "open healed" cavities has shown that the incidence is not negligible. In my own clinic, with approximately 1,000 patients on the tuberculosis register, we have 19 patients with "open healed" cavities, and no fewer than eight of these show evidence of aspergillus infection, six have a classical mycetoma demonstrated radiologically and have positive precipitin tests, and two have positive precipitin tests but so far no radiologically demonstrable mycetoma.

Resection in the presence of aspergillus infection is a more difficult and dangerous operation than resection in the absence of infection, and I submit that the likelihood of a young person left with such a cavity developing mycetoma in the future is sufficiently high to warrant resection of such residual cavities after adequate antituberculous chemotherapy, usually of two years' duration.—I am, etc.,

T. A. W. EDWARDS.

Chest Clinic,
St. Albans City Hospital,
St. Albans, Herts.

In Advance

SIR,—The correspondence on obstetric forceps or vacuum extractor (4 November, p. 292, and 11 November, p. 354) and on institutional care of the mentally subnormal (11 November, p. 355) reminds me of the

saying, "What Manchester thinks today London thinks tomorrow."

In the former, "the fact that it (the vacuum extractor) has largely replaced the forceps in several countries on the Continent" applies also to Northern Ireland and probably to other regions of the British Isles outside London.

In the latter, Northern Ireland for 10 years or more has cared for the mentally subnormal in the community with schools, and more recently with sheltered workshops and hostels.

Last month a swimming-pool exclusively for the use of the mentally subnormal was opened by Lady Wakehurst at Muckamore Abbey. Before this, hydrotherapy had been given at public swimming-baths, a treatment for the mentally subnormal which has been pioneered in Europe by Northern Ireland.

Several other advances in medical science have been instigated for the first time in the British Isles in Northern Ireland which I am reluctant to list for fear of appearing to boast. But the matters raised might indicate to your readers that here we appear to be in advance of, not behind, the times, and that the days of "pigs in the kitchen" have long passed away if they ever did exist.—I am, etc.,

Belfast 9.

MARY N. M. PAULIN.

North America Interview Board

SIR,—I would be grateful to be allowed to reply to the letters of Dr. J. Stanners and of Dr. C. D. H. Elton and Mr. I. W. M. Wright (18 November, p. 416).

The Interview Board's tour was arranged to meet the requests for interviews received in answer to the Ministry's advertisement of our visit published in the *B.M.J.* and other journals in July and August. Such requests were still reaching me when the Board left England on 30 September. At this time we had already invited 150 doctors to meet us for discussions of up to one hour each. It was possible to make only a few adjustments to this programme, because it was already very full and because the team's travelling schedule had to be adhered to. Every effort was made to accommodate doctors who approached the team at short notice, and where this was not possible informal meetings with individual members of the Board were arranged. I am sorry if some British doctors in Alberta were unaware of our visit before receiving a letter from the British Head of Post in Edmonton, but this, as I have said, was not the first intimation of our visit.

The Board would have gladly visited Edmonton if a sufficient number of doctors there had asked to meet us, but the centres chosen were necessarily locations which suited the convenience of the majority of doctors who had replied to the Board's advertisements. We sincerely regret that some of the doctors who approached us at very short notice could not be seen; this happened only where the Board's time was entirely taken up with appointments already arranged and confirmed.—I am, etc.,

R. H. BARRETT,

Chairman,
Interview Board, Ministry of Health.
London S.E.1.

Government-owned Health Centres

SIR,—It would appear that in the near future general practice will be conducted from well-equipped Government-owned health centres which will provide ancillary and laboratory facilities. At any rate I find that most of my colleagues are of the opinion that this transformation is in the natural process of the evolution of general practice, and that it is coming whether we like it or not. In fact it would also appear that the majority of general practitioners do like it. What is in no doubt at all is that the Government is keen on the idea and is offering financial inducements to general practitioners to form groups and go into health centres. Personally I am unable to view these inducements without a certain amount of misgiving—*timeo Danaos et dona ferentes*.

Nevertheless, I also feel that the "new general practice" is going to be a fact in a very few years from now, and that a salaried service will quickly follow. To my mind this change represents a possible threat to what is left of our independence and at the same time a possible chance to raise the status of family medicine and those who are expert in its practice. At worst, we can passively acquiesce to a take-over bid by a cynical Government aided by a handful of power-hungry medical politicians, in which case we shall have lost what little independence we have left, and our status will have become even lower than at present. At best, we can react in such a way to these imminent changes as to direct them towards the formation of a better type of general practice to the benefit of our patients and ourselves alike. I suggest that it would be worth our while to sacrifice a measure of independence (and this seems inevitable) for a career structure wherein an able doctor who had devoted eight to ten years of his life to general practice could expect to attain the rank of consultant (in family medicine) with the same pay, pension, and opportunity to win a merit award as his colleagues in the hospital service. It is quite unthinkable that we should be content to accept anything less than this. I would point out that there is nothing in the least inappropriate or even novel in this idea. The Indian Medical Service made the appointment of "Specialist in Family Medicine," which carried the same rank, pay, and kudos as any other specialty.

I also think that such a career structure would attract many of the best young doctors into family medicine—which could and should be the most rewarding of all the branches of our art.—I am, etc.,

Belfast 5.

J. D. H. MAHONY.

Practice "Twinning" Arrangements

SIR,—The health centre age is upon us, but what of those patients, those practitioners, and those areas where single-handed practice will continue to be a satisfactory, practical, and, in the case of country practice, an essential way of life.

Single-handed practice in future will be possible, and practicable, only if an efficient, reliable locum service is set up. Fewer and fewer young doctors, not forgetting their wives, will want to go to areas where they are isolated in terms of colleague contact and where in their isolation they are unable to

get time off for leisure, holidays, study, and illness. A patchy, unpredictable, sometimes unreliable and often absent locum service, as at present, will not do, as some areas will soon find to their cost.

I would like to suggest that consideration should be given to practice "twinning" arrangements whereby country doctors should be "twinning" with group practices in towns, even although these might be many miles away. The arrangement would cost little or nothing, but payment would be a problem, unless from central funds. Perhaps the Minister might be persuaded to put up a retainer for the involved parties. "Twinning" arrangements would allow country doctors to have freedom from the worry of personal illness and locum cover for holidays. Study courses could be regularly attended at the great teaching centres, and the country doctor could also, from time to time, work at the group practice with which he was "twinning," thereby having colleague contact which would be interesting, instructive, and stimulating for all concerned. Not all doctors in a group might wish to be available, and indeed not all might be suitable for what would be involved in taking over and running a single-handed country practice, sometimes at short notice in the case of illness. Experienced general practitioners in their forties would be best suited, and by repeated contact could get to know the particular practice well, and vice versa. How stimulating it would be for town general practitioners to practise real medicine occasionally in isolated country practice, especially if a cottage hospital was available.

Arrangements could be by mutual agreement and personal contact. Many single-handed doctors with doubts about the future of their practice might well be heartened by knowing that they were not alone and that a telephone call would bring a known, reliable, experienced colleague whose own work could be covered by his partners, helped by the local locum service of retired practitioners or retrained married women doctors, who would simply be required to help with the work at peak times and not have the considerable worry and responsibility of actually running the practice.

As a partner in a group practice I would welcome and be happy to participate in a properly organized practice twinning arrangement.—I am, etc.,

Musselburgh,
Midlothian.

CLIFFORD C. LUTTON.

"Mediflash"

SIR,—The "Mediflash" medical emergency light appears to be the subject of police criticism at present, and unless someone defends the scheme the authorities may well conclude that doctors do not care about being held up in traffic, so may I as originator of the design adopted by the B.M.A. comment on a few of the points in question?

In a letter to the B.M.A. (*Supplement*, 11 November, p. 50) the Chief Commissioner of the Metropolitan Police deprecates the use of the scheme because "... any further proliferation of flashing lights is bound to detract from the effectiveness of those that are already fitted to vehicles belonging to the fire, ambulance, and police services." This would be acceptable perhaps if the light was blue, but as it makes use of a different colour

surely this scheme cannot detract from the effectiveness of the blue light any more than the amber flashing lights permitted on vehicles such as gas works vans. Also, unlike the amber lights which are a permanent attachment, the green light will be seen only when required. Has not a doctor going to an emergency involving life a greater claim for this type of vehicle purpose identification than, for instance, a motoring organization's van attending a member's punctured car tyre? The letter also mentions that there may be no benefit without an audible warning device; the ordinary car horn, though not distinctive, will effectively draw attention to the flashing green light, which is.

A letter (18 November, p. 423) draws attention to the fact that the self-adhesive "Doctor-Emergency Duty" signs are "... almost invisible beyond the car's bonnet." Is this not strictly comparable to the abandonment of the old "Ambulance-Accident" sign in favour of the instantly recognizable symbol of the blue light, and should not doctors follow this example and adopt a symbol? If the doctor can be seen and helped by the police and motorists he can save much valuable time in difficult traffic, as compared with a small saving from just speeding in light traffic. Certainly the idea has been welcomed by the drivers of all three emergency services that I have spoken to, especially in the example of a doctor who when called to a bad road accident is readily visible to those already at the scene and to those motorists held up by the accident who have to be passed. This was confirmed when it was reported in the *Daily Mail* on 7 November that the medical officer in charge of the Lewisham Hospital major accident scheme (Hither Green rail disaster) was delayed by traffic and by police who had no means of knowing his identity until they had stopped his car and spoken to him. This resulted in a journey time to the control centre of over 30 minutes instead of the usual 15, and resulted in the first ambulance reaching the hospital with patients from the accident over 12 minutes before the arrival of the controlling medical officer.

If the profession is not allowed official recognition on the road then as traffic density problems increase so will delay times and the Documenta Geigy book on road accidents¹ confirms my own observations that delay in treating some emergencies can have very serious consequences. Granted these emergencies are not everyday occurrences, but this does not make them any less important when they arise.

If the green-light scheme is allowed to be quietly extinguished the parking badge will almost certainly suffer the same fate, and the doctor will then have no recognition at all even when dealing with a really urgent emergency.—I am, etc.,

Dunkerton,
Nr. Bath, Somerset.

R. SNOOK.

REFERENCE

- ¹ Gögler, E., *Road Accidents*, 1965, Documenta Geigy Series Chirurgica No. 5. Manchester.

Prospects for Hospital Doctors

SIR,—I was glad to see Dr. E. A. Harvey-Smith (11 November, p. 359) drawing attention to the failure of the consultant establishment to expand as it should.

I was puzzled, however, by his penultimate paragraph, in which he says, "... I am assured that the Central Advisory Committee on Consultant Establishments never turns down a needed consultant post. . . ." From this he draws the conclusion that either hospitals are not asking for them, or boards are failing to forward requests that are made. This is at variance with our experience in Chelmsford. The anaesthetic department, the medical advisory committee, the hospital management committee, and the regional board all agreed in February 1966 that another maximum part-time consultant anaesthetist was needed, but this has been twice turned down by the Ministry of Health.

Perhaps Dr. Harvey-Smith can tell us by whom he was assured that this does not happen; or perhaps it all depends on the Ministry's interpretation of "needed consultant post."—I am, etc.,

Chelmsford,
Essex.

D. A. WALMSLEY.

Seniority Payments

SIR,—I refer to the "Eligibility in Seniority Payments" being tied to the "stipulated average numbers of sessions per annum of approved postgraduate training." I strongly object to this provision on grounds of principle and practicability.

I have a 3,000-list single-handed practice in this designated area, with a high percentage of immigrants and over 65s, and qualify for maximum seniority payment. I have four morning and evening surgery sessions, plus two morning-only (each of 1½ hours) and two afternoon maternity sessions. I do only N.H.S. work and I find myself fully occupied in coping with this, my relaxation being one half-day away (from 3 p.m.) per week, and an hour's rest in the afternoons. I have for several years also had an annual two weeks' holiday. I may add that I find it pays me to visit on a Sunday morning, which I almost always do. Thus in practice I find that the only times I am not regularly occupied are Saturday afternoon and evening and Sundays, and, apart from the question of needing time for a break for health reasons, I find it difficult to pick out postgraduate training sessions to fit in with these periods. A further and by no means theoretical point is that I would be in breach of my contract with the executive council by attending these sessions, the majority of which are at a distance where I would not be readily available for possible calls.

On the principle involved, it seems clear that there should be no strings attached to a payment factor of this kind, especially those of a harassing nature. My case and views must be typical of many, and I should welcome the comments of others. I urge our negotiators to take up the cudgels again even at this late hour.—I am, etc.,

Wolverhampton, Staffs.

S. STOWE.

REFERENCE

¹ *Statement of Fees and Allowances payable to General Medical Practitioners in England and Wales, 1966.* Ministry of Health.

SIR,—Doctors who qualified in 1953 find themselves the first to have to fulfil the new regulations involving provisional registration for one year before full registration.

Next year these doctors will find that though they have been qualified for 15 years they are ineligible for seniority award, as the "New Deal" has based seniority on the number of years since full registration, not since qualification.¹ This must seem strange to us all, as their colleagues who qualified in 1952 have received payment for seniority *this year*. To rub salt into their wounds a large percentage of these doctors have been disallowed vocational awards, as their two years' National Service, compulsory in 1953, is not considered adequate enough experience. Either our negotiators are unaware of these glaring defects in our contract, in which case they are incompetent, or they have sacrificed considerable sums of money to the Ministry at the expense of the younger doctors for some motive which is beyond my comprehension. I cannot believe that the Review Body intended different sets of values for doctors qualifying before and after 1953.—I am, etc.,

Edgware,
Middx.

A. B. DAVID.

REFERENCE

¹ *Statement of Fees and Allowances payable to General Medical Practitioners in England and Wales, Ministry of Health, 1966.*

Improving General Practice

SIR,—The revisions of the last Charter¹ were designed to stimulate the provision of improved medical services under improved working conditions. As part of this policy group practice was encouraged. There is, however, an anomaly in this respect in the provisions relating to the reimbursement for the cost of a locum during sickness. At present this reimbursement will be given only if the average list size of the remaining partners is 4,000 or more. Thus a two-man partnership with an average list of 2,000 would be reimbursed for a locum, but a three-man partnership with an average list of 2,000 would not be reimbursed. In other words, the larger the group the more difficult for it to obtain financial help in this respect. One appreciates that the larger the group the easier it is for it to absorb the extra work occasioned by the incapacity of one partner. Nevertheless this is not in line with the general principles of the Charter to improve the standard of general practice.

I hope that this anomaly will be reconsidered by the next Review Body.—I am, etc.,

London N.W.10.

PETER G. BRENT.

REFERENCE

¹ *Brit. med. J. Suppl.*, 1965, 1, 89.

First Fellows of the Royal College of General Practitioners

SIR,—I was amazed to see a list of the first Fellows of the Royal College of General Practitioners elected (25 November, p. 498).

I have not seen any definite strict criteria laid down, such as original published work, etc., concerning general practice in the regulations of the Royal College of General Practitioners for such an election to Fellowship. No doubt most of the names of the newly elected Fellows are very familiar to us members of the College mostly for their various committee activities. The Fellows elected may be very deserving general practi-

tioners, but surely it is invidious to elect some members as Fellows because of their various committee activities or on some suchlike assessment.

This once again emphasizes how right the majority of we general practitioners were to overwhelmingly reject and throw out for ever the merit awards for general practitioners as proposed by the Ministry of Health and at that time accepted by our negotiators.—I am, etc.,

Nottingham.

B. I. KOHLINSKY.

Christmas Gifts Fund Appeal

SIR,—I should like to remind your readers who have not yet responded to the president's appeal (7 October, p. 57) that it is our custom to distribute the gifts in good time for Christmas.

In view of the rising costs of even basic necessities, it is the wish of the committee that the amount of the Christmas gift cheque given to each regular beneficiary should be increased this year, and it is hoped that the response will be even more generous than in previous years.

Please send contributions marked "Christmas Gifts" to the Royal Medical Benevolent Fund, 24 King's Road, Wimbledon, London S.W.19, as soon as possible.—I am, etc.,

GEOFFREY H. BATEMAN,

Honorary Treasurer,
Royal Medical Benevolent Fund.

London S.W.19.

Points from Letters

Deterioration of Professional Relationships

Dr. L. T. NEWMAN (London N.W.6) writes: "... It is becoming increasingly common, when one has referred a patient for a consultant opinion, for a general practitioner to be in the embarrassing position of not having a report on which to comment for a considerable period of time, even allowing for all the vagaries of our postal service. There is furthermore the appalling delay which takes place when a patient has been referred to a hospital before the hospital writes to give the general practitioner a report. I frequently have patients attending the surgery and have to contact the hospital before I am able to carry out their recommendations. Occasionally, one's patients have returned home after an operation before one is aware of the fact that they were even admitted to hospital. Naturally, the relatives concerned think that we are either callous or disinterested if, during the interim, we have made no inquiries concerning the patient's welfare.

There are, of course, many consultants who are both courteous and efficient, but I am afraid that, with the passing of time, these will become the exception rather than the rule, and thus widen the schism between these two branches of our profession. . . .

Reprints: Who Should Pay?

Mr. E. D. RUSKIN (Medical Librarian, Butterworth Hospital, Michigan, U.S.A.) writes: Dr. S. E. Browne's reply (7 October, p. 57) to the question: "Reprints: who should pay?" poses the problem of doctors finding time to answer requests, but neglects the difficulty of photocopying articles in journals that are so tightly bound (and lacking adequate margin-space) that at least a fraction of a page is lost in the process. Examples of this are the *B.M.J.* and the *New England Journal of Medicine*, both of which ought to consider reform—for the sake of the librarian who has to photocopy articles in bound volumes of them. . . .

Obituary Notices

G. H. BUCKLEY, M.B., CH.B., F.R.C.S.ED., F.R.C.S., J.P.

Mr. G. H. Buckley, formerly senior consultant surgeon to the Blackpool and Fylde hospital group, died at his home in Lytham on 17 November after a short illness. He was 71.

George Holden Buckley, son of a doctor, was born in Poulton-le-Fylde on 3 February 1896, and was educated at Blackpool



Grammar School and Manchester University. His medical studies were interrupted by the first world war, during which he served in the Royal Engineers. After demobilization he resumed his studies, and graduated M.B., Ch.B. in 1921. After holding junior appoint-

ments in the Manchester Royal Infirmary he took the F.R.C.S.ED. in 1925. He was greatly pleased by his election to the Fellowship of the Royal College of Surgeons of England, *ad eundem*, in 1949.

He joined the staff of the old Victoria Hospital, Blackpool—which at that time was virtually a cottage hospital—as an honorary consulting surgeon in 1927, and when he retired in 1961 he had been for a number of years the senior consulting surgeon to the Blackpool and Fylde hospital group. A superb technical surgeon, he devoted himself to raising the standard of surgery that then

prevailed in the provinces, and it is very largely due to his foresight, and to that of a few friends he gathered round him, that the Victoria Hospital has developed on its present site into the large specialist hospital that it is today.

Among his many activities, he was a Fellow of the Association of Surgeons of Great Britain, and was both a member and a past-president of the Provincial Surgical Club, with which he travelled widely. He was an original member of the Central Consultants and Specialists Committee which negotiated the terms of the National Health Services Act. He took a lively interest in the activities of the Blackpool and Fylde Division of the British Medical Association, and was chairman in 1938–9. He served throughout his active life on the Board of Management and after 1948 on the Hospital Management Committee of the Victoria Hospital, Blackpool, where his portrait now hangs in a position of honour as a tribute to his unique contribution to its progress over the years. In spite of the demands of a large consulting practice, he contrived to serve the community in other ways. He was appointed a magistrate in 1950, and on moving his home to Lytham St. Annes some ten years ago he began a new interest in local government and became chairman of the local health committee.

In 1928 he married Miss Eileen Heyworth, of Rossall Beach, who survives him. The deep sympathy of George Buckley's many friends and past patients will be extended to her and to her son and daughter in their sad loss.—D. K. L.

O. A. TROWELL, M.A., M.D., F.R.S.ED.

Dr. O. A. Trowell, an internationally distinguished senior member of the scientific staff of the Medical Research Council Radiobiological Research Unit at Harwell, died on 17 November. He was 58.



Oswald Arthur Trowell was born on 19 May 1909, and received his early education at King Edward VI School, Birmingham, and went to St. John's College, Cambridge, as an open exhibitioner in 1926. He became a scholar in 1928,

and obtained first-class honours in both parts of the natural sciences tripos. He did his clinical studies at Birmingham, and graduated M.B., B.Chir. in 1933. He proceeded M.D. in 1940, and was awarded the Raymond Horton-Smith prize for the best thesis of the year. He became a demonstrator in physiology at Liverpool, but in 1934 returned to

Cambridge. He was elected a Fellow of St. John's College, and later became director of medical studies. During the second world war he was lecturer in physiology in Edinburgh. From 1946 to 1948 he was reader in physiology at Bristol. During these years he soon gained recognition as an exceptionally lucid teacher of physiology.

In 1935 he published his first independent work in a paper on choline and liver respiration. This was followed in 1942 by a study of urea formation in the isolated perfused liver of the rat, and in 1946 by one on watery vacuolation of the liver, which is a classic. In these papers is ample evidence of the original approach, scrupulous attention to detail, and clarity of purpose which characterized all his later work.

In 1948 he embarked on a full-time career in research at Harwell at the comparatively late age of 39, and devoted himself to developing a method of maintaining lymph nodes for several days *in vitro* on a chemically defined medium. The method evolved had features in common with classical tissue culture technique and short-term methods for tissue slices. It is now widely used for many organs besides lymph nodes.

Being able to maintain lymph nodes *in vitro* enabled him to produce a formidable series of fundamental studies on the effects of x rays and numerous other agents on lymphocytes. The last of these studies was devoted to ultrastructural changes. His interests were by no means confined to lymphocytes, and he collaborated with others on papers dealing with subjects as diverse as the retina, the diaphragm, and the salivary glands. He also found time to write a review on the lymphocyte for the *International Review of Cytology* in 1958, and contributed several chapters to *Cells and Tissues in Culture*, which appeared in 1964–6. These are particularly valuable because of his clear, fluent style and complete mastery of the subject.

Despite his exceptional gifts, Ossie was a modest man. Behind his reserved, almost austere, demeanour he had a warm generous nature and a delightful dry wit. His personality was reflected in the happy atmosphere which prevailed in his laboratory; he was much loved by his staff. He was always ready to welcome to his laboratory the many other research workers who sought his advice, and he never grudged the time spent in giving help and advice—advice that was always sound and constructive.

Outside his work his tastes were simple and his interests wide. He was a talented artist with brush, pen, and pencil, and an expert gardener. Occasionally his scientific outlook intruded in his hobbies, as when he compared the "compost value" of the *Lancet* and the *Economist*. He was a great naturalist, and enjoyed an encyclopaedic knowledge of wild flowers and birds.

At home he was devoted to his family, and it is appropriate to conclude with a tribute to his wife, whose tireless love and patience helped him endure the distressing illness which marred the last year of his life. Our sympathy goes out to her and their two sons, the younger of whom recently qualified in medicine.—D. R. L.

E. N. W. writes: Trowell, whom I first met as a distinguished third-year student in physiology in 1929, joined Jacoby and myself in studies on fibroblastic growth in 1934, and we had a very fruitful triumvirate till Jacoby went to Birmingham three years later. Trowell stayed on for another year or two, and we worked together on the effects of tissue extracts on growth. He combined penetrating analytical powers with great technical skill and a scrupulous attention to detail. The minute and the precise fascinated him. He was an exceptionally clear teacher and writer, and took endless trouble to help his students. He was gloriously outspoken, and even his best friends were not spared the caustic edge of his tongue. While the latter knew that his bark was infinitely worse than his bite, unfortunately those who knew him less well were often put off by this mannerism. In fact, he was one of the gentlest and kindest people I have known. He had a very well developed sense of right and wrong, and would not tolerate humbug.

He had a delightfully pungent sense of humour, with a predilection for sophisticated puns, double meanings, and for the exploitation of the pompous and ridiculous. His letters were masterpieces of literary humour, and were often enlivened by highly skilful and apposite illustrations executed with a fine economy of line.

We had many interests in common. He and I constructed a rock garden together at his house in Cambridge. Bird-watching and indeed natural history in general were constant pleasures to him. Painting and drawing, too, held his attention for a time, and he brought to all these hobbies the same skill and precision that he gave to his scientific work. His death will be greatly mourned by his many friends, both at home and abroad.

DOROTHY C. HARE, C.B.E., M.D.
F.R.C.P., D.P.H.

Dr. Dorothy C. Hare, a former consulting physician to the Royal Free Hospital and Elizabeth Garrett Anderson Hospital, died on 19 November, at the age of 91.

Dorothy Christian Hare, daughter of Edward Hare, C.S.I., deputy inspector-general of hospitals in the Indian Medical Service, was born at Bath on 14 September 1876. She was educated at Cheltenham Ladies' College and the London School of Medicine for Women (now the Royal Free Hospital), graduating M.B., B.S. in 1905 and proceeding M.D. three years later. After holding early hospital appointments, she entered general practice at Cambridge in 1910, and in 1912 she took the D.P.H. She left her practice during the first world war and rendered distinguished service, first in Malta where in 1916-7 she was attached to the R.A.M.C., and later as medical director of the Women's Royal Naval Service in 1918-9. In recognition of these valuable services she was appointed C.B.E. in 1919. She took the M.R.C.P. in 1920, and the following year was appointed medical registrar at the Royal Free Hospital, later becoming assistant physician, and eventually consultant, to the Royal Free and Elizabeth Garrett Anderson Hospitals. She was elected F.R.C.P. in 1936.

Dr. Hare was a past-president of the section of therapeutics of the Royal Society of Medicine. She was the author of *Simple Instructions for Diabetic Patients*, which appeared in 1933.

Dr. Lilia Blackett Jeffries writes: When I reached the Royal Free Hospital—along with the first sizable group of women medical students following the pioneers—in 1905-6, Dorothy Hare was a house physician. She very quickly attracted our notice, partly for the sculptural correctness of her features, then for her calm and impressively confident manner, her obvious intellectual ability, and finally for the respect with which her chief treated her. She had a fine voice and gave a great deal of pleasure by her singing. None of her contemporaries were surprised by the professional honours she earned, and the recognition awarded her from her war service and public services. Many of us remember her guidance and help with gratitude.

W. BEAUMONT, M.R.C.S., L.R.C.P.

Dr. W. Beaumont, honorary consultant in physical medicine to the Westminster Hospital, died at the hospital on 14 November. He was 75.

William Beaumont was born in Huddersfield on 16 April 1892, and received his early education at Spring Grove Council School. He entered the London Hospital Medical College in October 1914. His studies were interrupted by the first world war, during which he served with the Royal Naval Volunteer Reserve. After demobilization he returned to the London Hospital, qualifying with the Conjoint diploma in 1922. He was house-surgeon to the ear, nose, and throat department at the London Hospital, and surgical registrar at the Throat Hospital, Golden Square. Subsequently he became interested in electrotherapy, and this was in the days when pyogenic infection was treated by rest, heat, and surgical drainage; surgical tuberculosis by rest and ultraviolet light; and wasted muscles by electrical stimulation. He soon became recognized as an authority on electrotherapy, and was one of the first medical examiners to the Chartered Society of Massage and Medical Gymnastics (now the Chartered Society of Physiotherapy). He published *Fundamental Principles of Ray Therapy* in 1931, *Diathermy* in 1939, and *Infra-red Irradiation*, which reached its third edition in 1951. During the second world war he served as a medical officer in the Emergency Medical Service.

Beaumont was instrumental in the establishment and became the first director of the Institute of Ray Therapy (now the Medical Rehabilitation Centre) at Camden Town, London. He was appointed consultant in physical medicine to the Westminster Hospital and to the Manor House Industrial Orthopaedic Hospital. He was a founder member of the British Association of Physical Medicine, in which he maintained an active interest after he had retired from hospital practice.

He leaves a widow and a son, to whom we extend our deepest sympathy.—F. S. C.

CHRISTINA B. BUCHANAN, M.B.
CH.B.

Dr. Christina B. Buchanan, a former consultant bacteriologist at the Royal Infirmary, Glasgow, died on 15 October after a short illness. She was 74.

Christina Blair Buchanan was born in Glasgow on 22 April 1893, and was educated at the Girls' High School and Glasgow University, graduating M.B., Ch.B. in 1916. After an appointment as medical officer at Ruchill Fever Hospital, she became assistant bacteriologist in the City of Glasgow Public Health Laboratory under Dr. R. M. Buchanan. She was later appointed assistant bacteriologist to Glasgow Royal Infirmary, where she reached consultant status. She also had a long association with the Federation of University Women.

Dr. Buchanan had a pleasant personality, and was very popular with a large circle of friends and colleagues, by whom she will be greatly missed.—M. H. M.

J. C. DICK, M.D., F.R.C.P. GLASG.
F.C.PATH.

J. R. McD. writes: As commanding officer of 19th General Hospital in the Suez Canal Zone I had the privilege of having John Dick (obituary, 4 November, p. 301) as pathologist in my hospital. I remember him with gratitude for three special reasons. When I went to the Middle East I knew very little about tropical medicine. John taught me all I know. Secondly, all German casualties came to our hospital, where we had 1,000 beds for them and a German staff, which included 13 German medical officers. It was almost self-sufficient, but despite repeated attempts we were unable to create a satisfactory pathology department. John solved the problem by accepting all their specimens in his own department. Thirdly, by his scrupulous care he established a department that was recognized by all as the "temple of truth."

F. A. PICKWORTH, B.SC., M.B., B.S.

Mr. W. STIRK ADAMS writes: I would like to offer my tribute to the memory of my old colleague and friend, Dr. F. A. Pickworth (obituary, 11 November, p. 363). In 1923 he joined Sir Frederick Mott as assistant pathologist to the Rubery and Hollymoor Mental Hospitals in Birmingham, and succeeded him as pathologist and director of pathological research in 1926. This research programme was sponsored after the first world war by Dr. T. C. Graves, F.R.C.S., medical superintendent, Sir Gilbert Barling, Pro-Chancellor of the University of Birmingham, and Sir Frederick Mott, who was in charge of the pathological services there after his retirement from London. Initially, under Sir Frederick's guidance, the special pathological investigation was directed to abnormalities present in the thyroid gland in the cadaver, and changes in its secretion. Later, similar studies were directed to possible abnormalities in the pituitary gland, which was excised with surrounding bone. Macroscopic evidence of chronic sphenoidal sinus infection and penetration by bacterial organisms into the surrounding bone and the brain stem was found in 24% of cases.

As a result of this finding a continuing clinical study of infections in the accessory nasal sinuses was made, and its extent recorded among the various types of mental disorder in the certified population of the hospitals. These investigations were carried out in every case under general anaesthesia. The recovery rate in these patients with certified mental disorders was found to be 10% better than the recovery rate published by any other hospital accepting similar cases, and this figure was maintained over many years.

Dr. Pickworth was an outstanding member of the team from 1923 to 1954, and by his continuing laboratory investigations he proved an essential guide in the clinical work, adding to its prestige. He also published numerous scientific articles, and later a summary of the pathological aspect of infective mental disorder in a *New Outlook on Mental Disease* (1955). Throughout he was a happy and friendly colleague and a loyal friend.

News and Notes

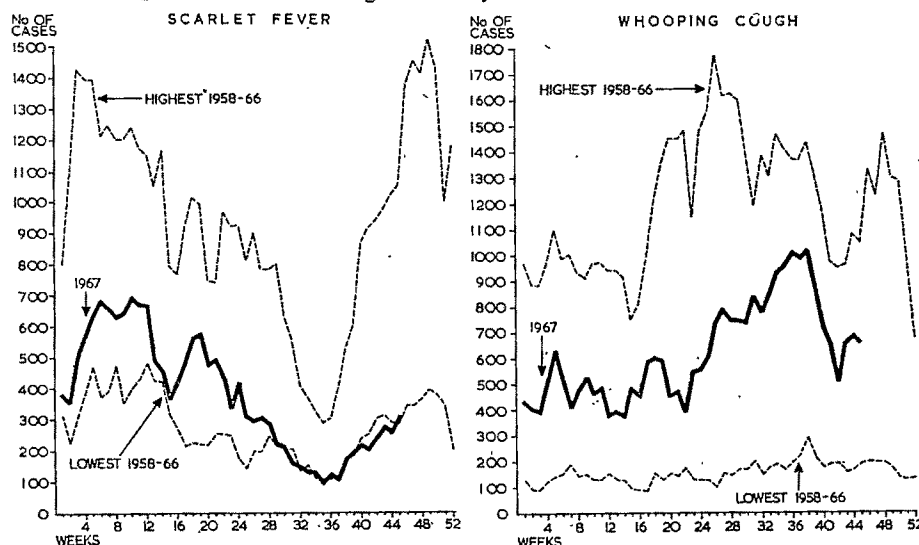
EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of scarlet fever and whooping-cough in England and Wales. Figures for

1967 are compared with the highest and lowest figures for each week in the previous

years shown. Areas where numbers of notifications were high in the latest two weeks for which figures are available.



Infectious Diseases

	Week Ending	
	10 Nov.	17 Nov.
Dysentery		
Durham ...	44	26
Blaydon U.D. ...	1	11
Stanley U.D. ...	5	10
Lancashire ...	103	51
Liverpool C.B. ...	8	11
Yorkshire West Riding ...	54	49
Leeds C.B. ...	17	14
Glasgow ...	44	30
Edinburgh ...	15	29
Diphtheria		
Brent (London) ...	1	1

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 11 November (No. 45) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	1	1	0	0		0	0	1	0	
Dysentery ..	326	32	94	4	4	299	65	73	4	3
Encephalitis, acute..	1	0		0		0	0		0	
Enteric fever:										
Typhoid ...	3	1	0	0		0	0	0	0	
Paratyphoid..	4	0	0	0		2	0	0	0	
Food-poisoning	208	30	3	0		115	38	40	0	
Infective enteritis or diarrhoea under 2 years				36	45				39	23
Measles* ..	1,110	51	60	24	59	9,147	1238	301	185	73
Meningococcal infection ..	10	0	5	0		7	2	2	1	
Ophthalmia neonatorum..	14	2	1	0		15	2	2	0	
Pneumonia† ..	100	12	90	4		125	14	109	3	5
Poliomyelitis, acute:										
Paralytic ..	0	0	0	0		0	0	0	0	
Non-paralytic	0	0	0	0		0	0	0	0	
Puerperal fever‡	66	22	1	0		88	38	4	0	1
Scarlet fever ..	312	50	25	11	10	431	61	26	9	11
Tuberculosis: Respiratory ..	225	54	35	8		236	82	33	6	
Non-respiratory ..	41	7	9	2		40	11	9	1	
Whooping-cough	656	84	62	13	32	436	53	90	4	23
DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	1	0		0		2	0		0	
Encephalitis, acute..				0						1
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	4	0	1	1	1	7	1	0	2	0
Influenza ..	2	0	0	0	0	14	3	2	0	0
Measles ..	0		0	0	0	0		1	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	604	101	22	11	6	759	158	23	19	8
Poliomyelitis, acute..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	38	5	4	0	0	41	5	3	0	1
Non-respiratory ..				0	0				0	0
Whooping-cough	1	0	1	0	0	1	1	0	0	0
Deaths 0-1 year	269	36	29	6	7	309	59	22	8	8
Deaths (excluding stillbirths)	10,679	1691	571	133	193	11,090	1855	595	133	180
LIVE BIRTHS	14,681	2419	819	259	347	15,195	2566	852	258	372
STILLBIRTHS	220	33	14			229	36	17		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

‡ Includes puerperal pyrexia.

MOTORING

Progress of the Wankel Rotary Engine

[FROM OUR MOTORING CORRESPONDENT]

Sooner or later it seems possible that some form of rotary power unit will supplant the reciprocating engine for motor-car propulsion. The most prominent contender in this field is the ingenious engine designed by Dr. Wankel, which has been the subject of a tremendous amount of research and development during the past 10 years—initially by N.S.U. Motorenwerke and more recently by Mercedes, Citroën, Curtis-Wright, Toyo Kogyo, and other companies.

N.S.U. were first in the field with a rotary-engined car for sale to the public in limited numbers. This had a Wankel engine with a single rotor, and in all some 2,500 cars were made. For the 1968 model year N.S.U. have announced a larger and much more ambitious front-drive car, designed to suit a twin-rotor Wankel engine, for which an output of 100 vehicles per day has been planned. Concurrently, the "Mazda Cosmo" sports model has been launched by Toyo Kogyo (in Japan) with a twin-rotor Wankel engine of their own design, based on six years of engineering development and testing.

Each of these projects ranks as a courageous, full-scale marketing evaluation of the technical and commercial merits of a power unit quite different in design from the reciprocating piston engine with which it competes. In fact the only principle in common is the thermodynamic operating cycle. In the car engines with which we are all familiar successive downward and upward strokes of each piston provide for the intake, compression, combustion, and exhaust of a mixture of petrol and air. The Wankel engine is a rotary machine, without pistons or valves, but the working cycle has four phases which correspond with those of the piston engine.

A photograph of the Mazda engine with an end cover removed shows the Wankel rotor and the curious "epitrochoidal" contour of the casing in which it turns (see Fig. 1). An eccentric shaft (not shown) adds the orbital motion to the rotation of the rotor, with the result that the three apex seals (S) make continuous rubbing contact with the curved inner surfaces. I should add that the sides of the rotor are flat and carry additional sealing devices which press against the ends of the "box" in which the rotor revolves.

Each of the three crescent-shaped chambers between the rotor and the casing alternately expand and contract in volume as the rotor turns. The one seen on the right is going through an expanding phase, in which a mixture of petrol and air enters through an intake port. A little later the continued movement of the rotor will close this port and the volume of the chamber will decrease, so providing the compression phase. This particular chamber will then occupy the position of the one seen at the top, where combustion is initiated by sparking plugs. As rotation continues the volume will first increase, completing the combustion or power phase, after which another port (not visible) is exposed to allow the exhaust gases to escape as the volume decreases again. The whole cycle is then repeated. Consequently, in each revolution of the rotor three charges of petrol and air are inspired, compressed, fired, and exhausted.

The unusual geometry of the engine requires that the eccentric shaft shall be geared to run at three times the speed of the rotor. Consequently, there is one firing impulse per shaft revolution in a single-rotor engine and two impulses in a twin-rotor design. If the volume displaced during each intake phase is,

for example, 500 c.c., a twin-rotor Wankel engine will burn 1,000 c.c. of mixture per shaft revolution, and is therefore equivalent in size to a four-stroke piston engine of 2,000 c.c. capacity. This is in fact the size to which both the N.S.U. and the Mazda engines approximate, and each of them develops about 110 b.h.p.

The principal advantages of the Wankel rotary engine can be summarized as:

- (1) Smooth, continuous rotation replaces the "stop-go" characteristics of a reciprocating engine.
- (2) Number of working parts is greatly reduced.
- (3) Engine is unusually light and compact.

The latest N.S.U. engine, for example, weighs only 265 lb. with all accessories; an equivalent piston engine would probably weigh an extra 150 lb. This saving in weight, together with compact overall dimensions, enabled the N.S.U. designers to install the engine ahead of the front wheels with an overall economy in space.

Problems in Design

Unfortunately, the engine presents some difficult problems to offset the impressive list of advantages. These are concerned with the sealing system, combustion efficiency, and production costs. No engineering training is needed to appreciate the difficulty of designing durable and effective sealing devices to prevent gas leaks from occurring between one chamber and another, remembering the extreme differences in pressure and temperature that exist during the various phases of the working cycle.

The development of piston rings to their present high standards of gas sealing, oil con-

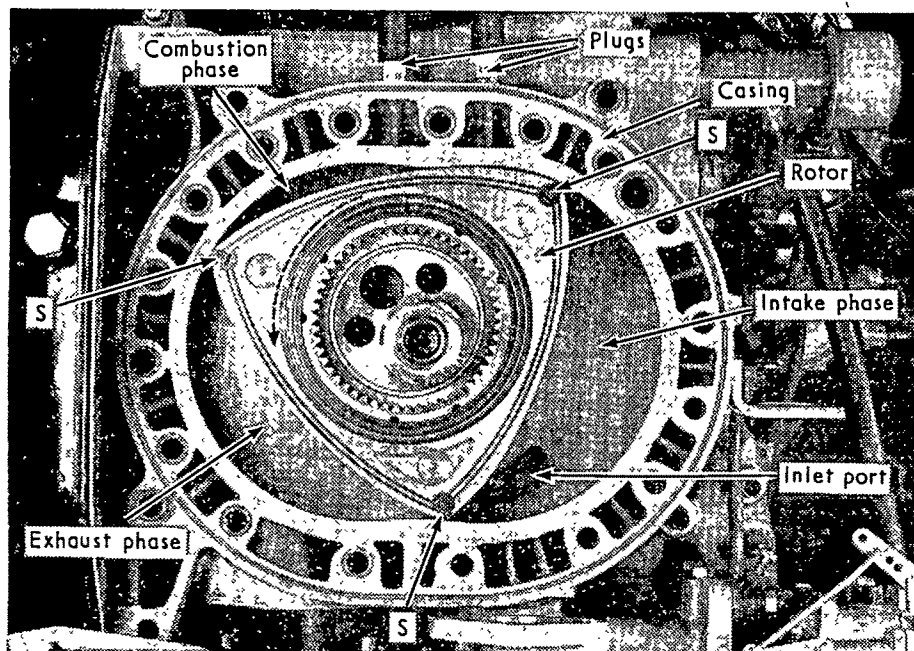


FIG. 1.—A Wankel engine with an end cover removed to show the three-cornered rotor and other mechanical details.

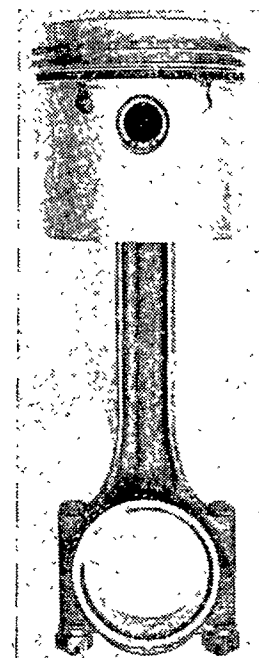


FIG. 2.—Typical reciprocating parts of a conventional engine (Jaguar) showing the three rings which provide a seal between the piston and cylinder.

tol, and durability has taken many years—and yet a springy circular ring is a simple device in comparison with the seals that must be fitted to the three longitudinal peaks, the flat ends, and the six corners of a Wankel rotor. Furthermore, the seal at each peak, or apex, presents only one line of defence, whereas three rings in series are usually fitted to a piston (see Fig. 2). Like piston rings, the Wankel seals are spring-loaded and must be lubricated in order to last for a reasonable mileage.

At the present time lubricant for the seals is provided by a metering pump which feeds oil into the fuel pump at a rate which varies according to engine speed and throttle opening. It has been claimed by N.S.U. that this system gives adequate seal lubrication in return for an oil consumption amounting to 1% of the fuel used; say 3,000 m.p.g. on oil for a car giving 30 m.p.g. on petrol. This is a higher oil consumption than in many piston engines, but is acceptable.

Casings are made of aluminium alloy, mainly for the reason that the good conduc-

tive properties of this metal help to lessen the temperature differences between the hot and cool sections of the engine. To provide the durable and smooth inner surface required for satisfactory sealing (and seal life) the interior of the casing is electroplated with a hard metal, such as chromium. This coating then has to be finished in a special grinding machine, which adds to the production costs.

Combustion is something of a problem because the shape of the chamber is largely predetermined by the geometry of the engine. In order to get regular firing and efficient burning at all speeds and loads, a dual carburation system has been found necessary. One part of the system has a restricted choke (and passage) which gives a sufficiently high gas speed for starting, idling, and light loads. A second and larger "channel" comes into action for full throttle operation. Latterly combustion problems have been accentuated by the legal restrictions on exhaust gas pollution which will come into force in the United States on 1 January next and which

will probably also apply, later on, in many other countries.

Two sparking plugs per rotor are used both by N.S.U. and by Mazda. The main reason is that the optimum position for the spark varies according to operating conditions. A second reason is the fact that the cycle of events in a Wankel engine provides no "rest period" for the plugs, so that failures occur more often than in piston engines.

Summing up, it would be rash at this stage to predict that the Wankel engine is destined to supersede piston engines. Much more will be known when service experience with thousands of rotary-engined cars (in private, inexpert hands) has been accumulated. The N.S.U. engineers also believe that, with further development, manufacturing costs will be reduced and may even turn out to be less than that of an equivalent piston engine.

It will be very interesting to follow the future progress of a design that has a great deal of merit but which also presents some formidable difficulties.

PARLIAMENT

Health Services Bill

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The Health Services and Public Health Bill, which the Government have introduced in the Commons (it was read a first time on 22 November) is an omnibus measure of 74 clauses, plus four schedules. Much of it is a collection of minor changes in health and welfare service administration that has accumulated on the Ministry shelves waiting the arrival of the rare legislative opportunity "Parliamentary Time" to be put right.

It does also, however, impose new powers and obligations on local authorities, and it introduces a new hospital designation.

"University Hospitals"

Clause 5 enables the Minister of Health to designate by order certain hospitals which provide teaching facilities as "university hospitals"—a designation which will be an alternative to that of "teaching hospital" under existing provisions. The hospital or group to be so designated will be those that provide, or are to provide, for a university "facilities for undergraduate or postgraduate clinical teaching." Such hospitals will be administered by hospital management committees and not boards of governors.

The Minister is enabled by clauses 1 and 2 to make accommodation in Health Service hospitals available for private patients, without the accommodation having to be especially set aside for the purpose. These facilities are to be available for "resident patients who undertake . . . to pay such charges" as the Minister may determine; and in so determining the Minister is authorized to classify hospitals and fix the charges to be made, making different charges for different accommodation, different services, and different circumstances. The clause retains the condition that the use of hospital accommodation

shall be determined by the urgency of the demand on it.

The power to fix charges for private non-resident patients, and for amenity beds, contained in clauses 2 and 4, is specifically attached to the Minister.

Local Authority Services

In the local authority services the Bill imposes on the authorities the duty of providing a domestic help service "on such a scale as is adequate for the needs of their area," and includes the provision of laundry facilities. It amends existing legislation by enabling midwives, health visitors, and nurses to attend patients elsewhere than in their own homes. Local authorities are also to be enabled to accommodate the elderly and the handicapped in registered homes run privately for profit, as well as in voluntary or local authority homes as at present.

Opticians, dentists, and pharmacists will be able under the new provisions to engage in private practice at health centres—there are new definitions of "dispensing" and "ophthalmic" opticians—on terms and conditions to be fixed by the Minister. The membership of executive councils is increased to 30 to include the general ophthalmic service now put on a permanent basis.

Questions in the Commons

Registration under Abortion Act

Dr. JOHN DUNWOODY (Falmouth and Camborne, Lab.) asked the Minister of Health on 27 November how many private nursing-homes had applied for forms to be registered under the Abortion Act 1967.

Mr. K. ROBINSON: I have had 100 applications, of which 89 are from private nursing-homes.

Sir JOHN GILMOUR (East Fife, Con.) asked for similar information for Scotland.

Mr. W. ROSS: So far applications have been received from five establishments, of which two are in the county of Stirling and one each in Edinburgh, Dundee, and the county of Dumfries. These applications have not yet been considered.

Doctor-Patient Ratio

Mr. A. BUCHANAN-SMITH (North Angus and Mearns, Con.) asked the Minister of Health if he would state the ratio of patients to general practitioners in 1967.

Mr. ROBINSON: Final figures are not yet available, but the estimated average number of patients on the lists of doctors providing full medical services in England and Wales on 1 October 1967 was 2,470. The true number of patients per doctor will be slightly smaller, since it is not possible to eliminate all duplicate entries from doctors' lists.

Mr. BUCHANAN-SMITH asked the Secretary of State for Scotland what was the number of doctors providing unrestricted general medical services in each of the past five years, and what was the average number of patients per doctor.

Mr. W. ROSS gave the following figures:

	Principals Providing Unrestricted General Medical Services	Estimated Average Number of Patients
1963	2,633	1,996
1964	2,656	2,005
1965	2,611	2,049
1966	2,573	2,083
1967	2,583	2,082

(The figures in the second column are inflated by up to 3%, since it is not possible to eliminate all duplicate entries from doctors' lists.)

MEDICAL NEWS

College of Pathologists

The College of Pathologists held its fourth annual general meeting on 22 November at the Royal College of Physicians, London. Dr. J. W. HOWIE, president, was in the chair. It was announced that the following had been re-elected honorary officers for the forthcoming year: Dr. J. W. HOWIE, *president*; Professor J. GOUGH and Professor N. H. MARTIN, *vice-presidents*; Professor T. CRAWFORD, *registrar*; and Dr. F. HAMPSON, *treasurer*.

In the afternoon Sir HANS KREBS, F.R.S., and Sir RUDOLPH PETERS, F.R.S., were admitted to the honorary fellowship of the College at a ceremony preceding the fourth Foundation Lecture, which was given by Professor R. R. A. COOMBS, F.R.S., his subject being immunopathology.

The annual dinner was held in the Royal College of Physicians the same evening. Sir HECTOR MACLENNAN proposed the toast of the College, to which the President responded. The toast of the guests was proposed by Professor N. H. MARTIN, and Sir HAROLD HIMSWORTH, F.R.S., expressed their thanks.

Brompton Hospital Extension

A new wing at the Brompton Hospital, London, was officially opened on 17 November by the MINISTER OF HEALTH. It houses a department of radiology, operating-theatre suite, cardiology department, and a paediatric unit, the cost of which is being met from the hospital's endowment fund. In his address the Minister referred to the discussions that were taking place about the future relationships between the Brompton Hospital, National Heart Hospital, Institute for Diseases of the Chest, and Institute of Cardiology. He was encouraged, he said, by the progress made on proposals for joint development. The extension has cost about £300,000.

Course in Basic Medical Sciences

A revision course in basic medical sciences will be held at Addenbrooke's Hospital, Cambridge. The course is intended mainly for anaesthetists preparing for the March 1968 primary F.F.A. R.C.S. examination, but others are welcome to attend. It will be held every Saturday from 30 December 1967 to 16 March 1968 and will consist of 60 lectures and demonstrations (anatomy and pathology, 11 each, pharmacology 16, and physiology 22). The fee for the course will be £20, which will include refreshments. Further details and programme may be obtained from the Secretary, Cambridge University Medical School, Tennis Court Road, Cambridge.

Importation of Carcinogenic Substances

An Order in Council prohibiting the importation into the United Kingdom of certain chemicals which can cause cancer and are used in the rubber, chemical, paint, and dye-stuffs industries was published last week. The chemicals are beta-naphthylamine, benzidine, 4-aminodiphenyl, 4-nitrodiphenyl and their salts and any substance or article containing any of these compounds. The order complements the carcinogenic substances regulations made in June prohibiting the manufacture and use of these chemicals in this country. Exemption from the prohibition may be granted when the material is to be used in medical or scientific research.

The order will come into operation on 9 December. (*Carcinogenic Substances (Prohibition of Importation) Order, S.I. 1967, No. 1675, H.M.S.O. 8d.*)

Irradiation of Food

The Advisory Committee on the Irradiation of Food (see *B.M.J.*, 27 May, p. 583) has prepared a memorandum outlining the functions of the committee and giving advice to those who seek any exemption from the regulations. Copies can be obtained from the Secretary to the Committee, Room D303, Division I.F.(B), Ministry of Health, Alexander Fleming House, London S.E.1.

N.Y. Recognition of British Graduates

The Secretary of the Board of Medical Examiners, New York, in reply to an inquiry about the recognition of British medical qualifications in New York State, makes the following observations:

"Each case of a British medical graduate is considered individually by the Board of Regents on the submission of completed petition forms. In certain instances in which there is evidence of advanced and extensive acceptable hospital training and in which the physician has obtained the F.R.C.S. of England, M.R.C.P. of London or Edinburgh, F.F.A. or the F.R.C., endorsement of the British registration may be considered by the Board of Regents.

"If a physician wishes to petition the Board of Regents for an evaluation of his education and training and a determination as to his eligibility for admission to the New York State medical licensing examination or to medical licensure, he should notify this office [State Education Department, Albany, New York 12224] giving the name of the medical school from which he graduated and the date of graduation. Instructions and appropriate forms will then be sent."

Singapore Academy of Medicine

The office-bearers of the Academy of Medicine at Singapore for the year 1967-8 are as follows: *master*, Professor K. S. RATNAM; *assistant master*, Dr. SEAH CHENG SIANG; *scribe*, Dr. LEE YONG KIAT; *bursar*, Mr. ROBERT C. K. LOH; *bedel*, Dr. CHEW CHIN HIN; *censors*, Lieut.-Col. CHOO JIM ENG, Mr. YAHYA COHEN, Dr. GWEE AH LENG, Dr. GEORGE TAY, and Dr. YEOW SEANG AUN.

Termination of Pregnancy

The Ministry of Health announces that applications for approval of premises for the termination of pregnancy should be made forthwith (see *B.M.J.*, 11 November, p. 368). It points out that if they are delayed, and the number is substantial, there may be difficulty in clearing them before the Abortion Act comes into operation.

Fellowships in Mental Research

The Mental Health Research Fund has announced the following awards: John Spedan Lewis Foundation Fellowship for Research into Psychosomatic Illness (£4,970) to Dr. ANDREW ZEALLEY, Royal Edinburgh Hospital, for study of the importance of anxiety in the cause and management of asthma; Brunner Fellowship for Research in Depression (£9,000) to Dr. BRENDA HERZBERG, Epsom, for study of the effects on emotional mood of certain forms of oral contraceptive pill; Mental Health Research Fund Senior Fellowship (£6,866) to Dr. JOHN OXBURY, Oxford, for study of the functions of the temporal lobe of the brain in relation to epilepsy.

People in the News

► Dr. JAMES PATTERSON has been appointed medical secretary of the Medical and Dental Defence Union of Scotland, Ltd. He will take up his duties on 1 February 1968.

Recent Publications

Current Medical Research: a reprint of the articles in the Medical Research Council's annual report April 1966 to March 1967. The articles review advances made in some of the subjects with which the Council is concerned, but the scope of the reviews is not confined to work sponsored by the Council. H.M.S.O., 8s. net.

British Hospitals—Home and Overseas (1967 edition), sponsored by the British Hospitals Export Council in association with the King's Fund Hospital Centre, demonstrates British achievement in hospital design, construction, and equipment. The volume, which is illustrated by numerous pictures and diagrams, is intended to be a source of reference for those concerned with the provision of hospital services anywhere in the world. It contains a bibliography. Published by Trafalgar Press Ltd., 29 Palace Street, London S.W.1, price £1 post free.

Therapeutic Diets in Hospitals: a nutritional guide for hospital caterers, published by King Edward's Hospital Fund for London, 14 Palace Court, London W.2, 8s. 6d. post free.

W.H.O. Guide to Ship Sanitation, by VINCENT B. LAMOUREUX, H.M.S.O., £1.

The Psychosomatic Disorders: a pamphlet published by the Mental Health Research Fund (38 Wigmore Street, London W.1), price 1s. 6d., plus 3d. postage.

Coming Events

Postgraduate Medicine, 1967 (T.V. Programme).—"Growth in Childhood," Scottish Television, 4 December (11.50 p.m.), repeat 6 December (1.10 p.m.). "Advances in Reconstructive Surgery," Tyne Tees Television, 5 December (1.15 p.m.), repeat 10 December (10.15 a.m.).

Hungarian Scientific and Technical Days in London.—13 December. Papers on "New System Cobalt Units" and "An Analysis of the Respiratory Function in Post-traumatic Failures." Tickets and full details from the London Chamber of Commerce (Inc.), 69 Cannon Street, London E.C.4.

Sheffield University Faculty of Medicine.—Course in dermatology for general practitioners, 1-5 April 1968. For details see advertisement on page xxix.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Sunday, 3 December

INSTITUTE OF LARYNGOLOGY AND OTOLGY.—10.15 a.m., seminar for general practitioners by Mr. A. Radcliffe.

Monday, 4 December

BLAIR BELL RESEARCH SOCIETY.—At Royal College of Obstetricians and Gynaecologists, 5.30 p.m., ordinary meeting.

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Professor A. S. Breathnach: The Melanocyte and Langerhans Cell.

INSTITUTE OF DISEASES OF THE CHEST.—6.15 p.m., Dr. J. N. Pattinson: Acquired Pulmonary Stenosis.

INSTITUTE OF LARYNGOLOGY AND OTOLGY.—5.30 p.m., Professor I. Friedmann, Dr. D. A. Osborn, Dr. M. I. Wright: clinicopathological conference.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. R. G. Chittam: Chromosomes—Methods of Study; 6.30 p.m., Dr. D. E. H. Tee: Cancer—Experimental Carcinogenesis. ●

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—8.30 p.m., FitzPatrick lecture by Dr. P. E. Thompson Hancock: Thomas Hodgkin, Physician and Philanthropist.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—5 p.m., Wade demonstration—I by Mr. A. A. Gunn: Surgical Pathology of the Gall Bladder.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—At Wolfson Institute, 4 p.m., Dr. Roger Bannister: Investigation and Treatment of Idiopathic Orthostatic Hypotension.

SCOTTISH TELEVISION LTD.—11.45 p.m., Growth in Childhood. (Sponsored by Glasgow Postgraduate Medical Board.)

SOCIETY FOR MEDICAL AND DENTAL HYPNOSIS.—At Royal Society of Medicine, 8 p.m., clinical meeting, cases will be presented.

Tuesday, 5 December

B.B.C. 2 TELEVISION.—1.15 p.m., medicine today: Parkinsonism. (Sponsored by A.S.M.E.)

BOLTON AND DISTRICT MEDICAL SOCIETY.—At Gymnasium, Bolton Royal Infirmary, 8.15 p.m., medico-legal lecture by Dr. L. A. Liversedge: Some Neurological Problems.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Kennedy Lecture Theatre, Institute of Child Health, 5.30 p.m., Dr. E. T. O. Slater: The Genetics of Schizophrenia.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Dr. E. A. Cronin: Mechanism of Pigmentation and its Anomalies.

MANCHESTER MEDICAL SOCIETY: SECTION OF SURGERY.—At Large Anatomy Theatre, Manchester University Medical School, 5 p.m., Mr. A. B. Wallace: The Plastic Surgeon in Paediatrics. NORTHAMPTON GENERAL HOSPITAL.—8 p.m., Professor P. B. Beeson: General Considerations in Management of Infections.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Professor

W. Linford Rees: Drug Addiction.

ROYAL COLLEGE OF GENERAL PRACTITIONERS: SOUTH LONDON FACULTY.—At General Practitioners Centre, St. Mary's Road, London S.E., 8.15 p.m., Dr. T. H. Bewley: Drug Addiction.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—5 p.m., Wade demonstration—II by Mr. A. A. Gunn: Surgical Pathology of the Gall Bladder.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. A. K. Monro: Tumours of the Colon.

St. CHARLES'S HOSPITAL MEDICAL CENTRE.—8.45 p.m., Dr. M. Feiwel: Dermatological Colour Slides.

WESTMINSTER MEDICAL SCHOOL.—At Keene Theatre, 5.15 p.m., Dr. J. G. B. Thurston: Intensive Coronary Care.

Wednesday, 6 December

BROOK GENERAL HOSPITAL.—8.15 p.m., neurology meeting with presentation of cases. Dr. D. Geraint James: Neurosarcoidosis.

CAMBRIDGE MEDICAL SOCIETY.—At University Arms Hotel, 7.30 p.m., supper meeting, Professor K. Simpson: Crime and the Doctor (illustrated).

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

INSTITUTE OF DERMATOLOGY.—4.30 p.m., Professor

F. A. Whitlock: Psychosomatic Disease—II.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. R. V. Gibson: Clinical Assessment of Heart Disease.

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

ANNALS OF THE RHEUMATIC DISEASES

Contents of the November issue are as follows:

Rheumatoid Pleuritis. W. C. Walker and V. Wright.

Clinical Background of Rheumatoid Vascular Disease. M. Wilkinson and W. N. Torrance.

Lipid Content of Human Costal and Articular Cartilage. R. A. Stockwell.

A Clinical and Serological Study of Rheumatoid Arthritis. Mary Corbett, June M. Downes, and F. R. Schmid.

Mefenamic Acid in Rheumatoid Arthritis. A. B. Myles, P. A. Bacon, and K. A. Williams.

An Investigation of the Prevalence and Significance of Gastric Parietal-cell Autoantibody in Rheumatoid Arthritis. E. M. Armstrong.

Influence of Lymphatic Tissue on the Development of Adjuvant-Induced Polyarthritis in Rats. A. G. Ryzewski.

Ultrastructure of Synovial Membrane in Osteoarthritis. S. Roy.

Haemolytic Complement Level and Ragoocyte (R A Cell) Concentration in Synovial Fluid. A. P. Felder, F. Delbarre, and G. Krassinine.

Influence of Trauma on the Development of Chronic Inflammatory Polyarthritis. K. A. Williams and J. T. Scott.

Rheumatoid Arthritis of the Temporomandibular Joints. J. J. Marbach and H. Spiera.

Immunological Characterization of Some Basement Membrane Antigens. G. Loewi.

Nature of Anaemia in Rheumatoid Arthritis. VII. Storage of Iron in Rheumatoid Disease. A. A. H. Lawson, E. T. Owen, and A. G. Mowat.

Ibuprofen in the Treatment of Rheumatoid Arthritis and Osteoarthritis. P. L. Boardman, G. Nuki, and R. Dudley Hart.

Shakespeare's Rheumatology. G. E. Ehrlich.

Book Reviews. Icterden Society. Abstracts. Index, 1967.

Volume 26, No. 6. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

JOURNAL OF CLINICAL PATHOLOGY

Contents of the November issue are as follows:

Activation of Lymphocytes. R. J. V. Pulvertaft and Isobel Pulvertaft.

Lipofuscinosis of the Gastrointestinal Tract in Man. Bernard Fox.

Tracheopathia Osteoplastica. S. P. B. Way.

Acute Necrotic Alveolitis and Perivascular Encephalomyelitis Associated with Hypertension and Renal Infection. A. A. Miller and F. Ramsden.

Incidence and Significance of Argentaffin and Paneth Cells in Some Tumours of the Large Intestine. N. M. G. Hiss.

Significance and Interpretation of Laboratory Tests in Pulmonary Aspergillosis. Mary P. English and A. H. Henderson.

Further Observations on Inclusion-bearing Cells in Urinary Sediment in Infectious Diseases. J. F. Boyd and Nada Nedelkoska.

Granulomatous Giant Cell Reticulosis Associated with Cases of Treated Leukaemia. G. Krasznai, S. Keresztury, and L. Szűcs.

Platelet Adhesiveness in Diabetes Mellitus. S. Shaw, G. D. Pegrum, Sylvia Wolff, and W. L. Ashton.

Red Blood Cell Abnormalities in Cardiac Valvular Disease. J. Forshaw and L. Harwood.

Hyaline Droplet Formation in the Renal Epithelium of Patients with Haemoglobinuria. S. J. Bryant.

Hyaline Cast Formation in Patients Treated with Cephaloridine. W. D. Linsell, A. Pines, and J. W. Hayden.

Observations on the Levels of γ G, γ A, and γ M Globulins, Anti-A and Anti-B Agglutinins, and Antibodies to Escherichia coli in Down's Anomaly. M. Adinolfi, Brigitte Gardiner, and Wendy Martin.

Mycoplasmas and Recurrent Oral Ulceration. A. M. Gordon, H. M. Dick, D. K. Mason, W. Manderson, and W. R. Crichton.

Resistance to Cloxacillin Among Hospital Staphylococci. G. C. Turner and P. E. Cox.

Serological Diagnosis of Amoebiasis by Immunofluorescence. Somnate Boonpucknavig and R. C. Nairn.

Evaluation of the Fluorescent Antibody Technique for the Diagnosis of Smallpox. A. L. A. El-Ganzoury.

Fatal Transfusion Reaction Due to Serratia marcescens. W. A. Black, A. Pollock, and Elizabeth L. Batchelor.

Importance of Potency in Typing by Colicine Production. J. McGeachie and W. McCormick.

Thyroid Disease Following the Administration of Thorotrast. A. O. Langlands and Kate Hermann.

Use of Diethylenetriamine Penta-acetic Acid (D.T.P.A.) in the Clinical Assessment of Total Body Iron Stores. L. W. Powell and M. J. Thomas.

Semi-automated Method for the Determination of Free Fatty Acids in Plasma. Joyce D. Baird, M. W. Black, and D. E. Faulkner.

New Automated Method for Measuring Glucose by Glucose Oxidase. D. G. Cramp.

Technical Methods

Red Cell Volume Distribution Histograms for Establishing the Normal Range Using the Coulter Plotter Model J. K. Crane and A. D. Welf.

Measurement of Red Cell Diameter by Image Shearing. P. N. Coleman.

The Association of Clinical Pathologists: 79th General Meeting.

Book Reviews.

Index to Volume 20.

Volume 20, No. 6. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

INSTITUTE OF NEUROLOGY.—6 p.m., Dr. J. Wilson, and 7 p.m., Professor J. N. Cummings: Genetically Determined Neurological Disease of Children.

INSTITUTE OF UROLOGY.—5 p.m., Mr. D. M. Wallace: Urinary Exfoliative Cytology and the Industrial Hazard in Carcinoma of the Urethelium.

MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—At Large Anatomy Theatre, Manchester University Medical School, 5 p.m., Dr. G. F. M. Russell: Metabolic Aspects of Anorexia Nervosa.

OXFORD UNIVERSITY MEDICAL SCHOOL.—At Nuffield Maternity Home Lecture Theatre, Radcliffe Infirmary, 5 p.m., Dr. G. Hamilton Fairley: Immunity in Hodgkin's Disease.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNARCOLOGISTS.—5.30 p.m., postgraduate Museum demonstration by Dr. F. A. Langley: Unusual Tumours of the Myometrium.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. E. H. Ahrens (New York): Raids on the Economy of Cholesterol in Man.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) Clinicopathological conference by Professor J. P. Shillingford: Arrhythmias. (2) 2 p.m., Renal Unit, urology seminar. (3) 2 p.m., pathology guest lecture.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE: EDINBURGH BRANCH.—At Postgraduate Board of Medicine, Hill Square, 7.45 p.m., Brigadier J. Mackay-Dick and Dr. Joyce Coghlan: Leptospirosis.

SCOTTISH TELEVISION LTD.—1 p.m., Growth in Childhood. (Sponsored by Glasgow Postgraduate Medical Board.)

STOKE MANDEVILLE HOSPITAL.—6 p.m., Squadron Leader A. McCracken: Virology of Respiratory Infections.

WEST MIDDLESEX HOSPITAL.—At Lecture Theatre, 5 p.m., Professor M. D. Milne: Drugs, Poisons and the Kidney.

Thursday, 7 December

ANGLO-AMERICAN MEDICAL SOCIETY.—At Paediatric Research Unit, Cameron House, Guy's Hospital Medical School, 7.30 p.m., scientific meeting.

DUNDEE UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Dr. G. de J. Lee: Blood Flow in the Lung.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—(1) 5 p.m., Erasmus Wilson demonstration by Dr. D. Haler: Some Unfamiliar Causes of Sudden Death; (2) 5.30 p.m., Otolaryngology lecture by Mr. J. S. Calnan: Wound Healing.

ROYAL PHOTOGRAPHIC SOCIETY: MEDICAL GROUP.—7 p.m., Mr. C. A. Duncan: Educational Technology Laboratories—Future Patterns for University and Hospital Illustration Services.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. J. S. Calnan: Advances in Understanding Lymphoedema.

St. MARGARET'S HOSPITAL.—At Epping, Essex, 8.30 p.m., Edward Sharp memorial lecture by Mr. G. F. Gibberd: Factors Concerned with the Progressing Safety of Childbirth.

Friday, 8 December

INSTITUTE OF CHILD HEALTH.—At Kennedy Lecture Theatre, 5.30 p.m., Dr. W. H. Hitzig (Zurich): Abnormal Susceptibility to Infections.

NORTHAMPTON MEDICAL SOCIETY.—8.30 p.m., Dr. J. D. N. Nabarro: Diabetes Mellitus.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Dr. J. W. Laws: An Assessment of the Value and Limitations of Arteriography. (2) 11.30 a.m., Mr. P. M. Martin: clinicopathological conference (vascular). (3) 4 p.m., lecture by Professor D. D. Reid.

WEST KENT MEDICO-SURGICAL SOCIETY.—At Medical Centre, Lewisham Hospital, 7 p.m., Purvis supper and oration by Dr. C. O. Carter: Genetics and Future Public Health.

Saturday, 9 December

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Board Room, Chesterton Hospital, 10.30 a.m., all-day symposium on Geriatrics.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—9.30 a.m., anaesthetic teaching meeting: Anaesthesia and the Burnt Patient and Aspects of Heart Disease.

Sunday, 10 December

ROYAL NORTHERN HOSPITAL LONDON.—10.15 a.m., Dr. D. Geraint James: clinical conference

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Atiology*, London W.C.1. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 9 DECEMBER 1967

Pointers

Cerebral Angiomas: Occurrence of fatal haemorrhage unpredictable and conservative treatment is justified in majority of cases. Bleeding from small angiomas is dangerous in children, but haemorrhage from large ones is more common in later life after years of progressive cerebral disability. (p. 571).

Coxsackie B5 Virus: Increased number of infections reported in summer of 1965, especially among children (p. 575). Leader at p. 570.

Subclinical Tropical Sprue: Nonspecific jejunal abnormalities are not evidence of this condition, according to results of tests on forty asymptomatic Thai subjects (p. 578).

Intensive Care: Report of B.M.A. Planning Unit. Leader at p. 569.

Bell's Palsy: Measurement of threshold for anodal galvanic stimulation gave accurate prognosis in 90% of cases. A.C.T.H. gel administration reduced overall incidence of denervation by two-thirds in a large group of patients (p. 581).

Antibodies to Meningococci: Gamma-M globulin is an important humoral defence mechanism, and its presence in the blood restricts systemic meningococcal infection to the C.S.F. (p. 583).

Permanent Arteriovenous Fistula: Surgical access to circulation for regular dialysis treatment successfully effected in 14 patients (p. 586).

Thyrocalcitonin Deficiency: Demonstrated by defective response to intravenous calcium infusion after radical treatment for thyroid disorders by surgery or radioiodine (p. 589).

Eyelid Retraction: Improvement obtained with local guanethidine whether aetiology was thyrotoxic or idiopathic, and precautions suggested to avoid toxic effects in long-term maintenance therapy (p. 592).

Pulmonary Embolism: Value of phlebography in determining source (p. 596); Successful late removal of pulmonary embolism (p. 598). Leader at p. 566.

Case Reports: Psychiatric drugs producing hypoglycaemic coma (p. 599); Cronkhite-Canada syndrome (p. 601); Haemoperitoneum associated with ruptured gall bladder (p. 602).

Tropical Medicine: Malnutrition in childhood (p. 603).

Postgraduate Medical Education: Proposals in report commissioned by the Nuffield Provincial Hospitals Trust (p. 613).

Conferences: Symposium on tropical splenomegaly (p. 614); Aspects of anxiety discussed at the Royal College of Physicians (p. 614).

Proceedings of Council: Public health dispute; administrative structure of N.H.S.; B.M.A. finances; Planning Unit (*Supplement*, p. 65).

Young Disabled and Sick in Hospital

In 1959 the welfare of children in hospital was the subject of a report¹ by a Central Health Services Council committee under the chairmanship of Sir Harry Platt, and subsequently the Minister invited hospital authorities to act on its recommendations. On a date in 1964, and on a further date in 1965, hospital authorities took a census of patients aged under 17 in National Health Service hospitals in England and Wales to obtain information about children and adolescents in hospital. The census² showed to what extent hospital practice accorded with the recommendations of the Platt Committee, and it disclosed 22,047 children and adolescents in hospitals in 1964, and 22,350 in 1965—or 1.8 children and adolescents per 1,000 of the population under 17 years of age. Most of them were under 12, and the census showed that 5% were being nursed in adult wards without any separation, while a further 13% were in adult wards but separated from adult patients. One-third of the adolescents were nursed in children's hospitals or in children's wards, one-tenth in adult wards but separated, and well over half in adult wards without separation.

The Platt Committee had recommended that the ward sister should be a registered sick children's nurse as well as S.R.N., but the census showed that only about half of the young children were under the care of registered sick children's nurses. Again, the committee had recommended that a children's physician should have a general concern with the care of all children, but this practice was not by any means evident. Other examples could be mentioned of failure to implement recommendations of an expert committee which the Ministry of Health had "invited" hospital authorities to do.

A pilot survey³ carried out by the two geriatric physicians in Fife, R. Rankine and R. M. L. Weir, with the aid of a grant from the South-eastern Regional Hospital Board (Scotland), adds to our knowledge about the plight of the younger disabled and chronic sick. It covered a sample population of 30,000–35,000 persons (about 10% of the total population of the county), and the two physicians had the assistance of 14 general practitioners as well as the local health departments. The survey included people aged 15 to 60 years suffering from long-term physical illness or disability to the extent that they were unable to take part in the normal activities of daily living. It revealed 87 cases, or 2.63 per 1,000 population, the lowest rate being in a rural practice and the highest in a practice largely confined to one of the older mining communities. The sexes were equally affected, and the incidence increased with age. Multiple sclerosis was the most common disability, closely followed by rheumatoid arthritis, cerebrovascular disease, and chronic bronchitis. Only 5 of the 87 patients were in institutional care; the care of the remainder devolved increasingly on the parents, usually the mother.

The authors of this report suggest that unsatisfactory housing conditions were of little importance, though they were distressed at the number

of persons who might have been rehoused in ground-floor accommodation. The patients themselves thought that the interests of the family had to be recognized, and were determined to be as independent as possible. The authors conclude that the number of such persons under the age of 35 was small and that in almost every respect they fared better than their elders, particularly in terms of medical care and of opportunities for employment. They confirmed the statement in the Piercy Report⁴ that "doctors still need to be better informed of the scope, nature and potentialities of rehabilitation," and suggested that local authorities needed to know more about the chronic sick and disabled in their areas. They considered that a hospital unit of 60 beds should be adequate to serve the needs of a population of about 300,000.

It is difficult to determine precisely the size of the problem. The number of substantially and permanently handicapped people aged between 16 and 65 years in Great Britain at the end of 1964 on the registers of local authorities was 164,000. In 1963 the Ministry of Pensions and National Insurance recorded 225,800 people in Great Britain between the ages of 18 and 65 years (60 for women) who had been receiving sickness benefit for two years or more, with perhaps a further 100,000 sick or handicapped people of this age group in receipt of National Assistance allowances for the same period. There are thus, possibly, some 500,000 people of working age in Great Britain so handicapped as to be incapable of paid employment, though with the exclusion of mental illness and mental subnormality the estimate might fall to 370,000. The most unsatisfactory position relates to the thousands of young chronic sick patients, of whom perhaps only one-tenth are in special units designated for their care. Many of the remainder are scattered through geriatric wards. Though some of these are middle-aged, this is no excuse for a lack of interest and drive that is an unhappy reflection on our hospital service.

It is often said that many such patients prefer to be in hospital wards, however unsuitable, near their homes and former environment. But this is not always borne out by experience, for many of the excellent homes provided by voluntary organizations attract patients from all over the country, who soon adapt themselves to the new community in which they are placed. This type of patient often comes to the hospital service as a social emergency. Consequently there might well be established in each region a hospital unit, or units, for the young chronic sick which would provide not only a hospital ward with single and double rooms and cubicles but occupational rooms of sufficient variety to recognize that the patient is usually going to spend the remainder of his days in that hospital, and needs an environment appropriate to his condition and to his mental faculties and interests. Such units might be of 25-50 beds, and without doubt relatives and friends would not resent travel if they were satisfied by the better conditions for the patients. The unit for young chronic sick could be in the environs of the general hospital rather than in an isolated institution, and the patients should be in the clinical charge of a special physician. More needs to be done to arrange temporary admissions of patients for their own benefit and for the relief of relatives, and to organize holidays in a new setting.

These two reports merit careful study, and point the way to a more active policy to alleviate the lot of these unfortunate, but not always recognized, children and young and middle-aged people suffering from long-term disability and sickness.

Pulmonary Embolectomy

When Trendelenburg¹ first told of his method of removing pulmonary emboli his vision and daring were received with enthusiasm. Sadly, the patient's strength was rarely able to match the surgeon's skill, and only a few cases of emergency embolectomy were successful. The development of cardiac surgery and the heart-lung bypass machine brought a new understanding of the physiology and surgery of the heart, and the possibility of successful pulmonary embolectomy became real. Now all cardiac surgeons practise emergency embolectomy, most of them using the heart-lung bypass,²⁻⁴ but some good results have been achieved without it.⁵ It is no longer a question of whether an embolectomy can be done, but when is the right time to do it.

Pulmonary embolism presents in four ways: firstly, sudden death; secondly, collapse, hypotension, and right heart failure followed by death or slow recovery over a few hours; thirdly, sudden severe pain, haemoptysis, and collapse followed by a steady, sometimes rapid, cardiovascular recovery; and, fourthly, without clinical disturbance of the cardiovascular system.

In making the diagnosis the surgeon will in some cases note the clinical signs of peripheral vascular collapse, high central venous pressure, third heart sounds, characteristic changes in the E.C.G., and the absence of vascular markings on the chest radiograph. These are diagnostic if they are all present, but unfortunately many cases do not have these physical signs. Consequently some surgeons advocate doing a preoperative pulmonary angiogram to avoid operating on a coronary infarction—the main differential diagnosis. This takes time, as does lung scanning after the injection of labelled macroaggregates of albumin,⁶ and often there is no time to spare.

The approach to the management of the four clinical groups is slowly evolving along the following lines. Sudden death from pulmonary embolism should be treated by external cardiac massage, for in some cases the massage will break up the thrombus, move it on, and so allow some pulmonary blood flow. If the circulation is restored and the patient responds, then the massage is continued until the patient is anaesthetized and either put on a heart-lung bypass or given supportive perfusion with blood taken from the femoral vein, oxygenated, and returned to the arterial circulation. There is obviously no time to confirm the diagnosis before operation, and so it must be accepted that a certain number of these patients will

¹ Trendelenburg, F., *Langenbecks Arch. klin. Chir.*, 1908, 86, 686.

² Hayward, J., and Howqua, J., *Lancet*, 1964, 2, 771.

³ Makey, A. R., and Bliss, B. P., *ibid.*, 1966, 2, 1155.

⁴ Paneth, M., *J. thorac. cardiovasc. Surg.*, 1967, 53, 77.

⁵ Vosschulte, K., Stiller, H., and Eisenreich, F., *Surgery*, 1965, 58, 317.

⁶ Wagner, H. N., Sabiston, D. C., McAfee, J. G., Tow, D., and Stern, H. S., *New Engl. J. Med.*, 1964, 271, 377.

⁷ Browne, N. L., and James, D. C. O., *Lancet*, 1964, 2, 1039.

⁸ Hirsh, J., Hale, G. S., McDonald, I. G., McCarthy, R. A., and Cade, J. F., *ibid.*, 1967, 2, 593.

⁹ Gorham, L. W., *Arch. intern. Med.*, 1961, 108, 8.

¹⁰ Paneth, M., *Ann. roy. Coll. Surg. Engl.*, 1967, 41, 370.

¹¹ Barker, N. W., and Priestley, J. T., *Surgery*, 1942, 12, 411.

¹² Phear, D., *Lancet*, 1960, 2, 832.

¹³ Allison, P. R., Dunnill, M. S., and Marshall, R., *Thorax*, 1960, 15, 273.

⁴ *The Welfare of Children in Hospital*. Report of Committee of the Central Health Services Council. 1959. H.M.S.O.

⁵ *Report on the Census of Children and Adolescents in Non-Psychiatric Wards of National Health Service Hospitals*. Ministry of Health. 1967. H.M.S.O.

⁶ Rankine, R., and Weir, R. M. L., *An Enquiry into the Incidence of Chronic Illness and Disability in the Young and Middle-Aged*. 1967. Victoria Hospital, Kirkcaldy, Fife.

⁷ *The Rehabilitation, Training and Resettlement of Disabled Persons*. Cmd. 9883. 1956. H.M.S.O.

be found to have a normal pulmonary artery and an infarcted myocardium.

Those who collapse and remain very ill require surgical treatment, or possibly thrombolytic therapy.^{7,8} But there is usually time for diagnostic investigations,⁹ and emergency pulmonary angiography is of great help. Embolectomy can then be done, and this is the group of patients in whom the best results are obtained.¹⁰ It is difficult to decide when to operate, but failure to improve over one to three hours, with hypotension and a raised central venous pressure, are sound indications for surgery.

The third group, collapse followed by fairly rapid recovery, presents many problems. Though surgery is not needed to save life, two great risks threaten these patients. Firstly, there may be another embolus waiting in the legs which, added to the first, could kill (second emboli occur in 30% of patients).¹¹ Secondly, early cardiovascular recovery does not mean that the patient will ultimately attain normal health. D. Phear¹² has shown that 30% of patients who survive a major embolism have persistent and sometimes disabling dyspnoea, due either to the initial embolus or to recurrent small subclinical emboli. It seems reasonable to suggest that these patients should have their peripheral veins studied, as suggested by N. L. Browse and his colleagues (p. 596), and a pulmonary angiogram done, and then be considered for thrombolytic therapy or surgery. How much time is available for these investigations before the thrombus becomes so adherent that it is irremovable? The paper by Lord Brock and his colleagues published at page 598 of the *B.M.J.* this week sheds light on this question, for it shows that emboli can sometimes be removed months after impaction. Many cardiovascular surgeons have operated on pulmonary and peripheral arterial emboli after impaction and found some to be irremovable and others loose. More information is required about the natural history of emboli. Though they undergo lysis spontaneously and rapidly in the dog,¹³ there is ample clinical evidence to prove that this does not always happen in man. The increasing use of pulmonary embolectomy should expand our knowledge of the local lesion in the pulmonary artery.

The present trend is to be bold not only to save life but also to reduce the late morbidity. But this approach needs to be continually reviewed in accordance with the findings at operation and the long-term results.

Doctors' Diseases

In the evidence which the B.M.A. submitted to the Goodenough Committee it deplored the failure of the medical schools to exclude men and women who, though able to pass examinations, have not the requisite aptitude, character, or staying power for a medical career. The Committee agreed, and recommended¹ that there should be machinery not only to select students from this standpoint but also to weed out students who prove unsuitable. No one, however, was bold enough to state the criteria of rejection, or, more specifically, to say whether a propensity to some form of psychological illness should be regarded as a sign of unsuitability. Deans of medical schools might have very discrepant views on this matter, and on their ability to look sufficiently into the future of some nervous aspirant aged 18 or 19 to foretell his professional fitness or inadequacy. Nevertheless, the attempt has to be made, for the health and mental stability of doctors are matters of public as well as

private concern. It is therefore understandable that the authors² of a recent inquiry should express their surprise that there have been few studies of the amount of psychiatric illness in the medical profession. Their own findings are not particularly encouraging.

A hundred and ninety-two doctors who had been treated at either St. Andrew's Hospital, Northampton, or St. George's Hospital, London, were compared with "control" groups, presumably free from psychiatric illness. There were no differences between the doctors and non-medical patients (matched for age, sex, and social class) in the frequency of most sorts of disorder, except that neurotic depressive reactions and drug addiction were more common in doctors. Psychiatrically disturbed doctors showed a greater tendency than usual to fall by the wayside professionally; only 70% were on the *Medical Register* when followed up in 1964.

The proportions in which various branches of the profession were represented in the sample do not permit any simple conclusion to be drawn. General practitioners made up 53%, 12% were psychiatrists, and 11% were surgeons. A similar investigation³ of 93 doctors admitted to the Mayo Clinic for psychiatric treatment between 1956 and 1963 showed that 44 were general practitioners (about the same proportion as in the profession as a whole), 15 were physicians, 17 were surgeons, and 4 were psychiatrists. Evidently no single branch of the profession has a disproportionate pre-eminence in this respect. A third of the doctors had some form of psychotic illness, a fifth were neurotic, and most of the remainder had personality disorders. Treating them was exceptionally difficult because the doctors found it hard to accept the status of a patient and tended to withdraw from treatment too soon.

There are two aspects of psychiatric illness which are painfully prominent in this connexion—suicide and drug addiction. Analysis of the *Registrar General's Decennial Supplement* earlier in this century⁴ showed that among the occupational groups with the highest suicide rates were doctors and lawyers. It has been conjectured that this was because they "work under some degree of nervous pressure" and witness much misery and suffering. In a recent study⁵ in Oregon the suicide rate for doctors and lawyers was found to be three times as high as in "white-collar workers." Despite the known unreliability of official statistics of suicide, it must be regarded as an occupational disease of medical practice.⁶

The problem of addiction in doctors has also been long recognized. The Rolleston Departmental Committee⁷ that reported in 1926 said that "questions of exceptional difficulty have presented themselves in the cases of doctors who are themselves addicts," and the Brain Committee⁸ echoed this, pointing out that the number of doctors known to be addicts was disproportionately high. There were in Britain in 1960 68 "professional" addicts—doctors, dentists, pharmacists,

¹ *Report of the Inter-departmental Committee on Medical Schools*, 1944. H.M.S.O., London. Out of print.

² A'Brook, M. F., Hailstone, J. D., and McLauchlan, I. E. J., *Brit. J. Psychiat.*, 1967, 113, 1013.

³ Duffy, J. C., and Liten, E. M., *J. Amer. med. Ass.*, 1964, 189, 989.

⁴ Dublin, L. I., and Bunzel, B., *To be or not to be—a study of suicide*, 1933. New York.

⁵ Blachly, P. H., Osterud, H., and Josselin, R., *New Engl. J. Med.*, 1963, 268, 1278.

⁶ *Brit. med. J.*, 1964, 1, 789.

⁷ *Report of the Departmental Committee on Morphine and Heroin Addiction*, 1926. H.M.S.O., London.

⁸ *Drug Addiction: Report of the Interdepartmental Committee*, 1961. H.M.S.O., London.

⁹ Ehrhardt, H., *Bull. Narcot.*, 1959, 11, No. 1, p. 18.

¹⁰ Pearson, M. M., and Strecker, E. A., *Amer. J. Psychiat.*, 1960, 116, 915.

¹¹ Putnam, P. L., and Ellinwood, E. H., *ibid.*, 1966, 122, 745.

¹² Evans, J. L., *ibid.*, 1966, 122, 159.

and veterinary surgeons—constituting 15% of the total number of known addicts. According to the report sent to the United Nations from the United Kingdom doctors made up 81% of all the known “professional addicts,” including nurses. As always where drug abuse is concerned, the number of officially known addicts is almost certainly a much lower figure than the real situation would disclose. M. F. A’Brook and his colleagues² had among their 192 patients 30 who were addicted to some drug other than alcohol.

In Germany³ there were in 1957 4,861 addicts, of whom 12% were doctors. One doctor in 112 was an addict. Reports from the United States deal for the most part with selected populations of doctors—those treated in private¹⁰ or in the special hospital for addicts at Lexington, Kentucky.¹¹ Many psychopathological explanations of the development of addiction in these doctors have emerged from the intensive study they received, but there can be little doubt that the most potent factor in giving them an unhappy pre-eminence among addicts has been the easy access to drugs (though this is not of course the only important factor). It is noteworthy in this connexion that in a study by J. L. Evans¹² of 50 doctors’ wives who received treatment in a private psychiatric hospital between 1960 and 1963 10 had overuse of drugs as their major presenting symptom, and 12 others had a history of overuse of addictive drugs (apart from alcohol). Fourteen of these 22 women had used morphine or morphine derivatives. Evans concludes that the addiction was related “dynamically and empirically to the profession of the husbands.” A number of the women had continued to have ready access to drugs after the addiction was evident.

Can nothing be done to reduce the numbers of doctors’ lives wasted by these occupational hazards? Too often, perhaps, colleagues who are aware that all is not well stand aside and refuse to interfere when early action is essential.

Arthritis and Sarcoidosis

Sarcoidosis is a widespread granulomatous process the signature of which is the sarcoid nodule. This is demonstrable by biopsy and sufficiently characteristic and uniform under the microscope to imply that sarcoidosis has a single cause, but the occurrence of an identical sarcoid reaction to beryllium disease and to some fungal infections proves otherwise. Beryllium disease and fungus infections of this type, however, are rare, and sarcoidosis without exposure to these agents is fairly common, so experts in the disease may be forgiven if they continue to write about sarcoidosis and not about the “sarcoidoses.” This apparently academic point is of practical importance in assessment of the prognosis of the condition and its associated manifestations such as arthritis.

A variety of quite different joint conditions have been described as associated with sarcoidosis. The value of studies of this kind is limited if several types of sarcoidosis are lumped together in the reported series. This is particularly so when the Kveim reaction (an artificially induced local sarcoid nodule) is used as proof of the disease. Statistics based on hospital studies are notoriously fallible when it comes to describing apparent association between diseases whose causes are unknown. The “two-disease fallacy” creeps in—the interesting possessor of two diseases is far more likely to be written about than the humdrum patient with only one. Epidemiological studies might be expected to help to clarify the association between arthritis and sarcoidosis, and a valuable survey has been reported by I. Sutherland, D. N.

Mitchell, and P. D’A. Hart, who looked for the development of sarcoidosis in a 14-year prospective follow-up study of 54,239 children and adolescents vaccinated against tuberculosis or observed as unvaccinated controls. They found 52 cases and mentioned that only three of them had joint pains. Nevertheless, workers in hospitals continue to find a high incidence of arthritis in histologically proved sarcoidosis, and in some patients this may be the presenting complaint.

The problem has been looked at both in rheumatism clinics (where the selection factor for arthritis is to be expected) and in specialized sarcoidosis clinics, as in a recent study by J. M. Gumpel and his colleagues.² If nonspecific or unrelated causes of joint symptoms are excluded at least three different presentations of arthritis emerge. The first, well-characterized, is an acute arthritis predominantly of the knees and ankles, occurring with or often before erythema nodosum. The characteristic patient is in the third or fourth decade and is more often a woman, and the associated clinical features include a painful oedema of the ankles and feet, marked and sometimes incapacitating stiffness of the limbs—especially in the mornings—fever, enlarged hilar lymph nodes, and general malaise. The response of the arthritis to corticosteroids is excellent and complete recovery is the rule, at least in Britain. Anergy to tuberculin and biopsy evidence of sarcoidosis in lymph nodes or other tissues in a small proportion of cases has led to this condition being classified as an arthritis of sarcoidosis, but neither the sarcoidosis nor the arthritis leaves any permanent residue. A positive Kveim test is common and by itself has been accepted as histological proof of sarcoidosis—for example, by Dr. D. G. James and his associates.³ Sutherland and his colleagues, however, thought that the Kveim positivity had “some immunological basis not directly related to sarcoidosis.” In other words, the presence of a positive Kveim test by itself should not be taken as histological proof of sarcoidosis. Many would feel that it would be preferable to regard this acute, early, and clinically distinct form of arthritis as no more than a part of the “erythema nodosum syndrome” and, as L. H. Truelove⁴ suggested, “as independent of the underlying cause of the syndrome, whether this be sarcoidosis, tuberculosis, or drug sensitivity.”

Two other forms of arthritis associated with sarcoidosis reflect the granulomatous invasion of the para-articular bone or of the synovium. They are much less common, much more likely to become chronic, and they are always associated with clinically apparent granuloma formation in the skin, lung parenchyma, eyes, lymph nodes, or peripheral nerves. Sarcoid dactylitis may give swollen painful fingers, which resemble rheumatoid arthritis superficially, but the radiograph will show the diffuse osteitis in the phalanges—an appearance which is seen much more frequently than the often quoted punched-out cysts. Synovial lesions⁵ may take the form of localized plaques of sarcoid-containing tissue, which replace part of the synovium and are associated with a nonspecific reaction elsewhere in the joints. The clinical course of such lesions is variable but usually takes the form of a subacute and recurrent hydrarthrosis. Both the arthritis

¹ Sutherland, I., Mitchell, D. N., and Hart, P. D’A., *Brit. med. J.*, 1965, 2, 497.

² Gumpel, J. M., Johns, C. J., and Shulman, L. E., *Ann. rheum. Dis.*, 1967, 26, 194.

³ James, D. G., Thomson, A. D., and Willcox, A., *Lancet*, 1956, 2, 218.

⁴ Truelove, L. H., *Ann. rheum. Dis.*, 1960, 19, 174.

⁵ Bianchi, F. A., and Keech, M. K., *ibid.*, 1964, 23, 463.

⁶ Bonnet, W. L., *Radiology*, 1946, 47, 175.

⁷ Kunkel, H. G., Simon, H. J., and Fudenberg, H., *Arthr. and Rheum.*, 1958, 1, 289.

⁸ Kaplan, H., and Klatskin, G., *Yale J. Biol. Med.*, 1960, 32, 335.

of the erythema nodosum syndrome and the arthritis of synovial sarcoid infiltration may precede the signs of illness elsewhere. Rheumatic fever, rheumatoid arthritis, and even of gout may be suggested diagnoses in this early phase and may on occasion be supported by nonspecific T-wave changes in the electrocardiogram⁶ or by positive tests for rheumatoid factor due to gammaglobulin changes⁷ or by elevation of the serum level of uric acid⁸ due to increased cell division. Isolated case reports have probably over-emphasized the importance of these instances of clinical overlap. Gumpel and his colleagues did not find that they were of much importance in practice.

Investigation of the Young Hypertensive

Despite intensive research into the aetiology of hypertension during the last two decades it is still unhappily true that only in some 10% of all hypertensive patients is it possible to identify a likely cause for their disease. Further, only in perhaps one-third of this 10% is it possible to cure or improve the hypertension by an operation on the kidney or adrenal glands. Nearly ten years ago Lord Platt¹ observed that the incidence of secondary hypertension was relatively high in patients under the age of 40 (in whom he reckoned only about 30% had primary or "essential" hypertension). Since then most physicians have adopted a conservative attitude to the investigation of hypertensive patients over the age of 40 but have continued to investigate their younger patients intensively. Everyone who does this has the occasional gratifying experience of curing a young hypertensive, but against every patient cured of his hypertension must be set the morbidity of renal investigations, especially aortography² and divided function studies, in the less fortunate remainder. As hypotensive drugs year by year become more effective and produce fewer side-effects the burden of lifelong treatment lessens and the necessity for surgical cure becomes less imperative.

From the Royal Postgraduate Medical School, A. Breckenridge and his colleagues³ have just reviewed their experiences in investigating intensively 229 hypertensive patients aged between 12 and 40. The balance sheet they have drawn up is instructive. Despite investigation as intensive as could reasonably be performed in such a group in only 73 patients (32%) was a possible cause for hypertension found. In addition there were a further 40 patients not subjected to intravenous pyelography because their renal failure was too severe when first seen or because they died before the investigation could be done. Of the 73 patients in whom a secondary cause of hypertension was suspected only nine were thought suitable for surgical treatment. Nephrectomy was carried out on six patients for renal artery lesions or unilateral pyelonephritis, and in the other three patients the adrenal gland was explored or a renal capsulotomy done. In only three cases was the treatment successful in that no further drug treatment was needed.

Three cures in 229 patients—it is not an encouraging record. A curious feature of the series is that there were so few patients with disease of the main renal artery (only 12 material lesions were identified), and none of these patients

is recorded as having had reconstructive renal artery surgery. The low incidence of disease of the renal artery would be met with amazement bordering on disbelief by American surgeons at Houston and at the Cleveland Clinic, who see a highly selected population. However, even those patients referred to the hypertensive clinic of Hammersmith Hospital are themselves probably a selected group, and it may well be that in a completely unselected population of young hypertensives the true incidence of remediable secondary hypertension is still less than in the Hammersmith series.

Breckenridge and his colleagues point out the moral: that youth alone is an insufficient recommendation for extensive investigation, especially aortography, in the hypertensive patient. Since by far the commonest renal lesion in these young hypertensive patients was chronic pyelonephritis, which could usually be diagnosed by the intravenous pyelogram and by examination of the urine, it seems that aortography or divided function studies can be therapeutically justified only under special circumstances. Patients suitable for intensive investigation are those with a loud renal artery bruit to whom surgery can be offered and by whom it might be accepted, and possibly also those who prove unduly resistant to drug therapy, those who find drug side-effects intolerable, or those whose occupation or domicile makes adequate supervision of their therapy impossible.

Young hypertensive patients should certainly not be denied the benefits of intravenous pyelography, urinalysis, screening of blood electrolytes to detect primary hyperaldosteronism, and, if possible, screening of the urine to detect pheochromocytoma. These tests are simple, safe, and reasonably inexpensive in time and money. Except under special circumstances investigation should stop at this point, and the patient should be treated with hypotensive drugs unless the reasons for proceeding further are unusually compelling.

Intensive Care

The value of intensive care units in hospitals has become generally recognized in Britain only in the last five years. As the equipment used in the management of patients with severe cardio-respiratory illness has become more complex so has special training and experience become necessary for those looking after the patients. The best use of men and machines can be made if they are concentrated into one unit and patients who need specialized treatment or monitoring are admitted to it.¹

Few units in Britain have been working for more than a year or two, but there is now widespread interest in their establishment. In 1962 the Ministry of Health gave its blessing² to hospitals wishing to set up units; now the B.M.A. Planning Unit has issued a useful report³ by a working party under the chairmanship of E. J. Moran Campbell which gives advice on the form that units should take, based on the experience of 17 hospitals in the British Isles. This is the first publication from the Planning Unit, and Professor Henry Miller, its director, stresses that the report is in no sense a statement of B.M.A. policy but is an informed assessment of

¹ Platt, R., *Quart. J. Med.*, 1948, 17, 83.

² Chamberlain, M. J., and Gleeson, J. A., *Lancet*, 1965, 1, 619.

³ Breckenridge, A., Preger, L., Dollery, C. T., and Laws, J. W., *Quart. J. Med.*, 1967, 36, 549.

¹ *Brit. med. J.*, 1966, 2, 1609.

² *Mth. Bull. Minist. Hlth Lab. Serv.*, 1962, 21, 218.

³ *Intensive Care*, B.M.A. Planning Unit Report No. 1, 1967, B.M.A. Price 3s. 6d.

⁴ *Organization of Medical Work in the Hospital Service in Scotland*, 1967. H.M.S.O.

⁵ *First Report of the Joint Working Party on the Organization of Medical Work in Hospitals*, 1967. H.M.S.O.

⁶ Lord Platt, *Brit. med. J.*, 1967, 4, 439.

current experience. The report defines the function of an intensive therapy unit (I.T.U.) as "the care of patients who are deemed recoverable but who need continuous supervision and need or are likely to need prompt use of specialized techniques by skilled personnel." When large hospitals have a divisional system the report suggests that specialties might have their own units, while in district general hospitals a communal I.T.U. might be better. The optimum size is said to be six to eight beds.

The report confirms earlier suggestions that the physician or anaesthetist in administrative charge of the unit should not have clinical responsibility for all patients, but it goes on to emphasize that the success of an I.T.U. depends on its staffing. "An I.T.U. succeeds if it has a dedicated staff who have the confidence and good will of the hospital—whatever formal arrangements are made." Two accounts published last month^{4,5} of the future organization of medical work in hospitals drew attention to the benefits of wider co-operation among hospital staff, and intensive therapy units will flourish only where this atmosphere exists. Perhaps most important, the report draws attention to the strain on patients and their relatives of the bustle of activity in these units, and the need for doctors to find time to explain what is going on. Technological medicine must not be allowed to become dehumanized.⁶

Outbreaks of Coxsackie B Infection

Nearly every year, generally in the summer months, outbreaks of infections caused by the enteroviruses make their appearance. Now that poliomyelitis can be controlled by immunization, the main pathogens are the E.C.H.O. and Coxsackie viruses. Fortunately these are more benign than poliovirus, but under certain circumstances severe and fatal disease can occur.¹ In the past few years laboratories throughout Britain have been sending in reports of micro-organisms isolated to the Central Public Health Laboratory at Colindale, and details of these are subsequently circulated weekly to many other laboratories and hospitals. This is a valuable and informative service.

Coxsackie viruses are isolated quite often in the summer and usually each year one or two strains are predominant. This year there were many isolations of Coxsackie B2 and B3 and of Coxsackie A strains from hand-foot-and-mouth disease.² In a report from the Public Health Laboratory Service published on page 575 of this week's *B.M.J.* it is clear that 1965 was a Coxsackie B5 year—the number of identifications made was greatly in excess of any year since 1960. A high proportion of the 1,160 reports came from London and the south-east, with very few isolations in the north of England, a few in Scotland, and none in Northern Ireland. The number of infections reported in 1965 started to increase in May and reached a peak in July and August. Infections were noted most frequently in children—41% of infections

occurred in children aged up to 9 years, and a further 19% in patients aged 10 to 19. Few were reported in patients over 50 years of age. The varied clinical features in the 900 cases ran true to form for Coxsackie B infections. Those observed most often were infections of the central nervous system (31%), with aseptic meningitis predominating. Next in order of frequency were cases of myalgia and Bornholm disease (23%), followed by respiratory disorders (15%), ranging from a cold, sore throat, croup, and pharyngitis to pneumonia. Gastrointestinal symptoms of diarrhoea, vomiting, and abdominal pain were encountered in 9%. Among the 48 patients (5%) with cardiac symptoms 41 had pericarditis, five had myocarditis, and in two a precise diagnosis was not made. In 13 patients a rash was the predominant symptom, usually rubelliform. Altogether there were six deaths, including two cases of myocarditis (one in an infant aged 11 days and one in an adult), and two infants died of "respiratory involvement." Respiratory and gastrointestinal symptoms were most common in children under 10, and next in order of frequency were disorders of the central nervous system. Over the age of 10 the systems most affected were the central nervous system and the muscles.

During the same epidemic a number of cases of Coxsackie B5 infection occurred in Essex, and in a recent study K. W. G. Heathfield and his colleagues³ report a detailed study on the neurological aspects of infection with Coxsackie B virus. Thirty-two patients were studied, and in 21 the central nervous system was clearly affected. Ten patients developed an aseptic meningitis with clinical features typical of this type of illness. Eleven patients were seen with a more extensive infection. These included three severe cases of acute meningoencephalitis in infants, all of whom recovered, though one remained retarded. In addition, there were four cases of acute meningoencephalitis in children, all of whom recovered, and two examples of a brain stem encephalitis in adults. Two fatal cases were observed: one, a patient of 28, died after four months in coma, and at necropsy the brain showed a severe necrotizing encephalitis, which affected in the main the medial parts of both temporal lobes. Coxsackie B5 had been isolated from the cerebrospinal fluid during life. The second death occurred suddenly in an adult; at necropsy an acute haemorrhagic leucoencephalitis was found. This account is of interest in the light of recent observations⁴ on the effect of herpes simplex virus on the central nervous system, for herpes virus can also produce a fulminating infection with sudden death and a subacute necrotizing lesion which seems to have a predilection for the temporal lobes. These reports remind us that though the non-polio enteroviruses are usually less virulent than poliovirus serious diseases can occur in which a brain-stem encephalitis and necrotizing encephalitis are among the more severe features

¹ Steigman, A. *J. Mt. Sinai Hosp.* (1958), 25, 391.

² *Brit. med. J.*, 1967, 4, 503.

³ Heathfield, K. W. G., Pilsworth, R., Wall, Barbara J., and Corsellis, J. A. N., *Quart. J. Med.*, (1967), 36, 579.

⁴ *Brit. med. J.*, 1967, 3, 812.

Papers and Originals

Natural History of Cerebral Angiomas

W. R. HENDERSON,* F.R.C.S.; R. DE R. L. GOMEZ,† M.D.

[WITH SPECIAL PLATE FACING PAGE 572]

Brit. med. J., 1967, 4, 571-574

This paper is based on 70 patients who were seen during 1946-61 and were followed-up in 1966. The main purpose is to assess the natural history of angiomas, with particular reference to haemorrhage; also to emphasize some aspects of management. Only six angiomas were removed.

The first comprehensive studies of angiomas were by Cushing and Bailey (1928) (Special Plate, Fig. 1) and by Dandy (1928), who described a few cases of epilepsy in which large angiomas were found during exploratory operation, usually for suspected tumour. The possibility of surgical removal, however, had to await the introduction of angiography by Egas Moniz in 1927; and later the widespread use of the percutaneous method in the investigation of subarachnoid haemorrhage revealed many smaller, previously silent, angiomas, and led to a pronounced increase in the numbers diagnosed during the past 20 years. Angiography enabled operations to be planned to ensure the essential early division of all feeding arteries, and it became possible to remove completely many small and medium-sized angiomas, and sometimes even the more challenging large angiomas (Norlen, 1949; Paterson and McKissock, 1956; Olivecrona and Ladenheim, 1957); fits, however, were not always abolished, and previous neurological disability often remained. Prevention of recurrent haemorrhage became the chief indication for operation, but the risk of haemorrhage had to be assessed against the possibility of operative damage.

More recently it became recognized that haemorrhage sometimes occurs from very small angiomas, designated "cryptic" hamartomas by Crawford and Russell (1956). They are often situated in the depth of a sulcus (Special Plate, Fig. 2) and are apt to produce a large intracerebral haematoma, sometimes without subarachnoid bleeding, that may be rapidly fatal (Margolis *et al.*, 1951; Kravenbühl and Siebenmann, 1965). It seems that minute angiomas are sometimes destroyed by the haemorrhage and consequently may not show on angiograms. They are an important cause of so-called spontaneous cerebral haematomas of unknown origin, especially in children and young adults, which, when diagnosed in time, are curable by urgent evacuation; haematomas caused most of the preventable deaths in this series.

Clinical Groups

Of the 70 angiomas 63 were found by angiography, 4 at necropsy, and 3 at operation. They varied in size from a few millimetres to 10 cm., and may be grouped into three sizes (Table I). The size of the angioma is important in relation to the incidence of epilepsy (Mackenzie, 1953); of cranial bruit, and of intracerebral haematoma, and to the possibility of surgical removal.

* Neurosurgeon, General Infirmary at Leeds.

† Neurosurgeon, Mexico City.

The first manifestations in 68 patients were: (1) haemorrhage in 53 patients (78%) from angiomas of all sizes but mainly smaller angiomas without cranial bruit; (2) epileptic fits in 11 patients (16%) with large angiomas and bruit; (3) progressive hemiparesis in two patients with basal angiomas; and (4) high intracranial pressure suggesting tumour in two patients.

TABLE I—Size of 70 Angiomas in Relation to First Symptoms

Size of Angioma	Haemorrhage	Epilepsy	Slow Hemiparesis	High Intracranial Pressure	No Symptoms
16 small (2 cm. or less)	16	—	—	—	—
35 medium (> 2—< 6 cm.)	30	2	—	1	2
19 large (6 to 10 cm.)	7	9	2	1	—
70	53	11	2	2	2

The ages at onset varied from 3 to 60 years; 21 patients were in the twenties and 16 were under 20. Silent angiomas were present in two patients with ruptured aneurysm.

Haemorrhage

Haemorrhage (subarachnoid, intracerebral, or intraventricular) occurred in 58 patients; in 53 it was the first manifestation, and five patients with large angiomas had late haemorrhage, many (10, 19, 23, 30, and 37) years after the onset of epilepsy or slow hemiparesis. After the first haemorrhage five patients died (three from intracerebral haematoma and two from late haemorrhage) and five angiomas were removed or clipped. There were 23 mild attacks of sudden headache without (or very brief) loss of consciousness or focal signs, and 21 moderate attacks with either loss of consciousness or focal signs, or both, that disappeared, so that 44 patients recovered completely; and there were nine severe attacks (four with known haematoma) followed by incomplete recovery.

A second haemorrhage occurred in 28 patients out of 48; five died from the haemorrhage (after intervals of five weeks, 15 months, two, seven, and nine years) and one angioma was removed. Further haemorrhages, making altogether three to six attacks, occurred in nine patients, one of whom died after the fourth haemorrhage; and another patient had nine almost certain haemorrhages (five proved by lumbar puncture), all followed by good recovery. Thus six patients (all with large or deep inoperable angiomas) died from recurrent haemorrhage. There were only seven short intervals, of less than six weeks, before 54 recurrent haemorrhages; 38 intervals were one year or longer, and 16 were 5 to 26 years. Only three of the nine patients who had severe first attacks had further haemorrhages. Seven patients had full recovery after all of three to nine

haemorrhages from medium-size inoperable angiomas (mostly supplied by choroidal arteries) and remained well 17 to 30 years after the first haemorrhage.

As regards permanent disability, 35 patients (60%) recovered completely from all attacks (Table II); and 12 had permanent residual signs, mainly hemiparesis or hemianopia, or occasionally cortical sensory loss or mild dysphasia, that were often slight and caused little or no disability. There was impairment of memory in one patient, and mild personality change in another. Eleven patients later developed occasional epileptic attacks. Two patients were not working.

TABLE II.—*Severity of Haemorrhage, Based on the Most Severe Attack, in 58 Patients*

Size of Angioma	Severity of Haemorrhage			Died	Total
	Mild	Moderate	Severe		
Small	5 (1)	7 (4)	3 (2)	2 (2)	17 (9)
Medium	10	9 (1)	7 (2)	4 (2)	30 (5)
Large	2	2	2	5	11
	17 (1)	18 (5)	12 (4)	11 (4)	58 (14)

The figures in parentheses are of known intracerebral haematomas.

It is well known that haemorrhages from angiomas are less fatal and cause less morbidity than haemorrhages from saccular aneurysms, that they occur at an earlier age, that recurrent attacks occur after longer intervals, often of many years, and that angiomas do not cause arterial spasm and cerebral infarction that sometimes produces severe permanent disability or fatality after rupture of an aneurysm. Haemorrhages from very small angiomas tend to occur in early life, as might be expected with a congenital lesion, but severe bleeding from large angiomas that contain so many abnormal vessels, surprisingly, often does not occur until later life, suggesting its dependence on degenerative changes; necropsies, however, often show evidence of previous clinically unrecognized slight leakages of blood (Russell and Rubinstein, 1963) that probably are more common than is known, especially from large angiomas. It seems from this small series that medium-sized surface angiomas often bleed into cerebrospinal fluid without causing permanent disability, and that their removal need not be attempted if the brain is likely to be damaged.

Intracerebral Haematoma

Haematomas were found at operation in 14 patients (Table II); four died. In five patients the cerebrospinal fluid was normal, which made early diagnosis more difficult, and in eight it contained blood; none had cranial bruit. Nine angiomas were small and five were of medium size (the largest was 5 cm.). There were no known haematomas with large angiomas that often extend from a wide base on the brain surface deeply to the ventricle and could bleed easily into cerebrospinal fluid, either directly or by tracking along the potential space between a dense angioma and brain. Blood may collect inside this space, forming a small haematoma that is discovered during removal of the angioma, or it may extend widely into the brain. A large haematoma occupies the white matter up to the cortex (Special Plate, Fig. 2), and the subependymal glia also seems to form a barrier; it is likely that fibre tracts at the site of bleeding are torn while nearby compressed tracts are capable of recovery, so that permanent focal signs are usually localized but may be severe—for example, monoparesis or quadrant hemianopia.

Clinically, there is great variation in the rapidity of onset. Usually sudden severe headache occurs with vomiting and perhaps neck stiffness, and, when the motor area is involved, rapid hemiparesis. Death may occur within a few hours, usually from ventricular haemorrhage (Crawford and Russell, 1956), and no effective treatment is possible. More commonly, and when operation is urgently necessary within a day or two, the sudden headache is followed after a delay of some hours

by progressive deterioration, with drowsiness deepening to coma, and with spreading signs and perhaps a dilating pupil which, when it occurs, is an important indication of haematoma; two such patients died in two and four days after late aspiration of 25 and 30 ml. of old blood (Special Plate, Fig. 2). With smaller haematomas improvement starts with return to consciousness within two days but focal signs often persist.

Large haematomas, up to 10 cm. long, are mostly in the central (sulcus) region, and there is early hemiparesis (nine haematomas arose from small convexity angiomas in the middle cerebral area), whereas haematomas nearer the poles of the hemisphere are usually smaller and have milder symptoms without focal signs. Diagnosis may be confused by a history of mild antecedent trauma to the head (as in two patients) that occasionally seems to precede haemorrhage (Margolis *et al.*, 1951; Crawford and Russell, 1956), and is probably coincidence, but if relevant it suggests that trauma may start bleeding from an angioma that is about to rupture spontaneously; negative burr-hole exploration for suspected extradural haemorrhage should include cerebral aspiration. In two patients with only drowsiness, inconspicuous signs, and normal lumbar puncture the symptoms appeared to have been gradual in onset, over a week or two, and were at first attributed to a rapidly growing cerebral tumour. Angioma should be suspected, first, when blood is obtained during burr-hole aspiration of a mass that produced symptoms of recent apparently gradual onset, because bleeding into a tumour is very rare; and, secondly, as a likely cause of cerebral stroke in children (six haematomas were in children aged 17 or younger). Permanent isolated focal signs—for example, hemianopia—in young patients after an uninvestigated acute cerebral illness, sometimes called meningitis, may have resulted from angioma haemorrhage.

Radiologically, there may be a laterally displaced pineal shadow. Angiography shows slight lateral displacement of the midline, which may be the only radiological evidence of haematoma, especially in the frontal or occipital region (a large angioma alone may produce a similar shift); but a haematoma in the central region, the common site, produces typical displacement of the middle cerebral artery, either downwards with parallel stretching of the ascending branches (Special Plate, Fig. 3) or upwards (Special Plate, Fig. 4).

Seven haematomas, sometimes unsuspected, were evacuated during craniotomy, and in seven patients up to 50 ml. of old blood was aspirated through a burr hole. Aspiration was sometimes late, or was inadequate, and probably all four deaths should have been prevented (two angiomas on the convexity were small and removable, and two were deep and inoperable). The patients who recovered remained well without recurrence

W. R. HENDERSON AND R. DE R. L. GOMEZ: CEREBRAL ANGIOMAS

FIG. 1.—Diagrammatic representation of medium-size superficial angioma showing enlarged feeding arteries and draining veins. Reproduced from Cushing and Bailey's *Tumours Arising from the Blood Vessels of the Brain*, by permission of the authors and of the publishers, Charles C. Thomas, Springfield, Illinois, U.S.A.

FIG. 2.—Intracerebral haematoma from small angioma (arrow) in a sulcus in a child aged 7 years who died 42 hours after haemorrhage (lumbar puncture normal).

FIG. 3.—Angiogram in boy aged 15 years showing feeding artery (arrow) to small angioma, characteristic early filling of draining vein during arterial phase, and stretching by intracerebral haematoma of ascending branches of depressed middle cerebral artery.

FIG. 4.—Angiogram in girl aged 10 years showing upward displacement of middle cerebral artery by large intracerebral haematoma without visible angioma which, at operation, was found histologically in adherent blood clot at anterior wall of haematoma.

FIG. 5.—Angioma in basal ganglia and internal capsule produced gradual hemiparesis for 19 years before fatal haemorrhage at age 45. The huge venous channel drained to the vein of Galen.

FIG. 6.—Angiogram (venous phase) of large 10-cm. angioma that caused focal epilepsy, showing drainage deeply to the vein of Galen and superficially to the sagittal sinus. Repeat angiography seven years later showed no change in size of angioma, but drainage through straight sinus was replaced by distended veins to skull base and behind orbit (associated with recent orbital congestion and proptosis).

W. R. HENDERSON AND R. DE R. L. GOMEZ: NATURAL HISTORY OF CEREBRAL ANGIOMAS

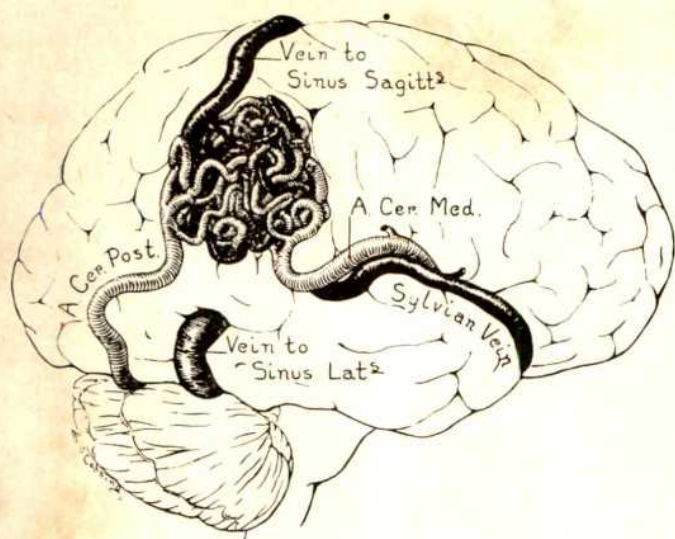


FIG. 1

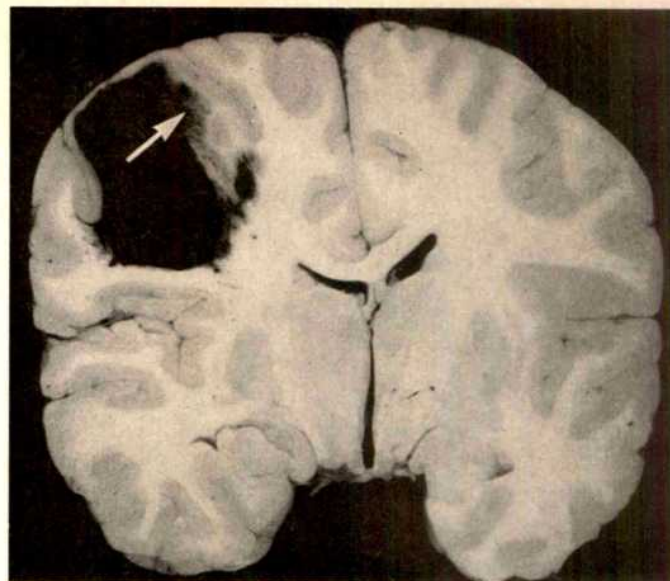


FIG. 2

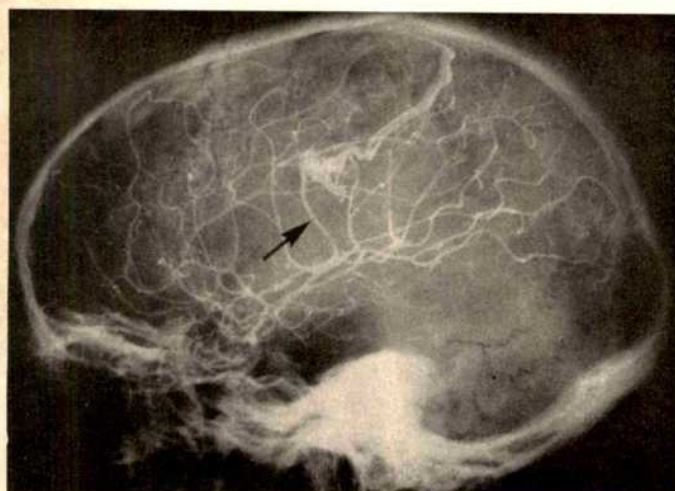


FIG. 3

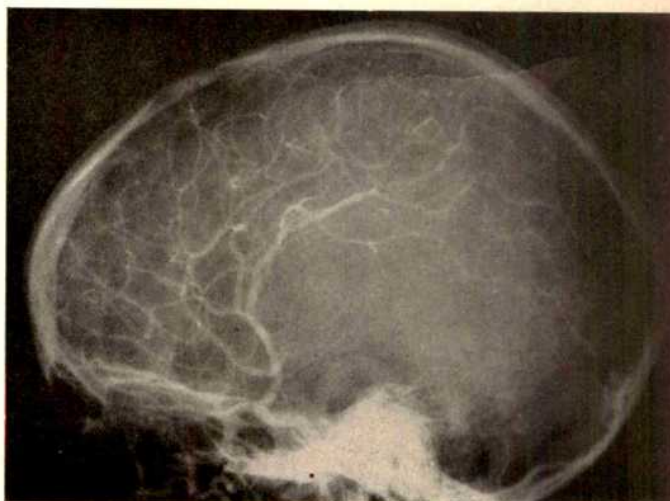


FIG. 4

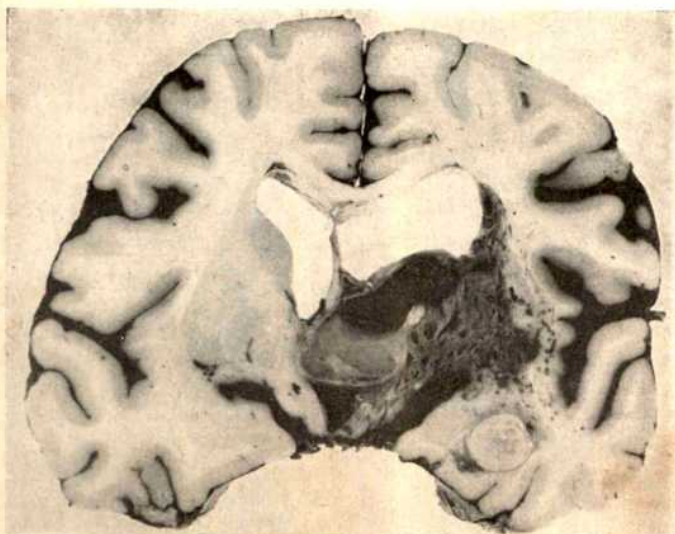


FIG. 5

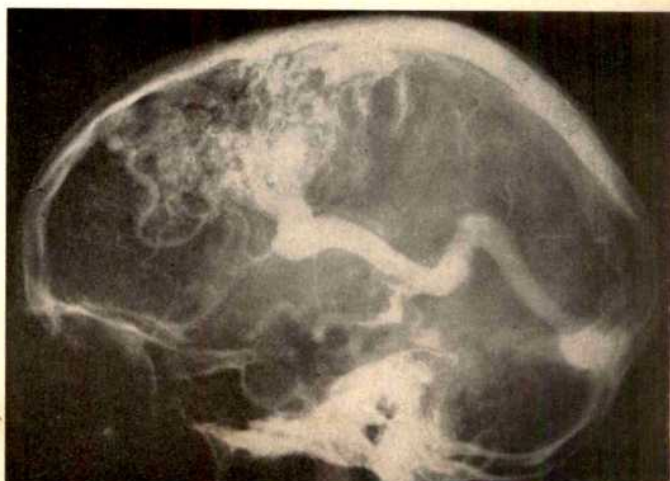


FIG. 6

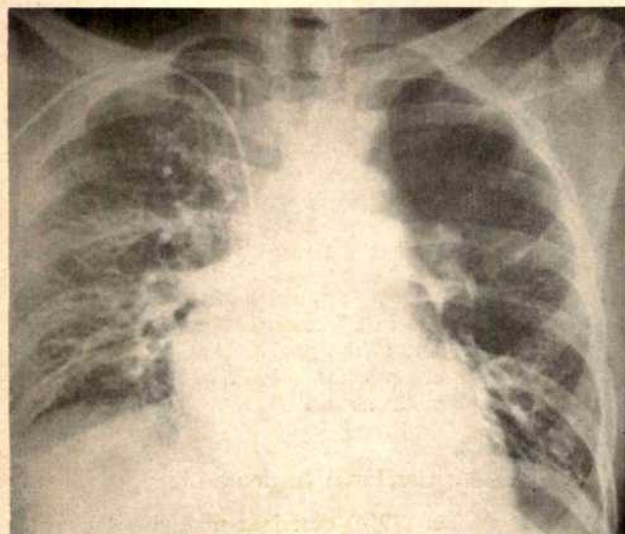
LORD BROCK *ET AL.*: CASE OF LATE PULMONARY EMBOLECTOMY

FIG. 1.—Angiocardiogram to show occlusion of main left pulmonary artery by an embolus. The small amount of lower lobe filling may be via bronchopulmonary anastomoses. A few small arterial branches in right lung are also not filled.

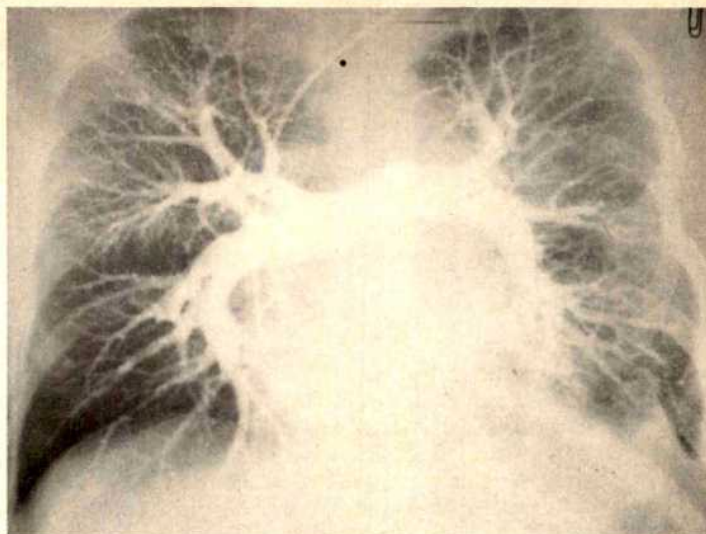


FIG. 2.—Angiocardiogram after embolectomy to show normal filling of the pulmonary arterial tree.

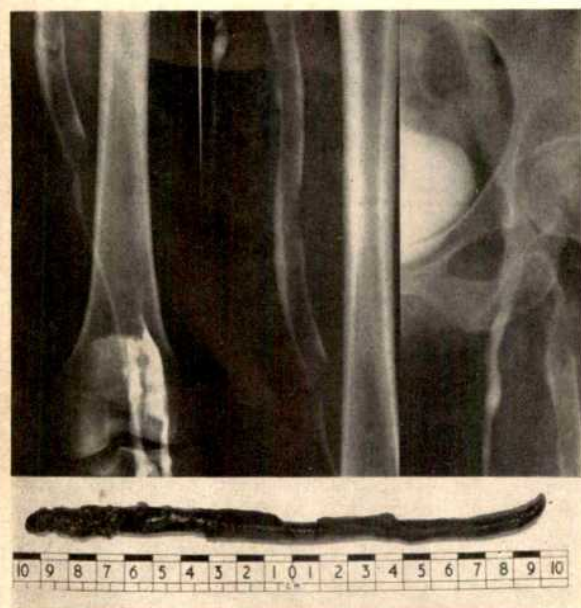
N. L. BROWSE *ET AL.*: MANAGEMENT OF PULMONARY EMBOLI

FIG. 1

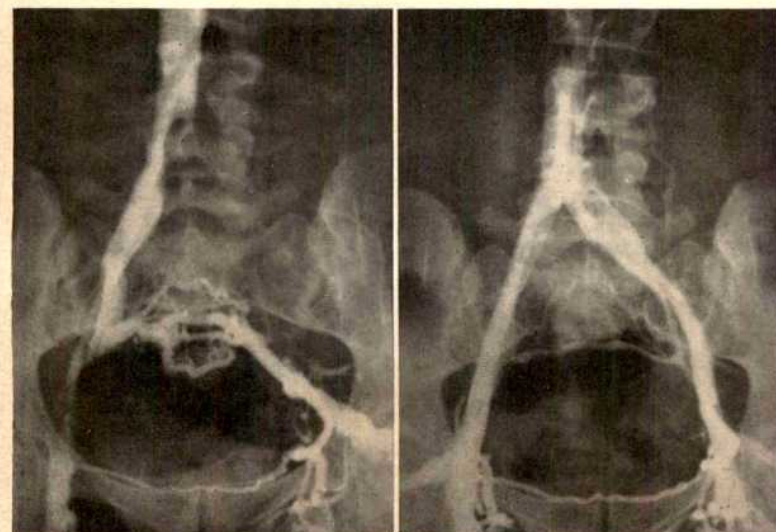


FIG. 2

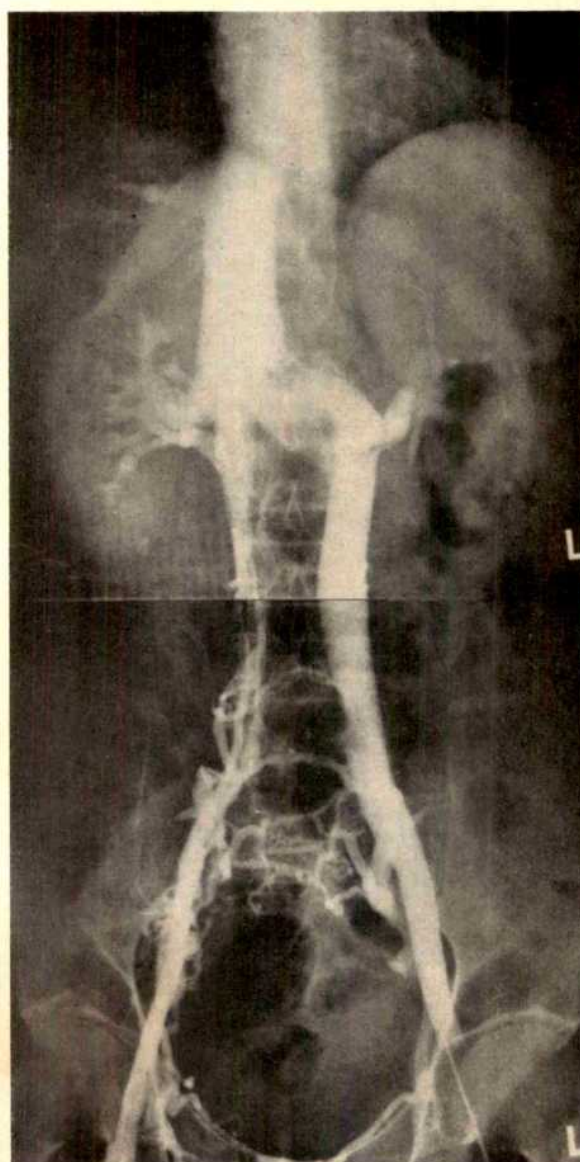


FIG. 3

of bleeding for 7 to 14 years. Burr-hole aspiration is sometimes satisfactory, but evacuation by craniotomy is usually better, especially when the angioma is removable; very small angiomas that are hidden in a sulcus may be traced by adherent clot inside the haematoma, as was proved histologically in one patient with a large haematoma but no angioma radiologically (Special Plate, Fig. 4). In very ill children with hemiplegia, dilated pupil, and possibly a history of recent mild head injury, it is probably safest to exclude a large central intracerebral (or extradural) haematoma by aspiration through two burr holes without angiography; an angioma can be removed after angiography later.

Epilepsy

Five of the 11 patients had no other complaint (except two with occasional migraine) during 10 to 40 years; four had late haemorrhage (two fatal) after fits for 10, 23, 30, and 37 years; and two patients died, one after epilepsy for 26 years (with, during the last nine years, gradual hemiparesis, dysphasia, and eventually mental deterioration), and the other (following rapid deterioration immediately after repeat angiography and subsequent radiotherapy) after mild epilepsy for about 10 years. The angiomas were superficial and large, 5 to 10 cm. in size (Special Plate, Fig. 6). Nine patients had cranial bruit. The classical combination of epilepsy and cranial bruit is strongly suggestive of angioma, but it may occur with a meningioma and is not diagnostic without subarachnoid haemorrhage. The fits, with or without loss of consciousness, were often Jacksonian; they were usually separated by intervals varying from months to several years, and were well controlled by anti-convulsant drugs. Removal of angioma was not attempted (occasionally the risk of producing increased disability may be justified when fits are frequent and disabling).

Eleven other patients had fits that started after, and presumably were caused by, haemorrhage, often within 12 months but occasionally after several years; usually, persisting signs of cerebral damage were present, and in five patients there had been a haematoma. In contrast to the epilepsy group, most of the angiomas were smaller, 4 cm. or less, and without a bruit. Posthaemorrhagic fits also were infrequent and were well controlled by drugs.

E.E.G. was of no value. In a few patients after epilepsy for many years it was normal; slow waves in two patients with gradual hemiparesis merely supported the obvious presence of a destructive cerebral lesion, but of course gave no indication of pathology.

Progressive Hemiparesis

Two patients with large angiomas in the basal ganglia had slowly progressive severe hemiparesis and sensory loss, without fits, for 20 and 19 years, when the latter patient died from haemorrhage; necropsy showed that the angioma was confined to and had destroyed the basal ganglia and internal capsule (Special Plate, Fig. 5). Slow hemiparesis was the initial symptom in five out of Paterson's (1955) nine cases of angioma in the basal ganglia.

N. L. BROWSE ET AL.: MANAGEMENT OF PULMONARY EMBOLI

FIG. 1.—Case 1. Ascending phlebogram of the clinically normal left leg showing typical recent thrombus. A loose thrombus of this size would probably be lethal if it broke free. The thrombus, easily removed, is shown below.

FIG. 2.—Case 2. Left, phlebogram showing a complete left iliac vein thrombosis with irregular fresh thrombus jutting into the vena cava. Right, phlebogram one year after plication of the inferior vena cava. The plication at the upper border of L3 is patent and the left iliac vein has fully recanalized.

FIG. 3.—Case 3. Percutaneous femoral puncture phlebogram of patient who had a pulmonary embolus six months after plication of the inferior vena cava without preoperative phlebography. The right inferior vena cava shows thrombosis and recanalization below the plication at the level of the body of L3, but there is a patent left inferior vena cava providing an unguarded route for emboli from the left leg.

High Intracranial Pressure

Two patients had high intracranial pressure with severe papilloedema and headaches of apparently gradual onset, without a history of fits or haemorrhage, that was suggestive of tumour. One very large space-occupying angioma was above the tentorium, and the other, of medium size, in the posterior fossa, obstructed the cerebrospinal fluid pathways.

Cranial Bruit

The presence or absence of a bruit, heard most easily over the eyeball, was recorded in 37 cases. It was nearly always present with large angiomas (the smallest was 4 cm.) but not with small ones (the largest without bruit was 5 cm.). Only one patient was aware of the noise.

Posterior Fossa Angiomas

Logue and Monckton (1954) described nine posterior fossa angiomas which usually produced cerebellar or lower cranial nerve signs; two in the cerebellum were removed and seven were in the brain stem. The clinical signs (without adequate history) may be wrongly attributed to tumour; similarly, intermittent symptoms from repeated small haemorrhages may be attributed to disseminated sclerosis. Our three patients with cerebellar angiomas remained well 7, 13, and 21 years after one or more mild haemorrhages; nevertheless their removal probably should have been attempted.

Angiography

Ideally, early management of subarachnoid haemorrhage rests on surgical observation from the day of haemorrhage, which is really the first investigation; the indication for and timing of angiography are based on the patient's (general and neurological) fitness primarily for possible operation and secondarily for angiography, which is potentially as risky as operation. Angiography should be regarded as a first-stage operation rather than as a diagnostic investigation.

Aneurysm is the commonest source of subarachnoid haemorrhage, and before angiography it is assumed that early operation may be required to prevent possible recurrent bleeding; on the other hand, a ruptured aneurysm often produces arterial spasm that may be dangerously increased by angiography during the first two or three weeks with resulting cerebral infarction (spasm sometimes spontaneously causes recurrent loss of consciousness and focal signs that are mistakenly attributed to recurrent haemorrhage). The third danger after haemorrhage is the formation of a large intracerebral haematoma (from angioma or aneurysm), which is very important because death from this cause can be prevented by prompt evacuation within a day or two; it is the most important complication of angioma haemorrhage. The suspicion of haematoma or of spasm, and therefore the timing of angiography, is based mainly on careful clinical observation for signs suggestive of progressive cerebral compression or transient increased spasm; the possibility of haematoma requires either immediate angiography or, when the patient is very ill, burr-hole exploration without angiography.

Angiography is not at any time without risk, and it is sometimes necessary to restrict it, or perhaps stop it after one injection, without completion of the series, which should never be routine. When an angioma is found on the first injected side, further injections are rarely required, either to demonstrate the complete blood supply of a large angioma, which is unnecessary except when the surgeon thinks it may be removable, or, unless there have been no focal manifestations, to exclude a coincidental ruptured aneurysm, which is rare. Such an aneurysm may be seen on the feeding artery to the angioma,

as in one of the two patients with silent middle cerebral angioma; the other patient had a ruptured posterior cerebral aneurysm that had produced partial oculomotor nerve paresis. Vertebral angiography was used conservatively because it seemed that the rare finding of a removable angioma or aneurysm in the posterior fossa (or occipital lobe) did not justify the added risk of routine complete four-vessel angiography.

The conventional three-exposure angiography seems to be adequate; rapid serial angiography is unnecessary even in the hope of showing with certainty a minute (not thrombosed) angioma, which, in any event, may be difficult to find at operation except in the wall of an obvious haematoma (Special Plate, Fig. 4). Repeat angiography after several years is also unnecessary and is inadvisable; in three patients the angioma showed no change in size after five to seven years. (In a 24-year-old patient with a 10-cm. angioma (Special Plate, Fig. 6) that had produced occasional mild focal fits for about 10 years, repeat angiography produced immediate severe hemiparesis and aphasia, followed by further rapid deterioration after radiotherapy, and death within a few months.) Post-operative angiography (a single lateral injection) was routine after excision or clipping of the angioma.

Operation

Removal of most deep (basal ganglia, choroidal, or brain-stem) angiomas is impossible, and there is no certainty that occlusion of a feeding artery that may give a branch to normal brain will not cause serious disability. Many superficial small and medium-size angiomas can safely be removed, but it is inadvisable to risk producing disability by attempting removal of large angiomas except perhaps when situated near a pole of the hemisphere.

There were 22 operations. Four angiomas up to 4 cm. in size were removed. The feeding arteries to six angiomas were clipped; two disappeared but four partially remained (without further bleeding during 9 to 13 years). In eight patients a haematoma was aspirated, usually through a burr hole. Three angiomas were found during exploratory operation, and one patient had flap decompression for high intracranial pressure but without improvement.

Radiotherapy was tried in five patients with large angiomas but produced no improvement, and four have died. McWhirter and Dott (1955) pointed out that the angioma blood vessels, though abnormal, are not neoplastic and that there is no reason to expect them to be more affected than the surrounding normal vessels. They stated that radiotherapy should not be employed, as have Paterson and McKissock (1956) and Olivecrona and Ladenheim (1957).

Follow-up

Twenty-one of the 69 patients followed up have died, 15 (22%) from the effects of the angioma and 6 from unrelated causes (four lived 7 to 11 years after subarachnoid haemorrhage and two with silent angiomas had ruptured aneurysm); one untraced patient was known to be alive eight years after haemorrhage. Most of the 15 patients died from haemorrhage: four from intracerebral haematoma, three from intraventricular haemorrhage, two from late haemorrhage (after 23 years' epilepsy and 19 years' hemiparesis), and one death followed vertebral angiography after full recovery from the third subarachnoid haemorrhage in eight years from a mid-brain angioma (previously shown by carotid angiography); all were proved at necropsy. Two sudden deaths without necropsy were assumed to have resulted from haemorrhage from large angiomas—one after epilepsy for 39 years and the other eight years after previous haemorrhage. The remaining three deaths (no necropsy) occurred in patients with very large supra-

tentorial angiomas after epilepsy for 10 and 26 years, and after a six-months' history of high intracranial pressure.

All 15 angiomas were thought to be either too large or too deep for removal except two small middle cerebral convexity angiomas with haematoma that should have been cured; and death after delayed evacuation of haematoma should not have occurred in two patients with deep angiomas. The five avoidable deaths were thus due to intracerebral haematoma or angiography. As regards intervals between first symptom and death, only 3 (4.4%) patients died, all from haematoma, within the first two months, and seven within 15 months; the remaining eight deaths occurred after 7 to 39 years. The earlier deaths were due mainly to haematomas from small angiomas, while the later deaths were in patients with large angiomas.

Conclusion

The natural history of angioma haemorrhage seems to be related to the size of the angioma. Haemorrhages from the common medium-size angiomas are usually mild and may recur at long intervals over many years. Small angiomas, on the other hand, are apt to bleed in children and rapidly produce a dangerous intracerebral haematoma in the first attack, whereas fatal haemorrhages from large (inoperable) angiomas often do not occur until later life, sometimes after fits or progressive cerebral disability for many years.

Forty-nine (84%) of the 58 patients who had haemorrhage were alive five years after the first bleeding; only two patients died from the effects of a safely removable angioma (with haematoma). These results probably justify a conservative surgical policy, but it is nevertheless believed that more angiomas should have been removed to prevent fatal haemorrhages that will no doubt occur in future years. Svien and McRae (1965) found that only 16% of 68 unoperated patients (out of a total of 95) seen at the Mayo clinic during 1920–61 had died from the angioma. We agree with their conclusion that, in retrospect, conservative treatment is appropriate for 80 to 85% of patients, but when patients are first seen the possibility of fatal recurrent haemorrhage is unpredictable, and some deaths will be prevented by excising the considerable number of angiomas that are removable without risk of producing serious neurological damage. It is, however, by the prompt evacuation of intracerebral haematoma that many avoidable deaths can be prevented.

It is emphasized that angiography should be used with restraint, especially in patients with large angiomas (and in the investigation of all subarachnoid haemorrhages), to avoid producing increased disability or fatality.

It is a pleasure to thank all the physicians who referred patients, and also the patients' general practitioners, for assisting with the follow-up.

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Coxsackie B5 Virus Infections during 1965

A Report to the Director of the Public Health Laboratory Service from Various Laboratories in the United Kingdom*

Brit. med. J., 1967, 4, 575-577

Many laboratories throughout the United Kingdom send regular reports of the micro-organisms they identify to the Central Public Health Laboratory, Colindale, London N.W.9. During the early summer of 1965 it became apparent that infections with Coxsackie B5 virus were being reported much more frequently than in previous years. Contributing laboratories were therefore invited to complete a standard record containing more information than that usually included in the routine reports. These special records were analysed centrally and the findings are reported below.

Period and Duration of Outbreak

Table I shows the total number of Coxsackie B5 virus infections reported to Colindale routinely in 1965 and in each of the previous five years. It is evident that the 1,160 reports during 1965 were greatly in excess of those recorded in any previous year. The last year in which a substantial number of infections was reported was 1960; in the intervening years the number of B5 infections was small, though the number did increase in the year before the epidemic. In contrast to the B5 isolations, the total number of other Coxsackie B isolations during 1965 was less than in the previous few years.

TABLE I.—Coxsackie B5 and Other Coxsackie B Infections According to Year

Year	Coxsackie B5 Infections	Other Coxsackie B Infections
1960	467	168
1961	46	83
1962	10	286
1963	26	316
1964	104	462
1965	1,160	188

Of the total of 1,160 isolations routinely reported the special record cards mentioned above were received for 900—that is, 77% of the total. Table II shows the isolations according to the month in which the specimen was obtained from the patient and sent for examination. Of the 900 reports 232 did not contain the requisite date. Few of the remaining 668 isolations were obtained before May. However, in that month there were 30 isolations; in June there were 85; in July and August—the largest numbers of any month—199 and 183 respectively. After August the numbers declined to 68 in September and October; in December there were only 2.

TABLE II.—Infections According to Region and Month—1965

Region*	Total	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Not Known
Northern	6	0	0	0	0	0	0	1	3	2	0	0	0	0
E. & W. Riding	12	0	0	0	0	0	2	4	1	0	0	0	0	5
N. Midland	55	3	0	0	0	3	5	7	12	3	2	3	0	17
Eastern	98	1	0	0	1	0	5	29	18	16	8	1	1	18
London & S.E.	278	0	0	0	1	10	26	54	37	13	19	3	0	115
Southern	82	0	0	0	0	0	15	30	17	3	3	0	0	14
S. Western	184	0	0	0	0	0	7	36	40	19	25	11	1	43
Wales	2	0	0	0	0	0	0	2	0	0	0	0	0	0
Midland	57	0	0	1	0	1	6	10	18	4	7	4	0	6
North Western	106	2	1	0	0	12	16	20	33	7	4	1	0	10
N. Ireland	2	0	0	0	0	0	0	0	1	0	0	0	0	1
Scotland	18	0	0	0	0	4	3	6	4	0	0	0	0	1
Total	900	6	1	1	2	30	85	199	183	68	68	23	2	232

* Standard Regions England and Wales as in 1965.

Table II also shows the number of reports received from each of the Registrar General's regions (Registrar General, 1965). At the outset isolations were reported from regions as far apart as London and the North-western Region. Taking the year as a whole the largest number of reports were received from the London and South-eastern, the South-western, the North-western, and the Eastern Regions of England and Wales.

Age

The age of the patients from whom the specimens were taken is shown in Table III. It is evident that infection was reported

TABLE III.—Infections According to Age and Sex

Age Group	Sex		Total Patients	
	M	F	No.	%
0-9 years	197	166	365†	41
10-19 "	92	75	167	19
20-29 "	57	80	137	15
30-39 "	69	55	124	14
40-49 "	22	13	35	4
50-59 "	4	5	9	1
60-69 "	5	3	8	1
70+ "	0	2	2	0.2
Not stated	29	22	53‡	6
Total	475	421	900	100

† Including 2 sex not stated. ‡ Including 2 sex not stated.

most frequently in children—365 isolations (approximately 41% of the total) were obtained from children 9 years of age and under. (Of these 68 about 7% of the total were from children under 1 year.) Seven hundred and ninety-three specimens (about 88% of the total) came from patients less than

* The reports on which this survey is based were submitted from Public Health and other laboratories in the following areas: Bath, Bedford, Belfast, Birmingham, Bournemouth, Bradford, Brighton, Bristol, Cambridge, Carlisle, Chelmsford, Chester, Cirencester, Conway, Cottingham, Coventry, Dundee, Epsom, Exeter, Glasgow, Guildford, Hereford, Hull, Ipswich, Kingston, Leeds, Leicester, Liverpool, London, Luton, Maidstone, Manchester, Middlesbrough, Newcastle upon Tyne, Northampton, Norwich, Nottingham, Oxford, Plymouth, Portsmouth, Preston, Salisbury, Sheffield, Shrewsbury, Southampton, Southend, Stafford, Sunderland, Swansea, Taunton, Truro, Wakefield, Winchester, Worcester.

The survey was planned and initiated by Dr. A. J. H. Tomlinson, P.H.L.S. Laboratory, County Hall, London S.E.1. The results were analysed and the report prepared by Mr. John G. Pope and Dr. T. M. Pollock, Epidemiological Research Laboratory, Colindale, London N.W.9.

40 years old. In most age groups there was a tendency for more isolations to be made from males than from females.

Predominant Clinical Features

A variety of clinical features of various degrees of importance was often noted on the record of a single patient. Table IV, in which each patient appears only once, shows only the most important feature in each patient. This predominant clinical feature was selected from the other clinical features noted on the record according to an order of precedence depending on the system affected as follows.

Conditions relating to the central nervous system took precedence as the predominant clinical feature over any of the other diagnoses noted on the record. Conditions of the central nervous system were followed in descending order by conditions affecting the cardiac, muscular, respiratory, and gastrointestinal systems, the skin, and, finally, general symptoms—for example, pyrexia. Thus a patient with a cardiac lesion and also gastrointestinal features appears in the cardiac group only. Similarly, a patient with muscular symptoms and general symptoms appears in the muscular group only.

TABLE IV.—Predominant Clinical Features in 900 Patients

System Affected and Diagnoses	Total Patients	
	No.	%
Central nervous: meningitis, encephalitis	280	31.0
Cardiovascular: myocarditis, pericarditis, unspecified	48	5.3
Muscular: myalgia, chest pain, Bornholm disease	204	22.7
Respiratory: cold, sore throat, croup, pharyngitis, pneumonia, bronchitis, pleural pain, pleurisy, unspecified respiratory	134	15.0
Gastrointestinal: diarrhoea, vomiting, gastroenteritis, abdominal pain	77	8.6
Skin: rash	13	1.4
General: pyrexia, headache, etc.	34	3.8
Other: arthritis, hepatitis, glandular fever	5	0.6
No symptoms	41	4.6
No information	64	7.1

As shown in Table IV, a condition affecting the central nervous system was recorded in 280 individuals (31% of the total). Of these 228 were diagnosed as meningitis, 38 as possibly meningitis, and 14 as encephalitis. A cardiovascular condition was the most important feature on 48 occasions (5%). Forty-one of these cardiac conditions were diagnosed as pericarditis and five as myocarditis; in the remaining two cases the precise diagnosis was not specified. Muscular conditions were the most prominent feature in 204 patients (23%). This group included myalgia, patients diagnosed as suffering from Bornholm disease without a description of the symptoms, and chest pain without features suggesting pleural involvement. Respiratory conditions, including colds, sore throat, pharyngitis, croup, bronchitis, pneumonia, pleural pain, or pleurisy, predominated 134 times (15%). Gastrointestinal conditions, including diarrhoea, vomiting, and abdominal pain, were the most prominent feature 77 times (9%). Rash was the most prominent feature in 13 patients: in seven of these individuals the rash was described as rubelliform and in one as maculopapular; in the remaining five cases the character of the rash was not specified. General symptoms—pyrexia, headache, and malaise without specific localizing symptoms—occurred as the predominant feature in 34 patients. Five other conditions were also reported—three diagnosed as arthritis, one as hepatitis, and one as glandular fever.

There were six deaths, but these included one after a serious operation. One of the remaining five deaths occurred in an adult patient with meningitis. Myocarditis was diagnosed in two patients who died; one of these was an infant of 11 days and the other an adult. In two very young infants death resulted from respiratory involvement.

Forty-one individuals had no symptoms. In most of these symptomless excretors the reason why the specimen was sent

for examination was not given in the report: in the few cases in which the reason was recorded the individuals without symptoms were contacts.

Main System Affected at Different Ages

The predominant system affected at different ages is shown in Table V. It is clear that the central nervous system was more often involved than any other system in every age group except early infancy. In the age group 10–29 years this system was involved in 39% of the group. Cardiovascular conditions were more commonly reported in the older than in the younger age groups. As might be expected, muscular conditions, which included myalgia and Bornholm disease, were diagnosed in infants infrequently (4% of all diagnoses in the 0–11 months group), though there were numerous reports in older children and also in adults (18 to 29%). In infants the respiratory system was more often predominantly affected than in any other age group (32%); respiratory conditions were also common in children (21%), but were much less common in the older groups. Gastrointestinal illness was the predominant diagnosis in 21% of all cases in young infants and in 15% of the younger children, but these made up only a small proportion of the diagnosis in older persons.

TABLE V.—Main System Affected According to Age

System Affected	0–11 Months		1–9 Years		10–29 Years		30+ Years		Not Known		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	
Central nervous	15	22.0	74	25.0	118	39.0	68	38.0	5	9.0	280
Cardiovascular	3	4.0	3	1.0	17	6.0	24	13.0	1	2.0	48
Muscular	3	4.0	53	18.0	88	29.0	46	26.0	15	28.0	205
Respiratory	22	32.0	62	21.0	27	9.0	15	8.0	7	13.0	133
Gastrointestinal	14	21.0	45	15.0	10	3.0	2	1.0	6	11.0	77
Rash	0	0.0	11	4.0	1	0.3	1	0.6	0	0.0	13
General	3	4.0	10	3.0	8	3.0	11	6.0	2	4.0	34
Other	0	0.0	1	0.3	3	1.0	1	0.6	0	0.0	5
No symptoms	0	0.0	29	10.0	1	0.3	1	0.6	10	19.0	41
No information	8	12.0	9	3.0	31	10.0	9	5.0	7	13.0	64
Total	68		297		304		178		53		900

In summary, therefore, over the age of 10 years the predominant features related to the central nervous system and muscular system. Under the age of 10 years the central nervous system and muscular system (except in infants) were also often mainly affected, but a common feature in infants and children was the predominant involvement of the respiratory system and gastrointestinal system.

Frequency of Symptoms

Though in some cases only the main symptom (see Table IV) was recorded, other reports did include one or more subsidiary clinical features. The total number of occasions in which each system was reported as affected is shown in Table VI. General symptoms were reported in 391 (43%) of the 900 cases, and it seems likely that such symptoms occurred more often but were not recorded. Next most frequent were reports of respiratory conditions—287 (32%) of the total cases. Conditions of the central nervous system and muscular conditions occurred in 31% and 30% respectively and gastrointestinal conditions in 20%. Cardiac conditions occurred in 6%.

TABLE VI.—Frequency of Reported Symptoms in 900 Patients

Category	Frequency	%
General symptoms*	391	43
Respiratory conditions	287	32
Central nervous system	280	31
Muscular conditions	271	30
Gastrointestinal conditions	180	20
Cardiac conditions	50	6
No information	64	7

* See text.

Comment

The findings of the survey show clearly that reports of isolations of Coxsackie B5 virus from laboratories in the United Kingdom were much more common during 1965 than in any other recent year. The real prevalence of illness due to infection with the B5 virus cannot be known from a survey concerned only with cases in which the diagnosis was confirmed by laboratory examination, but reports were sufficiently numerous to suggest the occurrence of a substantial outbreak in 1965.

Even at the outset this outbreak does not seem to have been confined to any one locality; apparently dissemination was rapid and widespread. In May, for example—the month in which an excess of Coxsackie virus isolations was first noted—reports were received from five widely separated regions and from all areas during the subsequent months. The reports, however, do not give a reliable indication of the relative prevalence of the morbidity in different regions. It is true that reports from laboratories in different locations varied substantially in number, but the differences were probably affected by factors which cannot be assessed in the circumstances of the investigation—for example, the relative frequency with which family doctors in each area requested virological examination for their patients.

The analysis indicates that the outbreak began in the early summer, reached its greatest intensity during the later summer months, and declined in the winter. This is in keeping with the general experience of infections with Coxsackie viruses. Vernon (1964) noted that laboratory reports were most frequent during late summer and autumn in the United Kingdom.

In considering the age groups affected it should be appreciated that the relative prevalence of illness as shown by laboratory reports is bound to be influenced by the proportion of sick persons in each age group for whom a virological examination was requested. For example, there might be a tendency for virological examination to be requested in a larger proportion of sick children as compared with adults. If this were so it would, of course, tend to increase the relative proportion of laboratory reports of infections in children. However this may be in the circumstances of the survey, there is no doubt that a striking preponderance of laboratory reports in 1965 related to young children. Moreover, it might be expected that this age group would be relatively susceptible, since, owing to the minor prevalence of the B5 virus in earlier years, young children must have had less opportunity than adults to acquire immunity by natural infection.

A first-hand and detailed account of clinical symptoms is not possible from this type of laboratory survey, but clinical descriptions of cases of Coxsackie B5 infection during 1965 have been given by Heathfield *et al.* (1967) and Brodribb (1966). The laboratory reports, however, do emphasize the wide variety

of symptoms with which Coxsackie B5 infection may be associated. A similar diversity of symptoms has been reported from other countries; Siegel *et al.* (1963), for example, in an outbreak in Virginia observed chest pain, abdominal pain, pleural effusion, pericarditis, fever, myalgia and headache, painful hepatic or splenic enlargement with fever, nausea and vomiting, usually with pharyngitis and conjunctivitis, and pneumonitis. Other reports of the varied symptoms associated with Coxsackie B5 infection have been published by Gordon *et al.* (1959). In assessing the relative frequency of specific symptoms it must be remembered that virological examination may have been requested more often from patients with certain clinical features. Laboratory reports therefore do not necessarily indicate the real prevalence of specific symptoms in the outbreak. Nevertheless, a striking feature of the reports is the large proportion—almost one-third of the total—in which symptoms indicative of meningitis were the principal feature of the illness. Rubin *et al.* (1958), who first recorded an outbreak of meningitis due to Coxsackie B5 virus, observed that children were principally affected. This may not be a constant feature of morbidity due to Coxsackie B5 involvement since in the cases reported from the laboratories the central nervous system was affected very often in young adults as well as in children.

The few cases without symptoms re-emphasize that, as reported by Spicer (1961), excretion of Coxsackie B5 virus need not necessarily be associated with illness.

Summary

Laboratory reports of Coxsackie B5 virus were much more numerous in the United Kingdom during 1965 than in any previous year, and a widespread outbreak seems to have occurred during the summer months. These reports were concerned with a selected group of patients from whom virus was recovered. Among these patients respiratory symptoms, meningitis, myalgia, and gastrointestinal symptoms were common. Children were especially susceptible.

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Normal Absorption in Thai Subjects with Non-specific Jejunal Abnormalities*

FRANK J. TRONCALE,† M.D.; GERALD T. KEUSCH,‡ M.D.; LOUIS H. MILLER,§ M.D.
RAY A. OLSSON,|| M.D.; RICHARD D. BUCHANAN,§ M.D.

Brit. med. J., 1967, 4, 578-580

There is a growing belief that subclinical tropical sprue is widespread in tropical countries (Klipstein, 1967). This opinion is based on studies of asymptomatic adults in India (Baker *et al.*, 1962), Pakistan (Russell *et al.*, 1966; Lindenbaum *et al.*, 1966b), and Thailand (Sprinz *et al.*, 1962), in whom jejunal histological abnormalities and impaired xylose absorption were frequently found. Recent studies in Haiti by Klipstein *et al.* (1966) show that this condition is very common in individuals complaining of one or more symptoms of the disease. The ease with which the same histological and biochemical abnormalities could be demonstrated in asymptomatic subjects led these workers to speculate that tropical sprue is a disease with a wide range of expression and that the overt cases represent only a fraction of the total number affected.

Because a jejunal lesion has been found commonly in asymptomatic subjects in Thailand (Sprinz *et al.*, 1962), we undertook to study its functional expression with a wider variety of tests than previously employed in order to assess the lesion as a possible precursor of tropical sprue.

Methods

Forty volunteer subjects, primarily from two villages on the outskirts of Bangkok, gave informed consent and were admitted to hospital for the studies to be described. There were 22 females aged 16-72 years and 18 males aged 13-45 years. History and physical examination were within normal limits. The following were performed in every subject: complete blood counts, total serum protein, protein electrophoresis, serum phosphorus, calcium, iron, and beta-carotene. Urinalysis and determination of blood urea nitrogen and serum creatinine were also carried out in all subjects and found to be normal by North American standards. Chest x-ray examinations, performed in all subjects, were also normal.

Five-hour urinary D-xylose excretion and two-hour serum xylose levels were measured in fasting subjects. All subjects received 25 g. of xylose, except for three who received 0.5 g./kg. (13.7, 22.0, and 22.6 g.). Urine and serum specimens were kept frozen after collection. The xylose determination (Roe and Rice, 1948) was performed within 24 to 48 hours after completion of the test.

Vitamin-B₁₂ absorption was measured by the Schilling (1953) technique, ⁵⁷Co vitamin B₁₂ (Racobalamin) with intrinsic factor being used. Vitamin-A absorption was tested in fasting subjects by the oral administration of a dose of 260,000 international units mixed in corn oil. Serum levels were measured before and five hours after ingestion of vitamin A (I.C.N.N.D., 1964).

* From the Clinical Research Center and Department of Pathology, Medical Research Laboratory, S.E.A.T.O. Medical Project, Rajavithi Road, Bangkok, Thailand.

† Captain, Medical Corps. Present address: Harvard Medical Unit, Boston City Hospital, Boston, Massachusetts 02118.

‡ Present address: New England Medical Center Hospitals, Boston, Massachusetts.

§ Captain, Medical Corps.

|| Lieutenant-Colonel, Medical Corps. Present address: Walter Reed Army Institute of Research, Washington, D.C.

For the lactose-tolerance test an oral dose of lactose (1.5 g./kg. body weight) was administered. The glucose-tolerance test was performed with an oral dose of 0.75 g. of glucose/kg. body weight, an amount equimolar to the glucose content of the lactose in the lactose-tolerance test. Blood glucose was estimated (Technicon AutoAnalyzer method, 1937) before and 15, 30, 45, 60, 90, and 120 minutes after each sugar was administered.

Stools were collected for three to six days and were analysed for fat by the method of van de Kamer *et al.* (1949). Because fat intake in the average Thai diet is low (I.C.N.N.D., 1962), a daily supplement of 75 g. of butter was given during the collection period. Carmine red dye was given orally to mark the beginning and end of the collection periods.

Fluoroscope examination of the upper gastrointestinal tract, with small-bowel follow-through studies, was also made. (We are indebted to Major Chitti Palavatana for carrying out the x-ray studies.)

Small-bowel biopsy specimens were taken from the jejunum with a Crosby biopsy capsule (Crosby and Kugler, 1957) after x-ray verification of the position of the capsule. The specimens were orientated with the mucosal side up on filter paper and were fixed in 10% buffered formalin. Haematoxylin and eosin, periodic acid-Schiff, and iron stains were done on all material. In order to minimize artifacts resulting from tangential cutting, care was taken to ensure that the plane of sectioning was parallel to the long axis of the villi and perpendicular to the luminal surface (Rubin and Dobbins, 1965). Measurements of overall mucosal thickness and villus/crypt ratio were made in eight patients by methods similar to those of Swanson and Thomassen (1965).

Results

Laboratory data are shown in the Table. Urinary excretion of D-xylose after a 25-g. dose was 5.84 ± 1.54 (S.D.) g. in 36 subjects. The mean two-hour serum level was 39.8 ± 7.5 (S.D.) mg./100 ml. The percentage of xylose excreted by the three subjects given the smaller dose (0.5 g./kg. body weight) was comparable to that after a 25-g. dose. Mild diarrhoea consisting of two to four watery stools occurred after ingestion of the 25-g. dose in three subjects. Five-hour urine volumes were above 225 ml. in all subjects tested.

Little or no increase in blood glucose occurred after oral lactose administration in the 39 subjects tested (Fig. 1), the mean maximum rise being 2.97 ± 3.07 mg./100 ml. Diarrhoea, consisting of up to 10 loose stools, or abdominal cramps, or both, occurred in 28 of the 39 subjects.

In contrast with the flat lactose-tolerance test, glucose absorption was usually normal. The mean maximum rise in blood sugar after ingestion of 0.75 g./kg. body weight of glucose was 42.5 ± 20.5 (S.D.) mg./100 ml. in 33 subjects (Fig. 1). Only four subjects showed a rise of less than 20 mg./100 ml. (7, 15, 16, and 19 mg./100 ml.). In four other subjects given 100 g. of glucose the mean maximum rise in blood sugar was 61.5 mg./100 ml.

Vitamin-B₁₂ absorption was normal in 33 out of 34 subjects tested (Fig. 2). One subject with a haemoglobin of 12.4 g. excreted 4% of the dose.

Stool fat excretion averaged 2.31 ± 1.37 g./day in 35 subjects tested. The values were below 5 g. in all except two, in whom the fat excretion was 6.3 and 6.8 g./day (Fig. 2).

Vitamin-A tolerance in 24 out of 27 subjects showed a rise of more than 125 μ g./100 ml. above the control value (Gardner and Perez-Santiago, 1956).

The mean serum total cholesterol was 177.5 ± 31 mg./100 ml. in 25 subjects tested. There was no correlation between xylose excretion and serum cholesterol (Robins et al., 1967).

The following mean levels ($\pm$ S.D.) were obtained (the number of subjects tested is in parentheses): serum calcium, 9.31 ± 0.49 mg./100 ml. (29); serum beta-carotene, 133.1 ± 65.0 μ g./100

ml. (34); serum albumin, 4.18 ± 0.56 g./100 ml. (32); haemoglobin, males 13.8 ± 1.9 g./100 ml. (18), females 12.1 ± 1.2 g./100 ml. (22).

Fifteen subjects were found to harbour the following small-intestinal parasites: *Ascaris* alone in 11, *Ascaris* and hookworm in one, hookworm alone in one, hookworm and *Strongyloides* in one, and *Giardia lamblia* in one. No difference in absorption tests was noted between these subjects and the 24 whose stools were negative for parasites, with one exception. Subject 8, whose stools contained *G. lamblia*, excreted the lowest xylose recorded—2.99 g.

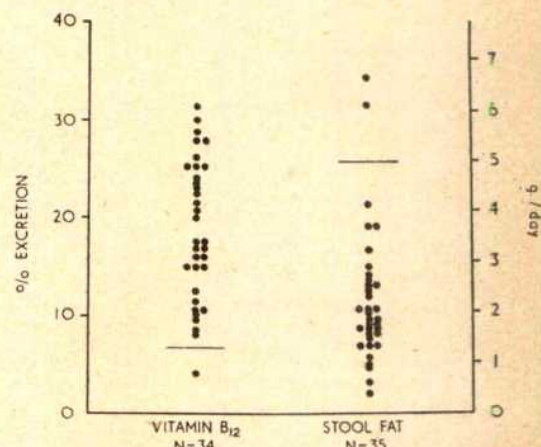


FIG. 2.—Individual values for cobalt-57 vitamin B₁₂ urinary excretion (Schilling test) and for stool fat excretion in Thai subjects. Horizontal lines indicate lower and upper limits of normal, respectively, by Western standards.

The small-bowel pattern by x-ray examination was normal in the 29 subjects studied, except for mild mucosal irregularity in the ileum of one. In six subjects wormlike objects, probably ascarids, were seen in the mid-ileum.

A jejunal biopsy was obtained in each of the 40 subjects. The specimens were reasonably uniform in appearance, with the same mild histological abnormalities as noted in a previous report from Thailand (Sprinz et al., 1962). Under the dissecting-microscope the villi were irregular in height and thickness

Laboratory Investigations

Subject No.	Age	Sex	Urine Xylose Excretion After 25-g Dose (g)	Schilling Test with Intrinsic Factor (%)	Vitamin A Tolerance* Max. Rise (μ g./100 ml.)	Lactose Tolerance† Max. Rise Blood Sugar (mg./100 ml.)	Glucose Tolerance‡ Max. Rise Blood Sugar (mg./100 ml.)	Stool Fat (g./day)
1	31	F	4.05§	15.8	444	0	42	3.79
2	24	F	6.98	17.3	190	5	61	3.30
3	27	F	4.73	—	307	1	16	2.4
4	22	F	5.06	7.8	455	3	56	2.08
5	46	F	3.59	29.8	180	0	67	1.88
6	22	F	5.70	—	—	0	—	—
7	46	F	6.77	4.0	156	8	57	2.07
8	43	F	2.99	—	—	0	57§	—
9	31	F	4.05	—	—	—	—	—
10	17	F	9.39	10.3	252	0	19	1.82
11	72	F	3.22	9.5	343	8	84§	—
12	25	F	4.43	11.3	276	8	79	0.6
13	29	F	4.85	15.2	242	5	98	2.7
14	16	F	6.30	—	421	3	33	1.00
15	32	F	4.30	—	190	0	—	1.40
16	16	F	7.00§	31.3	345	0	34	0.93
17	40	F	7.77	16.8	227	0	21	2.46
18	18	F	7.80	19.9	—	3	66	1.94
19	25	F	6.66	8.4*	—	2	33	1.60
20	35	F	5.97	12.3*	—	5	27	1.84
21	27	F	—	14.9	49	0	28	2.14
22	19	F	4.73	17.6	—	0	66	1.70
23	15	M	7.40	25.7	225	0	51	2.61
24	16	M	6.50	29.0	1,266	5	60	1.40
25	16	M	4.70	28.0	262	0	56	2.80
26	17	M	5.55	23.0	95	0	15	1.14
27	16	M	5.50	10.7	429	0	23	1.71
28	18	M	8.59	28.0	—	5	62§	6.30
29	17	M	6.87	15.0	—	2	43§	3.00
30	17	M	7.27	26.5	280	6	58	3.80
31	13	M	4.41§	10.0	235	8	30	0.44
32	17	M	7.39	24.0	205	6	28	2.00
33	45	M	7.20	25.7	—	2	32	1.65
34	40	M	4.16	20.8	217	6	7	4.26
35	42	M	4.48	17.0	112	0	44	6.81
36	15	M	6.16	23.6	145	4	52	—
37	17	M	6.04	15.8	355	10	44	1.58
38	17	M	4.16	21.7	—	3	42	2.63
39	19	M	5.94	25.7	—	1	23	1.45
40	17	M	7.01	22.8	—	7	34	1.62

* Test dose 260,000 I.U. † Test dose 1.5 g./kg. body weight. ‡ Test dose 0.75 g./kg. body weight. § Test dose 0.5 g./kg. body weight. ¶ No intrinsic factor given. ¶ Test dose 100 g.

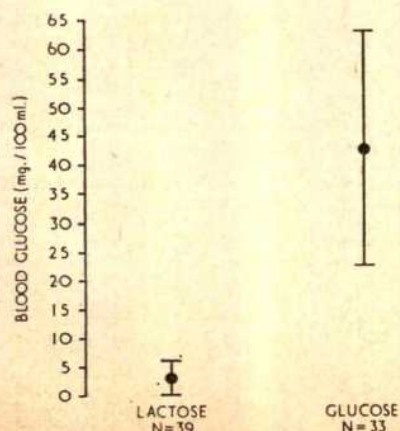


FIG. 1.—Comparison of mean maximal rise in blood glucose over fasting value in Thai subjects after lactose- and glucose-tolerance tests ± 1 S.D.

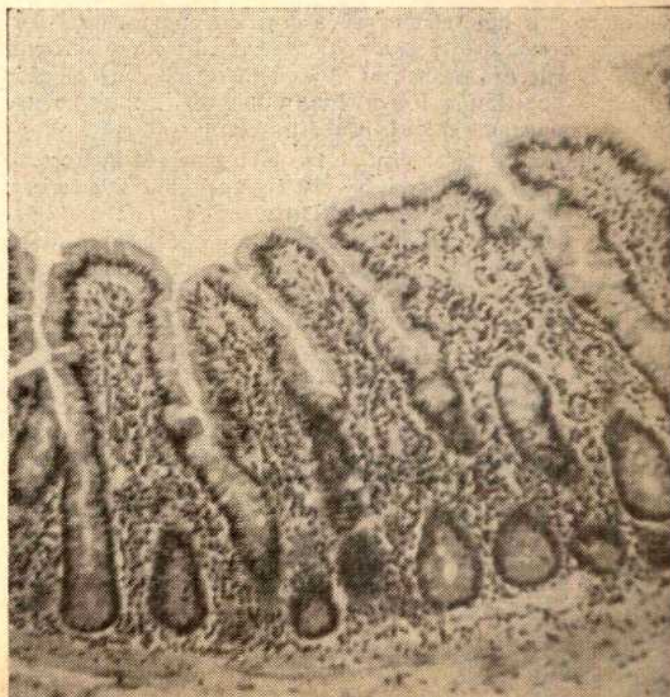


FIG. 3.—Biopsy showing villus shortening, decreased villus/crypt ratio, and increased cellularity of the lamina propria. (Haematoxylin and eosin. $\times 125$.)

and usually leaflike or tongue-like in overall shape. In no specimen did fingerlike forms predominate. A flat or convoluted mucosal pattern was not seen in any patient. Under the light microscope the most impressive changes were villus-shortening with a decrease in the villus/crypt ratio, and uniform infiltration of the lamina propria with plasma cells and lymphocytes (Fig. 3). In the eight biopsies measured the average total villus/crypt thickness was $520\ \mu$ (range 420 – $630\ \mu$) and the average villus/crypt ratio was $2.3:1$ (range $1.9:1$ – $3.1:1$). Periodic-acid-Schiff and iron stains were unremarkable. No correlation was noted between the degree of microscopic or gross abnormality of the biopsies and any of the laboratory findings.

Discussion

In this population of asymptomatic Thai subjects the results of fat, vitamin-B₁₂, vitamin-A, and glucose-absorption tests were comparable to the results obtained in North American subjects (Sheehy and Floch, 1964). Xylose and lactose absorption and the histological appearance of the jejunal mucosa were different, however. Changes of similar degree have been found by others in apparently healthy subjects and interpreted as indications of subclinical intestinal disease (Baker *et al.*, 1962; Russell *et al.*, 1966; Lindenbaum *et al.*, 1966b). Is there any evidence to support this contention?

Urinary xylose excretion after a 25-g. dose in this population (5.84 ± 1.54 g.) is essentially the same as Gardner and Perez-Santiago (1956) (5.60 ± 0.60 g.) and Butterworth *et al.* (1959) (5.70 ± 1.40 g.) have reported from Puerto Rico, and Lindenbaum *et al.* (1966b) from East Pakistan (5.38 ± 1.57 g.). The Thai results are significantly lower than those of a group of North Americans studied in our laboratory (Keusch *et al.*, unpublished data). A similar difference was found by Lindenbaum *et al.* (1966b) between "protected" Westerners living in Pakistan and Pakistanis. While the reasons for this mild reduction in xylose excretion are not apparent, it is important to point out that these results are clearly higher than values found in classical tropical sprue (Sheehy and Floch, 1964).

The xylose excretion in the present study and in Pakistanis (Lindenbaum *et al.*, 1966a) has a bell-shaped distribution. Therefore it is not valid to use a criterion of normality—for example, greater than 5 g. excretion—derived from a different group (North Americans), as is customary in many clinics. Arbitrarily applying such a criterion would divide these homogeneous populations studied in the tropics.

Though lactose malabsorption has been observed in tropical sprue (Bayless *et al.*, 1964), it has also been described in a variety of other gastrointestinal diseases (Haemmerli *et al.*, 1965), as a possible genetically controlled enzyme defect (Cook and Kajubi, 1966), and in a surprisingly high percentage of normal adults (Friedland, 1965). The cause in the Thai is not clear. However, in view of what is apparently a universal occurrence of lactose malabsorption in Thais, the test is of no value in this population as a screening test for tropical sprue (Sheehy and Anderson, 1965).

Interpretation of the very mild non-specific jejunal abnormality is also difficult. Similar histological changes have been reported in kwashiorkor (Burman, 1965), hookworm disease (Tandon *et al.*, 1966), viral illnesses (Sheehy *et al.*, 1964), rosacea (Watson *et al.*, 1965), acute diarrhoea (Lindenbaum, 1965), and after triparanol administration (McPherson and Summerskill, 1963). None of these conditions was present in our subjects. What, then, is the relation between this non-specific histological abnormality and tropical sprue? It has been suggested that there is a spectrum of small-bowel disease in the tropics which ranges from mild and asymptomatic malabsorption to overt sprue (Klipstein *et al.*, 1966). Furthermore, this coexistence of tropical sprue and milder forms of

jejunal abnormality in the same tropical population has been cited as evidence for an association between the two processes (Klipstein, 1967). However, our results fail to support this contention, since intestinal function in Thai subjects with non-specific jejunal abnormalities is different from that in overt tropical sprue. Furthermore, Pakistanis with similar histological changes failed to show improvement in absorption tests after treatment with tetracycline or folic acid, which are usually effective in tropical sprue (Lindenbaum *et al.*, 1966a).

Summary

Forty asymptomatic Thai subjects were studied for evidence of tropical sprue by means of the following tests: xylose excretion, ⁵⁷Co vitamin-B₁₂ and vitamin-A absorption, faecal fat excretion, lactose and glucose tolerance, small-intestine radiographs, and jejunal biopsy. Xylose excretion was lower than in North American subjects but above the range expected in tropical sprue. Lactose malabsorption and mild non-specific histological abnormalities of the jejunal mucosa were present in all. The other studies showed nothing abnormal. These findings were considered insufficient to support a diagnosis of subclinical tropical sprue, and thus we have no evidence for sprue as a widespread disease in Thailand.

We are indebted to Colonel Edward H. Johnston for helpful criticism of the manuscript; to Captain S. W. Nye for helpful discussion in the early stages of the work; to Mrs. Yupa Kasemsant for her help in providing the subjects used in the study; to Miss Natamnuay Soparpun for providing nursing supervision of the study subjects; and to the Laboratory Service of the Clinical Research Center, S.E.A.T.O. Medical Research Laboratory, for performing the chemical analyses.

Requests for reprints should be addressed to Lieutenant-Colonel Ray A. Olsson.

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Prognosis and Treatment of Idiopathic Facial (Bell's) Palsy

D. TAVERNER, M.D., F.R.C.P.; F. KEMBLE,* M.D., M.R.C.P.; S. B. COHEN, M.B., CH.B.

Brit. med. J., 1967, 4, 581-582

Previous reports from this department based on controlled clinical trials (Peiris and Miles, 1965; Taverner *et al.*, 1966) have described methods for the early establishment of an accurate prognosis in idiopathic facial palsy and for the reduction in the incidence of denervation, with permanent sequelae, in this common condition. The present communication describes our experience of the use of these two methods in the routine management of facial palsy in the two years following the controlled trials. The results support the claims previously made, and we are now confident that these methods should be introduced into routine medical practice.

Material and Methods

All patients attending the department of electromyography in the 23 months following the conclusion of the previous study (Taverner *et al.*, 1966) who were suffering from their first attack of idiopathic facial paralysis of not more than five days' duration are included. It was laid down that patients known to be in early pregnancy or to be suffering from diabetes mellitus, severe hypertension, or active peptic ulceration were to be excluded. Four patients were affected. The criteria for diagnosis were the same as those previously used (Taverner, 1955). The patients were allocated to treatment or observation groups on the basis of the threshold to anodal galvanic stimulation of the tongue by the method of electrogustometry (Krarup, 1958; Peiris and Miles, 1965). Treated patients were given five daily intramuscular injections of 80 units of adrenocorticotrophic hormone (A.C.T.H. gel), then 60, 40, 20, and 10 units on successive days. In 26% of the cases the injections were given in the outpatient department of the General Infirmary at Leeds. The remainder were given by the patients' general practitioners or by the district nurse. Some patients were examined electromyographically as described by Langworth and Taverner (1963).

At least three months after the onset of paralysis the final evaluation was made on clinical grounds, and patients with evidence of denervation were followed until no further improvement could be detected. In all except a few very mild cases each patient was seen by more than one observer. Two patients failed to reattend and have been excluded. Three others defaulted from the final assessment, but a reasonable conclusion seemed possible by combining the last clinic record with a report from the family doctor.

Clinical assessment of function in the facial muscles was estimated in terms of a percentage of the normal function of the orbicularis oris, orbicularis oculi, and frontalis muscles on the unaffected side. The results were classified as complete recovery or denervation. Denervation was recorded in the presence of any permanent defect of voluntary movement or any degree of associated movement, however slight.

Results

A study was made of 383 consecutive patients with idiopathic facial palsy of not more than five days' duration. Two de-

faulted—one treated and one observed—leaving 381 for analysis (Table I). There were 191 females, mean aged 42.4 years, and 190 males, mean age 40.1 years.

TABLE I.—Age and Sex Distribution of 381 Consecutive Patients With Idiopathic Facial Palsy

Category	Males		Females		Total
	No.	Age	No.	Age	
Treated	116	42.1 (10-77)	100	42.8 (10-77)	216
Untreated	74	37.0 (4-73)	91	41.8 (2-83)	165
Whole group ..	190	40.1	191	42.4	381

Prognosis.—Satisfactory normal responses to the anodal galvanic threshold test were obtained in 165 patients. The threshold was less than 10 μ A, and there was less than 5 μ A difference between the two sides. The remaining patients were unable to co-operate, were heavy smokers with high thresholds, or had large differences in threshold between the two sides. They were treated with A.C.T.H. gel because of the risk of denervation. The sex and age distribution in the two groups was essentially the same (Table I). Of the 165 untreated patients 153 (93%) recovered completely, as predicted, and 12 underwent denervation, only two seriously (Table II). The 10 with more than 70% recovery of function were fully satisfied with the outcome and considered themselves cured. Six of these 10 patients recovered more than 90% of normal power, and previous denervation was revealed by trivial flickers of associated movement. Retrospective analysis of the clinical records of the two patients with moderate to severe denervation showed that both had admitted subjective disturbance of taste when first seen. The more severely affected had also described hyperacusis and had later developed a significant difference in anodal galvanic threshold between the two sides.

TABLE II.—Outcome in the 12 Patients Who Developed Denervation Among the 165 Untreated Patients

Degree of recovery	..	..	..	<30%	30-70%	>70%
No. of patients ..	..	..	..	1 (8%)	1 (8%)	10* (84%)

* Six of these patients recovered more than 90% of their normal function.

Treatment.—Of 216 patients treated with intramuscular injections of A.C.T.H. gel 178 (82.5%) recovered completely and 38 developed denervation. Only 11 of the latter were affected to a moderate or severe degree (Table III); 27 were only slightly affected and considered themselves cured, and 14 of them recovered over 90% of normal function.

TABLE III.—Outcome in the 38 Out of 216 Patients Treated with A.C.T.H. Who Developed Denervation

Degree of recovery	..	..	..	<30%	30-70%	>70%
No. of patients ..	..	..	..	6 (15%)	5 (13%)	27* (72%)

* Fourteen of these patients recovered more than 90% of their normal function.

Overall Outcome.—The results can best be illustrated by contrasting them with the null hypothesis that neither the prognostic testing nor the treatment had any influence whatever on the outcome. In a series of controlled therapeutic trials over many years we have repeatedly found that the proportion of unselected patients with idiopathic facial palsy developing denervation, using the very strict criteria here applied, is very

Departments of Electromyography and Medicine, The General Infirmary at Leeds 1.

* Present address: Department of Neurology, Queen Elizabeth Hospital, Birmingham 15.

close to 40% (Taverner, 1954; Mosforth and Taverner, 1958; Langworth and Taverner, 1963; Fearnley *et al.*, 1964; Taverner *et al.*, 1966). Taverner (1959) studied 164 successive patients with denervation and found less than 30% recovery in 38%, 30–70% recovery in 23%, and over 70% recovery in 39%.

In the present inquiry 381 patients were studied. In all, 50 (13%) of them developed denervation in contrast to the 150 (40%) that might have been expected. In addition, the degree of denervation was much less severe than could have been expected—a “shift to the right” (Table IV). The proportion of patients with severe denervation—that is, less than 30% of return of function—has fallen from 15% to 1.8%.

TABLE IV.—Observed Outcome in 381 Consecutive Patients with Idiopathic Facial Palsy Compared with the Expected Result (See Text)

Degree of Recovery:				< 30%	30–70%	> 70%
Expected	..	..	..	57 (15%)	34 (9%)	61 (16%)
Observed	..	..	..	7 (1.8%)	6 (1.6%)	37 (10%)

Side-effects.—Two patients complained of dyspepsia suggestive of peptic ulceration, and one of them probably bled fairly severely. Both recovered spontaneously and no permanent ill effects were observed.

Discussion

The method of anodal galvanic testing provides a means of selecting those patients with idiopathic facial palsy who are going to recover completely, with an accuracy of nearly 95%. Its reliability can be increased by noting those patients with a normal threshold who admit to subjective disturbance of taste or to hyperacusis. Daily testing of the threshold will increase its accuracy still further. The importance of the test lies in the fact that it justifies the omission of A.C.T.H. gel therapy from a group of patients who do not need it. The converse proposition, that patients with an abnormal galvanic threshold will develop denervation, is not strictly true. In a few patients seen after five days of paralysis, differences of up to 25 μ A in the threshold on the two sides have been followed by complete recovery. If the threshold is “off scale”—that is, over 300 μ A on the affected side—denervation is invariable in untreated cases. However, our information on this point is scanty because in such patients the clinical picture has usually been modified.

Anodal galvanic stimulation tests the integrity of the chorda tympani nerve (Taverner, 1965), which leaves the facial nerve at a variable point along its descending course through the mastoid air cells (Anson *et al.*, 1963). The section of nerve running from the geniculate ganglion to a point between the branch to the stapedius muscle and the chorda tympani has a special microscopic structure (Sunderland and Cossar, 1953). This section of the facial nerve forms a single bundle with a dense, thick, perineurial sheath surrounded by a thicker but less dense epineurium merging with the walls of the bony canal. The rest of the nerve consists of a plexus of tiny nerve bundles with many anastomoses. Each small bundle has a thin perineurium and the whole is surrounded by a loose perineurium. It seems from our results that complete recovery is likely when the lesion causing the paralysis is situated distally. In this section of the nerve any swelling of the nerve bundles is con-

tained by the perineurium rather than by the bony walls of the Fallopian canal. It is probable that the mid-portion of the nerve, with its dense perineurium surrounding a single, compact bundle of fibres, may be especially liable to internal damage secondary to swelling. This would explain the high liability to denervation when the chorda tympani is involved (Peiris and Miles, 1965).

The results of A.C.T.H. therapy can be regarded as satisfactory in that the overall incidence of denervation has been reduced by two-thirds and of severe denervation with permanent disfigurement by 90%. There is no evidence that the severity of Bell's palsy has changed spontaneously in recent years. It has been shown that the prognosis is better in younger patients, but the age distribution of the various groups of patients in the present series is exactly the same as in the past. Further improvement is to be expected if treatment is begun on the first day of palsy. This would be justifiable in all cases of severe facial palsy if facilities for anodal galvanic testing are not immediately available.

It is still not clear why A.C.T.H. should succeed when oral corticosteroids fail (Taverner, 1954), but this effect has been noted before in neurological conditions (Miller *et al.*, 1961). A rigorously controlled trial to test this point has now been instituted in this department.

Summary

The results obtained in the management of 381 consecutive patients with idiopathic infranuclear facial (Bell's) palsy are reported.

Measurement of the threshold for anodal galvanic stimulation established the prognosis for recoverable conduction block with an accuracy of over 90%.

Treatment with A.C.T.H. gel intramuscularly was given to 216 patients. The results in the whole group of 381 patients show a reduction in the overall incidence of denervation by two-thirds and of severe denervation by 90%.

We thank Miss L. Lodge and Mr. M. Twitchett for their expert technical assistance. We are indebted to the many doctors who have referred patients so promptly. We are grateful to the chairmen and secretaries of the local health committees in Leeds, Bradford, Barnsley, Dewsbury, and the West Riding for their enthusiastic co-operation.

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Gamma-M Deficiency Predisposing to Meningococcal Septicaemia

J. R. HOBBS,* M.D., B.SC., M.R.C.P., M.C.PATH.; R. D. G. MILNER,*† M.A., M.B., M.R.C.P.

P. J. WATT,*‡ M.B., M.R.C.P.

Brit. med. J., 1967, **4**, 583-586

Before his death from cerebrospinal fever Dr. G. D. Heist showed that he was one of the rare individuals whose blood had no bactericidal action on meningococci (Heist *et al.*, 1922). His father and four uncles also died of illnesses resembling meningococcal infections. We have observed two patients with fulminating meningococcal septicaemia who had abnormally low serum γ M globulins. Noting the susceptibility of Dr. Heist and possibly his family to meningococcal infections, and the possibility of a causal relation between a deficiency of serum γ M globulin and meningococcal infection, we carried out a survey of the immunoglobulin levels in the relatives of our two patients and made a study of antibodies to meningococci.

Subjects

Propositi

The immunoglobulin levels of five children suffering from meningococcal meningitis or septicaemia were studied. Brief summaries of their case histories are shown below.

Case 1.—An 8-year-old West Indian boy was admitted in a state of shock with an ecchymotic rash which had started 12 hours earlier. Waterhouse-Friderichsen syndrome was diagnosed, and treatment with intravenous antibiotics, hydrocortisone, and plasma expanders started immediately, but he became comatose and died four hours later. Before treatment started the plasma cortisol level was 61 μ g./100 ml. and the neutrophil count 9,000/cu. mm., with a marked left shift. Meningococci were isolated from blood cultures. Necropsy revealed bilateral haemorrhagic necrosis of the adrenals, fibrin occlusion of subcutaneous and dermal vessels with haemorrhage into the dermis, pulmonary congestion, and oedema.

Case 2.—A 5-year-old boy was admitted because of generalized convulsions, neck stiffness, and a fever of 107.4° F. (41.9° C.) which had begun eight hours earlier. Cerebrospinal fluid was normal and antipyretics were effective initially, but eight hours later hyperpyrexia returned accompanied by coma and a purpuric rash. A diagnosis of meningococcaemia was made and was later confirmed by blood culture. The neutrophil count was 5,000/cu. mm. and showed an extreme left shift. Despite treatment he died two hours later. The plasma cortisol level just before treatment with corticosteroids was 208 μ g./100 ml. Necropsy revealed no important abnormality apart from purpura.

Case 3.—This patient was a first cousin of Case 2. When 4 weeks old and asymptomatic she was found to have normal immunoglobulin levels for her age during screening of the relatives of Case 2. At the age of 9 weeks she was admitted because of neck stiffness and fever. The neutrophil count was 7,000/cu. mm., with a marked left shift. Blood and C.S.F. cultures grew meningococci. She responded to antibiotic therapy and made a complete recovery.

Case 4.—An 11-month-old girl was admitted because of a two-day history of fever and neck stiffness. Her blood showed a neutrophilia with a left shift. Meningococci were grown from both blood and C.S.F. cultures. Chemotherapy resulted in a slow but complete and uneventful recovery.

Case 5.—An 8-week-old baby was admitted because of fever which had not responded to penicillin. Examination showed a

petechial rash and a bulging anterior fontanelle. The C.S.F. contained moderate numbers of neutrophils, some of which contained Gram-negative diplococci, glucose 35 mg./100 ml., and protein 335 mg./100 ml., but yielded no bacterial growth. A clinical diagnosis of meningococcal meningitis was made, and with intensive chemotherapy she recovered completely.

Families

A survey of the immunoglobulin levels of all the available relatives of Cases 1 and 2 was carried out shortly after the death of these patients. The parents of Case 5 had normal immunoglobulin levels, but both the mother and father of Case 4 had γ M levels of 30 mg./100 ml. with normal γ G and γ A levels.

Positive Controls

Sera taken from four patients (A, B, C, and D) two to three weeks after the onset of meningococcal meningitis were kindly supplied by the Standards Reference Laboratory, Colindale, and were tested for meningococcal antibodies and immunoglobulin levels.

Normal Sera

Pooled serum from 10 mothers and pooled cord serum from their babies were tested for bactericidal action on meningococci under varying conditions. Cord serum contains half the adult level of haemolytic complement (Ewald *et al.*, 1961), has the same γ G content, but is deficient in γ A and γ M.

Idiopathic Isolated γ M Deficiency

Serum immunoglobulin levels were measured in over 3,000 miscellaneous hospital patients. Among 350 patients with deficiencies most had subnormal levels of γ G, γ A, and γ M all together. However, in 76 patients subnormal levels of γ M globulin occurred alone. In 47 of these the abnormality was thought to be secondary to pre-existing diseases such as myelomatosis, chronic lymphatic leukaemia, lymphoma, renal failure, idiopathic steatorrhea, etc. In 29 patients there was no known predisposition. Of these, 18 were asymptomatic, but among 11 who were symptomatic were three of the propositi (Cases 1, 2, and 4), two with pneumococcal meningitis, one with *Escherichia coli* meningitis, one with recurrent *E. coli* pyelonephritis, and four with mixed respiratory infections. Bacteraemia was proved in 10 of these 11 patients.

Methods

Immunoglobulin Measurements.—Immunoglobulin levels were measured by a modified Mancini method (Goldman and Hobbs, 1967). All sera were separated at 37° C. and when possible tested the same day to avoid loss of γ M. Aliquots were stored at -20° C, thawed once only for tests, and then discarded. Our own log-normal ranges are given for adults and throughout childhood in Tables I and II. In the families

* Royal Postgraduate Medical School and Institute of Child Health, Hammersmith Hospital, London W.12.

† Present address: Department of Biochemistry, University of Cambridge.

‡ Present address: The Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London W.2.

of Cases 1 and 2 some sera showed low or borderline γ M levels. After ABO grouping of the red blood cells of such relatives of Case 1, isoantibody titres were measured as one way of assessing the quality of what little γ M globulin the subject had.

Meningococcal Antibodies.—Antibodies to meningococci were sought by the indirect fluorescence method. In Cases 2, 3, and 4 the organisms grown from the patient were tested against the patient's serum. Otherwise serum or C.S.F. was tested against four strains of meningococci—groups A and B, a non-groupable strain isolated from Case 2, and the strain isolated from Case 4. Air-dried smears of the organisms were exposed to the serum or C.S.F. to be tested, washed, then exposed to fluorescent rabbit antisera monospecific for human γ G, γ A, or γ M globulin and finally washed. Results were graded as negative (0) or positive (+, ++, +++). Rabbit γ -globulin fractions were conjugated to both fluorescein and lissamine rhodamine B200. The specificity and efficacy of the antisera had been verified many times on human myeloma marrow samples, etc.

Complement-fixation Tests.—Meningococci of groups A and B and of a non-groupable strain were grown as shake cultures in brain-heart infusion broth enriched with 20% horse serum. Antigens were extracted by a modified Price method (Ross and Stevenson, 1962), and complement fixation was tested as described by Ross (1961).

Bactericidal Activity of Sera.—Two pools of maternal and umbilical cord serum were treated by adsorbing lysozyme and β -lysin on to bentonite (Muschel and Jackson, 1966). Complement was inactivated by heating the serum to 56° C. for 30 minutes. The bactericidal activity of the unabsorbed, absorbed, and heated serum was tested by adding 3×10^5 meningococci to 1 ml. of serum and performing duplicate pour-plate counts at 5, 10, 20, 40, and 60 minutes thereafter.

Results

Table I summarizes the immunoglobulin levels and the results of meningococcal fluorescent antibody and complement-

fixation tests in the nine patients who suffered meningococcal infection. In the fatal cases (Nos. 1 and 2) and in the patient who survived (Case 4), the γ M serum levels were subnormal at the start of the illness, and in Cases 3 and 5 and the positive control A the γ M was low because they were only 2 months old. Case 4 had low serum γ A levels during the acute illness and convalescence. During convalescence γ G or γ M meningococcal antibodies appeared in the serum of survivors and a complement-fixation test was positive in Case 4 and all of the positive controls. In Case 5, the only patient from whom meningococci were not cultured, the nature of the bacterial meningitis was confirmed by the presence of γ M antibodies to meningococci in both serum and C.S.F. during convalescence. Neutropenia, commonly associated with septicaemia, was not present in the five *propositi* in whom phagocytosis appeared to be normal.

The family trees of the relatives of Cases 1 and 2 are shown in Figs. 1 and 2 respectively. The father, paternal uncle, and

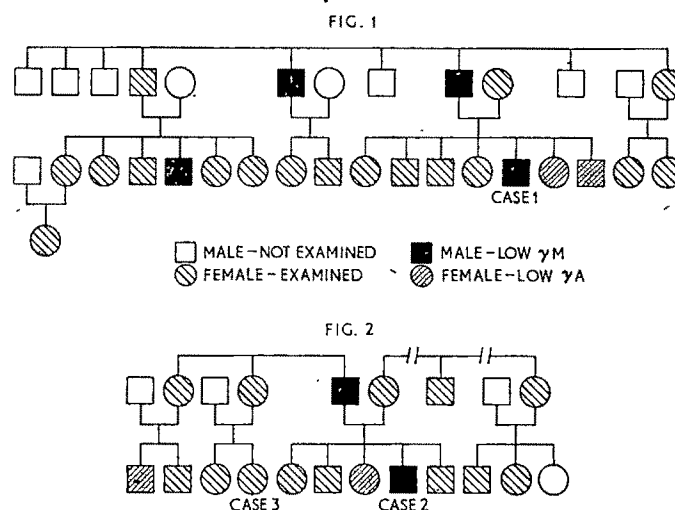


FIG. 1.—Family tree of Case 1. FIG. 2.—Family tree of Case 2. Key as in Fig. 1.

TABLE I.—Immunoglobulin Levels, Meningococcal Antibodies, and Meningococcal Complement-fixation Tests in *Propositi* and Positive Controls. Normal Ranges of Serum Immunoglobulins $\pm$ 2S.D. are Shown in Parentheses

	Age in Years	Sample and Time of Collection After Onset of Infection	Immunoglobulins (mg./100 ml.)			Meningococcal Fluorescent Antibody			Meningococcal Complement-fixation Test		
			γ G	γ A	γ M	γ G	γ A	γ M	Group A	Group B	Non-groupable
Case 1	8/10/12	Serum, day 1	560 (600–1,600)	70 (65–250)	4 (50–170)	0	0	0	0	0	0
" 2	5/2/12	" " 1	1,120 (600–1,600)	190 (55–215)	12 (50–170)	0	0	0	0	0	0
" 3	4/52	" " 6	480 (350–900)	40 (5–40)	25 (10–40)	0	0	0	0	0	0
" 4	9/52	" " 8 months	400 (200–700)	70 (8–45)	130 (15–150)	0	0	0	0	0	0
" 5	10/12	" " day 4	600 (300–1,300)	60 (25–95)	100 (50–170)	+	0	+	0	0	0
" 6	11/12	" " day 27	350 (300–1,300)	<2 (25–95)	21 (50–170)	+	0	0	0	0	0
" 7		" " day 1	300 (300–1,300)	19 (25–95)	50 (50–170)	++	0	0	1/16	1/32	1/32
" 8		" " day 6	70	<1	<1	0	0	0	0	0	0
" 9		" " day 7	50	<1	25	0	0	+++	0	0	0
" 10		" " day 13	230 (200–700)	7 (8–45)	53 (15–50)	0	0	0	0	0	0
" 11		" " day 13	290 (200–700)	7 (8–45)	28 (15–50)	0	0	++	0	0	0
" 12		" " day 13	300 (200–700)	<15 (8–45)	50 (15–50)	+	0	0	1/8	1/32	1/4
" 13		" " day 13	600 (600–1,600)	160 (60–240)	120 (50–170)	0	0	++	1/8	1/16	1/4
" 14		" " day 13	800 (600–1,600)	180 (125–425)	90 (50–170)	+++	0	0	1/128	1/128	1/256
" 15		" " day 13	960 (600–1,600)	300 (125–425)	100 (50–170)	++	0	+	1/128	1/128	1/128

TABLE II.—Cases 1 and 2 and Their Relatives with Abnormal Immunoglobulin Levels, ABO Isoantibody Titres of Relatives of Case 1 with Low γ M Levels. Normal Ranges of Serum Immunoglobulins $\pm$ 2S.D. are Shown in Parentheses

Identification	Age in Years	Serum Immunoglobulins (mg./100 ml.)			ABO Group	Isoantibody Titre	
		γ G	γ A	γ M		Anti-A	Anti-B
Case 1	8	560 (600–1,600)	70 (65–250)	4 (50–170)	0	<1	<1
Father	A	1,300 (600–1,600)	320 (125–425)	40 (50–170)	0	16	16
Paternal uncle	A	1,100 (600–1,600)	125 (125–425)	40 (50–170)	0	512	32
First cousin	A	1,600 (600–1,600)	125 (125–425)	45 (50–170)	0	512	32
Brother	6	1,600 (600–1,600)	48 (60–230)	100 (50–170)			
Sister	8	1,600 (600–1,600)	<15 (65–250)	125 (50–170)			
Case 2	5	1,100 (600–1,600)	190 (55–215)	12 (50–170)			
Father	A	640 (600–1,600)	480 (125–425)	40 (50–170)			
Sister	7	1,300 (600–1,600)	48 (60–240)	125 (50–170)			
First cousin	1½	900 (350–1,400)	<15 (30–120)	75 (50–170)			

paternal first cousin of Case 1 and the father of Case 2 had γ M levels more than 2 S.D. below our normal range (Table II) but were asymptomatic and had uneventful past histories. Two siblings of Case 1 and a sibling and first cousin of Case 2 had abnormally low serum γ A levels. Case 1 had a lower titre of ABO isoantibodies than his relatives with low γ M levels (Table II).

The bactericidal activity of normal serum to meningococci was investigated with pooled maternal or umbilical cord serum. The destruction of complement by heating removed bactericidal activity to meningococci. Fig. 3 shows that unadsorbed umbilical cord serum had a moderate bactericidal activity but that this disappeared after the adsorption of lysozyme and β -lysin. Maternal serum, on the other hand, had a much greater bactericidal activity, which was only slightly lessened after adsorption of the serum.

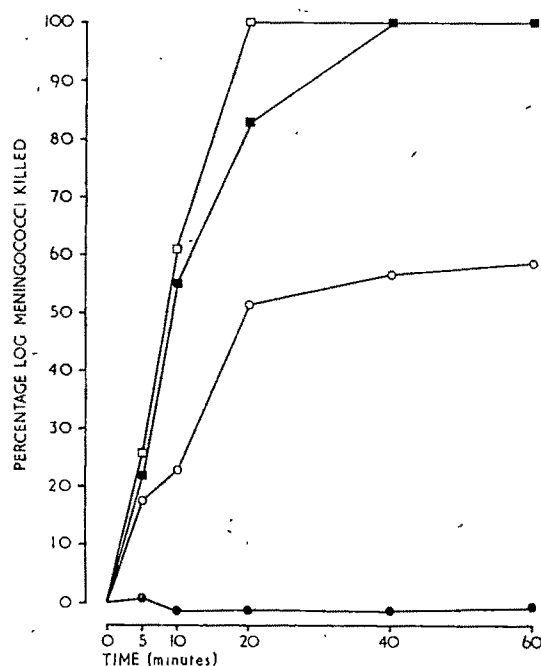


FIG. 3.—Bactericidal activity to meningococci of pooled maternal (squares) or cord serum (circles). Results from unadsorbed serum are shown by open symbols and from serum after bentonite adsorption by solid symbols.

Discussion

The observation that two boys who died from the Waterhouse-Friderichsen syndrome had a deficiency of serum γ M globulin led to an investigation of the role of γ M globulin as a humoral defence mechanism against meningococci. Neither of the boys died from acute adrenal failure, for plasma cortisol levels shortly before death were normal or raised. Neutropenia was not responsible for the rapid multiplication of meningococci, and in the case of Dr. Heist normal phagocytosis of meningococci was observed. It was postulated that the fulminating meningococcal septicaemia was due to a lack of bactericidal antibody and that death probably resulted from endotoxaemia or a generalized Schwartzman reaction. The post-mortem finding of fibrin occlusion of small vessels in Case 1 was in keeping with the view that death in a generalized Schwartzman reaction may be due to widespread intravascular coagulation (Skjörten, 1966).

Immunoglobulin levels and meningococcal antibodies were studied in three children admitted to hospital suffering from meningococcal meningitis and in the sera of four patients who were convalescing from meningococcal meningitis. None of the three children had meningococcal antibodies on admission to hospital, but γ M and/or γ G antibodies were detected in all

seven patients during convalescence. In a 2-month-old baby (Case 5) γ M meningococcal antibodies were found in the C.S.F. on the sixth but not on the first day after admission. Normally, γ M is not present in the C.S.F. (Schultze and Heremans, 1966), and the finding of C.S.F. γ M antibody in one patient suggested that the concentration had risen either as a result of active transport of γ M across the blood-brain barrier or, more likely, by secretion from cells which had migrated into the sub-arachnoid space. It was thought unlikely that γ M (mol. wt. 1,000,000) had entered the C.S.F. by simple diffusion, for it was present at half the serum concentration whereas γ G (mol. wt. 160,000) was present at one-fifth the serum concentration.

The detection of both γ G and γ M meningococcal antibodies prompted a study of the meningococcal activity of normal maternal and umbilical cord serum. The cord serum had the same γ G as the maternal serum but negligible amounts of γ A or γ M.

The meningococcal activity of both adult and cord serum was dependent on complement, but the activity of adult serum was not greatly affected by bentonite adsorption of lysozyme and β -lysin (Fig. 3). The weaker activity of cord serum was completely abolished after bentonite adsorption. This suggested that the meningococcal activity of adult serum did not reside in γ G globulin, and since fluorescence had failed to detect γ A antibodies the evidence favoured γ M as the site of meningococcal activity. Bactericidal antibodies against other Gram-negative organisms have been found mainly in the γ M fraction of the serum (Michael and Rosen, 1963; Evans *et al.*, 1966) and are absent in the γ A fraction (Adinolfi *et al.*, 1966).

Cohen and Norins (1966) demonstrated by immunofluorescent techniques that there were natural antibodies to *E. coli* and *Neisseria gonorrhoeae* in the γ A, γ G, and γ M fractions of normal serum and suggested that γ G antibodies had a critical role in the bacterial recognition system of the host. However, in a prospective study Sample *et al.* (1966) showed that prophylactic pooled human gammaglobulin (virtually only γ G globulin) offered no protection against the development of meningococcal meningitis and septicaemia.

In a study of the epidemiology of meningococcal infection more than 90% of Army recruits entering a training camp were found to become nasopharyngeal carriers of the endemic group B meningococcus (Brown and Condit, 1965). Despite the almost universal colonization of the upper respiratory tract of recruits entering an endemic area, only 1 in 400 got systemic disease, and of these only 10% had fulminating meningococcaemia. It is possible that the very small percentage of people who develop fulminating meningococcaemia lack an effective system for destroying meningococci in the blood stream which may be γ M globulin. The colonization of the nasopharynx by meningococci in most of the recruits suggests that γ A globulin, the immunoglobulin which normally protects mucus surfaces (South *et al.*, 1966), does not afford protection against meningococci. Our failure to detect γ A antibodies to meningococci is in keeping with this suggestion, which also lends support to the theory that meningococci gain access to the C.S.F. via the cribriform plate.

In the retrospective survey of immunoglobulin levels in over 3,000 hospital patients, 29 had an idiopathic isolated γ M deficiency. A third of these had proved bacteraemia, confirming the importance of γ M antibody in blood-stream defence. Further, pronounced increases in γ M levels occur in infections mainly confined to the blood stream such as malaria, trypanosomiasis (Mattern *et al.*, 1961), bartonellosis, and rickettsial endocarditis (Hobbs *et al.*, 1967b).

The discovery that the fathers of the two fatal cases and two male relatives of Case 1 also had γ M deficiency suggested that the abnormality might be inherited. This could offer an explanation of why Heist, whose blood had no meningococcal activity, and his five male relatives, all died of illnesses resembling cerebrospinal fever.

This isolated and severe γ M deficiency can be classified as a dysgammaglobulinaemia. It is distinct from the Giedion-Scheidegger variety (type 1), where γ A is also very low and where there is a continual history of all kinds of bacterial infections from birth. Case 4 initially showed a low γ A and γ M, but this may have been due to delay in immunological maturation, for both are now developing normally. Cases 1 and 2 are also distinct from the Wiskott-Aldrich syndrome (type VA), a sex-linked recessive condition usually fatal to affected males before 10 years of age, where though γ M deficiency appears it is usually associated with a marked increase of γ A. Clinically there is a long history of eczema, thrombocytopenia, and recurrent infections from soon after birth. Cases 1 and 2 have therefore been classified as type VB by Hobbs *et al.* (1967a). Furthermore, it is realized that isolated deficiency of γ M can be found in apparently healthy subjects (type VO) and can be associated with defects of other classes of immunoglobulins in both sexes of given families (Burtin *et al.*, 1964). Thus the finding of γ A deficiency in four other relatives of Cases 1 and 2 adds support to a genetic basis for their fatal abnormality.

Summary

Serum immunoglobulin levels and meningococcal antibodies were measured in nine patients suffering from meningococcal infection. The bactericidal activity of normal serum to meningococci could be attributed largely to γ M globulin. Severe γ M deficiency, probably inherited, was found in two boys dying from fulminating meningococcal septicaemia. Other evidence supported the view that γ M antibodies are an important humoral defence mechanism and that the normal

presence of these antibodies in the blood stream restrains systemic meningococcal infection to the C.S.F.

We thank Professor J. P. M. Tizard and Dr. J. A. Davis for allowing us to study patients under their care; Dr. S. Worledge, who estimated the blood groups and isoantibody titres; and Professor L. P. Garrod for his advice. Requests for reprints should be addressed to Dr. J. R. Hobbs, Department of Chemical Pathology, the Royal Postgraduate Medical School, Ducane Road, London W.12.

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Access to Circulation by Permanent Arteriovenous Fistula in Regular Dialysis Treatment*

J. S. HANSON, M.B., B.SC.; M. CARMODY, M.B.; B. KEOGH, M.B.; W. F. O'DWYER, M.D.

Brit. med. J., 1967, 4, 586-589

Regular dialysis therapy has now become the accepted treatment of selected cases with end-stage renal disease.

Hitherto, repeated access to blood vessels for dialysis was achieved by means of the conventional Teflon or Teflon-Silastic prosthesis, establishing an external semipermanent arteriovenous shunt (Quinton *et al.*, 1960, 1962; Hegstrom, 1961). In spite of its considerable success this technique is far from perfect, and problems of infections and clotting remain as a major cause of trouble in the management of these patients. The average survival rate for external shunts varies considerably from one centre to another. In a series published from the Swedish Hospital in Seattle the mean shunt life for both arteries and veins varied from 11 days to 11.4 months (Murray *et al.*, 1964). In a more recent review from the same centre (Pendras and Smith, 1966) an average cannula survival of 12 to 14 months was reported. This they attributed to the prevention of infection in the patient before and shortly after operation, and also by avoiding cannulation in the severely uraemic state.

We have been unable to achieve a similar standard of shunt survival since we began regular dialysis therapy in November 1964. Our survival rates in arteries and veins were 3.8 and 3.6 months respectively, the majority of the failures occurring

in the first six weeks after surgery. The longest surviving shunt was 16 months. Infection and clotting, the major causes of our failures, were responsible for a high morbidity and often long periods of immobilization in hospital for surgical revision of the cannulas. This was particularly true for those in the lower limbs. The frequent manipulations involved in declotting were also a contributory factor to the psychological fixations which some of these patients developed about their cannulas. Our relative failure with the Quinton type shunt prompted us to adopt the surgically created arteriovenous fistula as described by Brescia *et al.* (1966). As a result of the arteriovenous fistula so created the arm veins are distended, allowing dialysis to be carried out by venepuncture. The veins are then in effect an extension of the arterial system.

Surgical Technique

Anaesthetic.—Brachial plexus block by the axillary route has been used routinely and has proved very satisfactory. Firstly, the accompanying sympathetic block dilates the blood vessels and prevents vascular spasm until the vein has been denervated by the stripping of its fascia. The sympathetic blockage may lead to free bleeding from the line of incision, but

* Department of Surgery and Renal Unit, Jervis Street Hospital, Dublin.

this can be controlled by circumvential infiltration around the wound with a local anaesthetic containing adrenaline. Secondly, the muscular paralysis enables the patient to lie in comfort with an outstretched arm for prolonged periods. Thirdly, the sensory effects of the brachial plexus block extends well into the postoperative period, and the analgesic effect is much appreciated by the patients. Fourthly, when performing this procedure under brachial block it is not necessary to admit the patient to hospital. Also it can be carried out at a time convenient to the patient and therefore does not interfere with his normal working hours.

Choice of Vessels and Site of Fistula Formation

In the early stages of this project we received patients who had had repeated shunt insertion. Frequently only ulnar arteries remained patent, the radial arteries having been cannulated. This does not make fistula formation impossible. Neither does it appear to impair seriously the blood supply to the hand if the sole remaining main vessel is used for fistula formation. In Tables I and II are given particulars of a series of 14 patients on regular dialysis treatment in whom an arteriovenous fistula was created surgically.

TABLE I.—Permanent Arteriovenous Fistula (A.V.F.) in Regular Dialysis Therapy

Case No.	Sex	A.V.F. Formation	Artery Used	Complications
1	M	28/12/66	Radial	None
2	M	2/1/67	"	Left A.V.F. non-function
3	F	16/1/67	"	Right A.V.F. successful
4	M	17/1/67	"	None
5	M	18/1/67	"	"
6	F	21/1/67	"	"
7	M	21/1/67	"	"
8	M	16/2/67	Ulnar	Right A.V.F. infection and haemorrhage
9	F	23/1/67	Radial	Left A.V.F. successful
10	M	24/1/67	Ulnar	None
11	F	31/1/67	"	Transplanted 5/4/67
12	M	20/3/67	"	A.V.F. non-function (Quinton shunt replaced)
13	F	9/4/67	Radial	None
14	F	10/4/67	"	"
15	F	15/4/67	"	"
16	M	14/6/67	"	"

TABLE II

No. of patients	14
No. of arteriovenous fistulae	17
No. of dialysis months	67
No. of dialyses	561
Failed arteriovenous fistula	3*

* Two successful repeats, opposite limb.

New patients introduced to the regular dialysis therapy programme cause no problem in respect of suitability of artery and vein, as they are initially fitted with a temporary Carmody (1964) type shunt, leaving a virgin arm for fistula formation. When available the radial artery and cephalic vein are used routinely, but, as mentioned, the ulnar artery and any superficial vein in close proximity may be used. Venae comitantes do not give the flow required in the superficial veins. When using an ulnar artery it is preferable to avoid use of the small superficial veins in the area of the skin creases on the ventral carpal surface. In this situation the skin is tethered to the deep fascia, making dissection difficult and increasing the possibility of vessel spasm due to excessive handling. Again, the veins in this area form a branching network; therefore without ligating some branches it is unlikely that a segment of vessel adequate for fistula formation will be obtained. Finally, in association with brachial block there appears to be more superficial bleeding in the area.

In choosing a suitable vein a venous tourniquet is applied and the arm inspected. The availability of a suitable vein really dictates the site of fistula formation, but it is desirable to create it as far distally as possible in the arm to facilitate future venepuncture and tourniquet application. The depth

of the artery from the surface does not militate against the use of a suitable vein.

A transverse incision is used routinely. Longitudinal incisions have to be of greater length to provide adequate exposure; also, they heal badly. The incision is made at the point of nearest proximity of artery and vein, unless the vein has an excessive number of branches in the area. A segment of vein without branches and sufficient for an anastomosis is necessary, as it is desirable to leave as many patent tributaries as possible. In the virgin arm the cephalic vein is constant in position and generally of good calibre, but in patients who have repeated shunt insertion and intravenous therapy most subcutaneous veins may be occluded. With an adequate cross anastomosis, veins that are quite minute enlarge and it seems that large thrombosed veins may recanalize. The skin incision should be of sufficient size to ensure that an adequate segment of vessel may be mobilized without tissue distortion due to retraction. Caution must be exercised to limit the incision to skin only, as otherwise the veins in the superficial fascia may be severed.

When the skin has been incised the superficial fascia is opened as far as the lateral margin of the vein on both sides. The skin and superficial fascia are undermined on both sides of the wound, leaving the vein encased in its own fascia. A venous tourniquet is applied to dilate the vein. The fascia on the vein is incised down to the adventitial layer at a central point and a sling is positioned here. From this point the vein is cleared by sharp dissection. Once the correct plane has been entered it is quite easy to clear the vein. To ensure maximum mobilization adjacent tributaries are cleaned in similar fashion. Another sling is now inserted and the vein is swung to the area of the artery, indicating the degree of mobility and adequacy of dissection. The vein lies in superficial fascia. In order to achieve approximation with the artery it must be slung deep to the fascia. This makes adequate undermining of the fascia a matter of paramount importance if "kinking" of the vein is to be avoided.

It must be emphasized that the completed arteriovenous fistula will be between deep and superficial fasciae, and "kinking" may occur at the junction of dissected and undissected segments of the vein. The tourniquet is now released, there being no danger of vessel spasm in the segment of vein to be used. The fascia over the artery is incised longitudinally. At one point the artery is freed from the venae comitantes and the sling inserted round the artery; the artery is dissected free. Only tributaries that will definitely interfere with its mobility are cut and tied. A second sling is inserted. With the use of both sets of slings, artery and vein are approximated (Fig. 1). The vessels must lie parallel for a distance of at least 2.5 cm. between slings without tension or angulation if adequate fistula

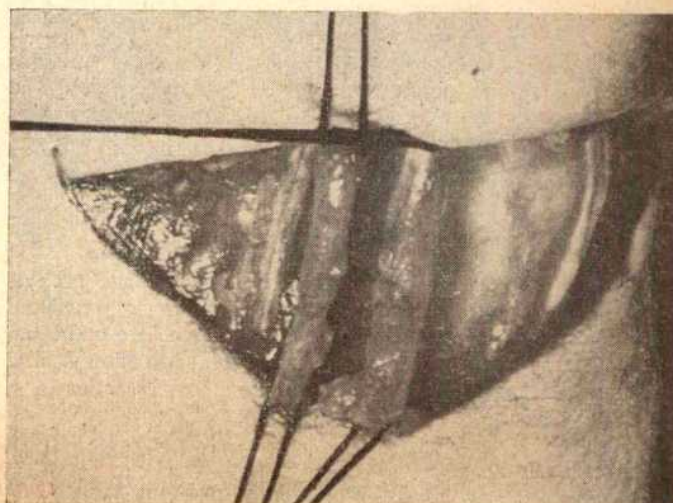


FIG. 1.—Vessels dissected and approximated. Use of slings indicating adequacy of dissection.

formation is to be obtained. This is a critical point, as an equal flow in the vein, both proximally and distally, will otherwise not be obtained. Where the artery leaves and enters its own proper tissue plane an edge of fascia remains; this may "kink" the artery. It may therefore be necessary to extend the fascial incision proximally and distally. Both sets of slings are now replaced with De Bakey peripheral arterial clamps. These clamps are introduced from the assistant side. Longitudinal incisions 0.5 cm. in length are made in corresponding lateral surfaces of vein and artery (Fig. 2). The lumen of both vessels is washed out with heparinized saline and a side-to-side anastomosis made in continuous fashion with 00000 polyethylene (Fig. 3). On release of the clamps there is an immediate bruit and thrill. The wound is sutured in two layers.

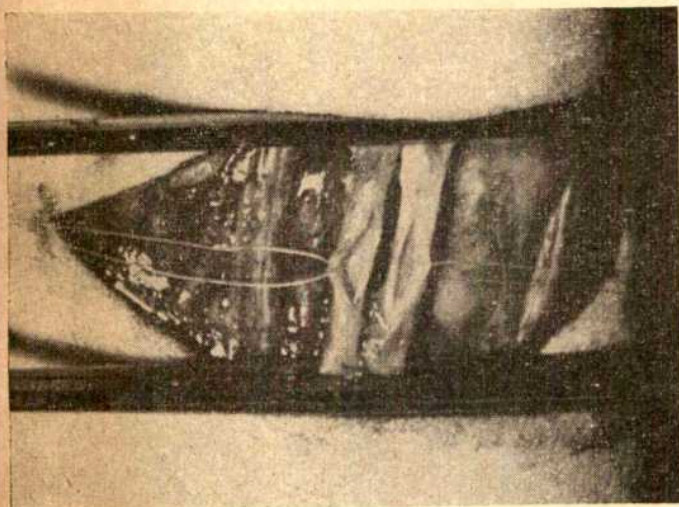


FIG. 2.—De Bakey clamps in position before suturing.

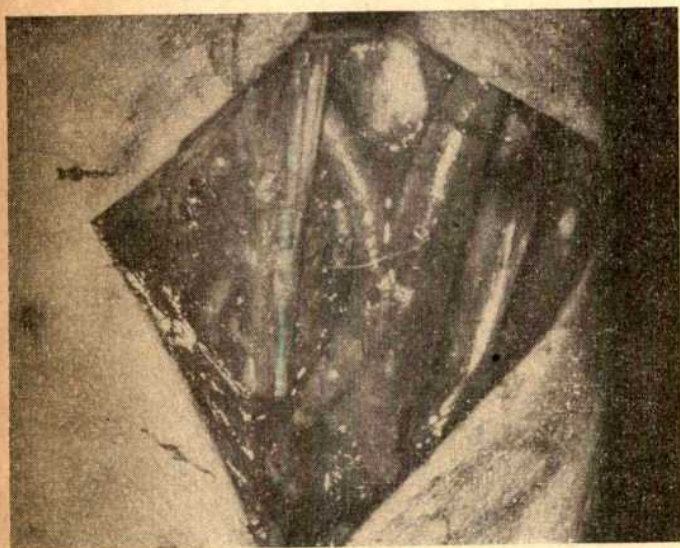


FIG. 3.—Arteriovenous fistula completed.

Management

Postoperative Care.—We feel it is necessary to use prophylactic antibiotics for five days after the operative procedure. It is essential that patients are well dialysed before operation, as this greatly lessens the hazard of infection. To allow healing and vein distension the fistula is not used for seven days.

Dialysis Technique

Previous to venepuncture a tourniquet is applied to the upper arm to obtain venous engorgement. The puncture sites are

infiltrated subcutaneously with 0.5% lignocaine without adrenaline. Initially the obtaining of a suitable puncture needle was a major problem. We tried a variety of needles, but were continuously faced with the problem of clotting of the needles in the lumen despite increasing the standard dose of heparin by 10,000 units. However, we realized that the quality of our needles was at fault, the surface of the inside of the lumen being rough. We now satisfactorily use a 1½-in. (3.8-cm.) 14 gauge thin-walled smooth-bore needle (Bardic). The needles are attached to Tomac extension tubes (Fig. 4). Firstly, the return-flow needle is inserted cephalically below the antecubital fossa and advanced maximally. The tourniquet is released and the standard dose of heparin is infused through this needle. Adequate time for heparinization is allowed. The tourniquet is now reapplied below the proximal needle and the outlet venepuncture is performed. If the needle is inserted proximal to the fistula it should be directed towards the hand, while if inserted distally it should point cephalically. The predialysis blood samples are taken from this latter tube.

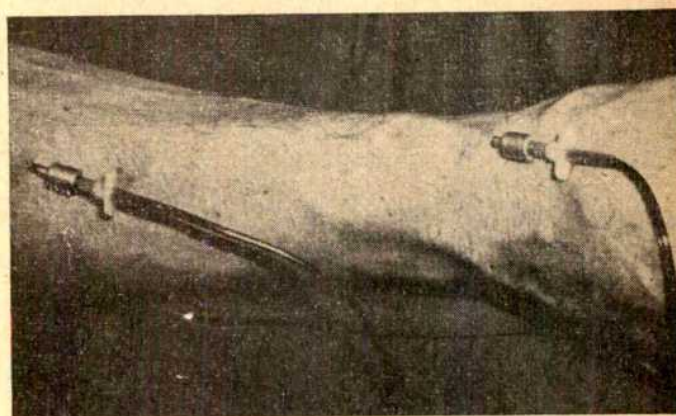


FIG. 4.—Needles in situ—dialysis in progress.

A light venous tourniquet is occasionally necessary between the needle insertions to ensure adequacy of flow. This is particularly so in the first few weeks after fistula formation, but later is unnecessary as the veins become distended and arterialized. Blood flow rates of 300 ml. per minute are easily obtainable by means of a roller type blood pump. Each dialysis lasts nine hours, and there is no falling off in the blood flow rates. At the completion of dialysis, protamine sulphate is infused. Each needle is removed at intervals of 10 minutes and digital pressure is applied by the patient along the line of venepuncture until haemostasis is obtained. This requires three to five minutes on an average. A light dressing is applied to the puncture sites, and the patient discards it after a few hours.

Comment

On our dialysis programme we use Kolff twin-coil machines, similar to those used by Brescia *et al.* (1966), who pioneered this technique of access to the circulation. In order to maintain an adequate flow rate with this technique some form of pump on the "arterial" side is necessary. Therefore the technique is not suitable for use on patients dialysed on a conventional Kiil type machine. In our experience with the external arteriovenous shunt (Quinton-Scribner) we must admit that our earlier regular dialysis therapy patients were inadequately dialysed owing to very demanding acute renal failure commitments. For the past eight months we have been able to correct this, and we recognize that inadequate frequency of dialysis may have increased our incidence of clotting and infection in the original external shunts. We are none the less impressed, however, by the Brescia-Cimino fistula, which allows much greater comfort and freedom for the patient. One woman on our programme has taken up golf since discarding her external shunt for the fistula.

Since we adopted this method of access to the circulation for haemodialysis, the morale of each patient has changed considerably. Patients no longer live with their fears of an artificial Teflon shunt with its possible hazards and complications. They can rehabilitate themselves more easily and their lost working hours have decreased considerably. Similarly, life for members of the staff is no longer punctuated by frustrating crises of clotted shunts and infection.

We have not observed any evidence of cardiac embarrassment in spite of the alteration in circulatory dynamics produced by the introduction of the arteriovenous fistula.

We would like to suggest that this technique might be of value in circumstances other than haemodialysis where repeated access to the circulation is required—for example, repeated transfusions in aplastic anaemia. In this regard Williams *et al.* (1967) and Anderson *et al.* (1967) have reported on the successful use of the conventional type of Quinton-Scribner Teflon shunt in a total of three patients with aplastic anaemia requiring regular transfusions. It is noted, however, that in two cases the problem of clotting occurred. From our experience we would suggest that a permanent surgically created arteriovenous fistula as described here would be a less troublesome method of obtaining access to the circulation when repeated transfusions are required.

Summary

An arteriovenous fistula was created surgically in 14 patients on regular dialysis treatment in order to provide repeated access to the circulation. In 11 patients the initial arteriovenous fistula functioned satisfactorily and without complica-

tions. In two patients in whom the initial fistula failed to function, success was achieved in the opposite forearm. In one patient in whom the procedure failed initially a second attempt to create a fistula has been postponed owing to the poor calibre of her veins and the urgency of maintaining adequate haemodialysis.

ADDENDUM.—Since this communication was submitted for publication two further patients have had successful arteriovenous fistulas established. In addition one patient (Case 9) in whom arteriovenous fistula formation on 31 January 1967 was unsuccessful and in whom a Quinton shunt was replaced has recently had a functioning fistula established by use of her remaining ulnar artery. In September 1967 the total number of patients with successful fistulas was therefore 16.

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Thyrocalcitonin Deficiency after Treatment of Thyroid Disorders by Surgery or Radioiodine

R. N. SMITH,* M.B., CH.B., B.SC., M.R.C.P.ED., D.OBST.R.C.O.G.; H. C. K. LALJEE,† M.B., CH.B., B.SC., M.R.C.P.ED.

Brit. med. J., 1967, **4**, 589–591

The isolation of thyrocalcitonin from human thyroid tissue (Hirsch, Voelkel, and Munson, 1964; Milhaud, Moukhtar, Bourichon, and Perault, 1965; Smith, Laljee, and Dorrington, 1966; Aliapoulos, Voelkel, and Munson, 1966; Tashjian, Frantz, and Lee, 1966; Mazzuoli, Coen, and Baschieri, 1966; Laljee, Smith, and Dorrington, 1967) and the demonstration of its hypocalcaemic action in man (Foster, Joblin, MacIntyre, Melvin, and Slack, 1966; Bell, Barrett, and Patterson, 1966) have stimulated interest in the importance of this hormone in human physiology.

High serum calcium levels stimulate the release of thyrocalcitonin (Foster, Baghdiantz, Kumar, Slack, Soliman, and MacIntyre, 1964; Care, 1965). If the calcium-lowering effect of this hormone was absent the serum calcium might rise higher and fall more slowly after an intravenous calcium load in comparison with a normal response. Deficiency of thyrocalcitonin might occur after removal or destruction of most of the thyroid gland, as may occur after surgery or radioiodine therapy. This possibility has been investigated by studying the response of patients to an intravenous calcium infusion (Smith and Laljee, 1967).

Patients and Methods

Subtotal Thyroidectomy Group.—Patients received intravenous calcium infusions two or three days before and at the same interval after subtotal thyroidectomy for thyrotoxicosis (five) or non-toxic goitre (four); thus each patient acted as his own control. Antithyroid drugs and potassium iodide were given preoperatively to patients with thyrotoxicosis.

Radioiodine Therapy Group.—Our studies included 24 patients who had been treated with radioiodine for thyrotoxicosis from 2 to 15 years previously and a group of seven patients of similar age without any evidence of thyroid disorder who agreed to help in this investigation after its value had been fully explained to them.

Technique.—The intravenous infusion of calcium was given at a constant rate over four hours by means of a D.C.L. micro-pump type T (Messrs. F. A. Hughes & Co. Limited). The dose of elemental calcium was 15 mg./kg. body weight given as a calcium gluconate solution (15 mg. of calcium per 5 ml.). Blood samples were taken before (0 hours) and immediately after the infusion (4 hours), and subsequently at 8, 12, and 24 hours. The serum calcium was estimated by an edetic acid titration with calcichrome as indicator and a manual titrator (Messrs. Evans Electroselenium Ltd.). The rise in serum calcium and elevation above pre-infusion level was plotted at four-

* Lecturer in Pharmacology and Therapeutics, University and Royal Infirmary, Sheffield.

† Formerly Boots Research Fellow, Department of Pharmacology and Therapeutics, University and Royal Infirmary, Sheffield.

hourly intervals up to 12 hours. The area beneath the graph was calculated, and it represented the response to the calcium infusion (Fig. 1).

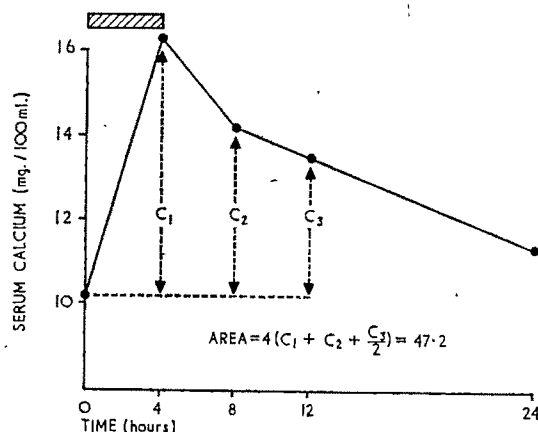


FIG. 1.—Representation of response to four-hour calcium infusion and calculation of the area below the curve of serum calcium values.

Results

Subtotal Thyroidectomy.—There was no significant difference between the preoperative and postoperative responses to the calcium infusion in nine patients (Fig. 2). No difference was apparent between the patients with thyrotoxicosis and those

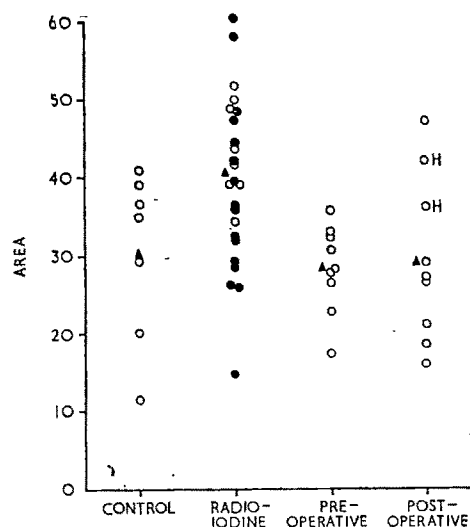


FIG. 2.—Responses to calcium infusion. O = Euthyroid patients. ● = Hypothyroid patients on thyroxine. ▲ = Mean value of each group. H = Hypothyroidism developed six months later.

Details of Patients and the Response After Intravenous Calcium Infusion

Groups	No. Studied	Mean Age ± S.D.	Mean Serum Calcium Values (mg./100ml.) ± S.E.		Mean Area of Graph ± S.E.
			Before Infusion (0 hours)	Rise After Infusion (4 hours)	
Subtotal thyroidectomy:					
1. Thyrotoxicosis:					
Before operation	5	37 ± 5	9.84 ± 0.24	4.59 ± 0.44	27.65 ± 1.56
After operation			9.44 ± 0.20	4.59 ± 0.55	28.75 ± 3.8
2. Simple goitre:					
Before operation	4	46 ± 5	9.85 ± 0.09	4.46 ± 0.51	28.08 ± 3.52
After operation			9.05 ± 0.12	3.92 ± 0.61	28.55 ± 5.6
Radioiodine therapy:					
1. Euthyroid	8	62 ± 7	10.49 ± 0.12	6.54 ± 0.36	43.17 ± 2.05
2. Hypothyroid on thyroxine	16	59 ± 7	9.96 ± 0.15	5.61 ± 0.37	38.80 ± 2.71
Control	7	55 ± 5	9.77 ± 0.34	4.58 ± 0.73	30.13 ± 4.28

with non-toxic goitres (see Table). Three patients had higher calcium levels postoperatively after the infusion compared with their preoperative values. Two became hypothyroid six months after the operation (indicated by H in Fig. 2); the other had a large multinodular goitre. The small portion left appeared grossly disorganized, and accordingly the patient was started on thyroxine immediately after operation.

Radioiodine Therapy.—The response to calcium infusions in 24 patients after radioiodine therapy (Fig. 2) differed significantly from both the preoperative and postoperative surgical groups ($P < 0.005$) and the control group of similar age ($P < 0.05$). There was a positive correlation ($r = +0.50$, $P < 0.02$) between the response to the calcium load and the time interval since the irradiation of the thyroid (Fig. 3). No correlation was apparent in the radioiodine group when the results were plotted in relation to the age of the patients or the total dose of calcium administered.

Discussion

Intravenous calcium infusions were used to assess thyrocalcitonin secretory capacity because the release of this hormone is stimulated by high serum calcium levels and its calcium-lowering action corrects experimental hypercalcaemia (Foster *et al.*, 1964). It does not influence renal excretion of calcium directly but acts by inhibiting the resorption of bone (Friedman and Raisz, 1965; Milhaud *et al.*, 1965; Aliapoulos and Munson, 1965; Gaillard, 1966; Foster *et al.*, 1966; Johnston and Deiss, 1966). The most sensitive measurement of its action is the serum calcium level. The greater rise of

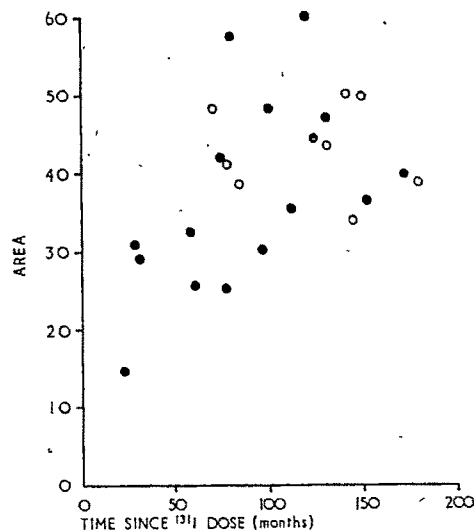


FIG. 3.—Correlation of response to calcium infusion represented by area below serum calcium curve and time interval (months) since radioiodine therapy ($r = +0.50$, $P < 0.02$).

serum calcium and the persistence of elevated readings after intravenous calcium loading are consistent with a deficiency of thyrocalcitonin.

Surgical and radioiodine treatment of thyrotoxicosis may damage the parathyroids (Adams and Chalmers, 1965), but there was no clinical or biochemical evidence of this in our patients. In fact, parathyroid damage would not influence the speed of recovery from hypercalcaemia after calcium loading (Hahnemann and Friis, 1965). Hypothyroidism will alter the response to a calcium infusion (Krane, Brownell, Stanbury, and Corrigan, 1956; Lowe, Bird, and Thomas, 1962). Our patients were all euthyroid, including those with post- ^{131}I hypothyroidism who were on adequate replacement doses of thyroxine.

The effect of subtotal thyroidectomy on the response to an intravenous calcium load was insignificant in most cases. These

patients were left with an amount of thyroid tissue thought to be sufficient to keep them euthyroid. However, two patients who became hypothyroid six months later did not lower the calcium level so efficiently as others in this group. The other patient with a defective response had a radical excision of a multinodular gland, and the tissue left was severely deranged. In these three patients little or no active thyroid tissue was left in the body. In pigs and in rats similar results were found after total thyroidectomy (Care, Duncan, and Webster, 1967; Gittes and Irvin, 1965). Similar calcium infusion studies on 14 patients who had subtotal thyroidectomies have shown defective handling of the calcium load in five (Hahnemann and Friis, 1965). In other infusion studies four out of seven hypothyroid patients receiving thyroxine had delay in return to preinfusion calcium levels (Williams, Hargis, Galloway, and Henderson, 1966). Finally, Ibbertson, Roche, and Pybus (1967) have shown failure to lower promptly the serum calcium after an infusion of calcium in patients with spontaneous hypothyroidism when on thyroxine.

Antithyroid medication has been reported to reduce the release of thyrocalcitonin in pigs (Duncan and Care, 1967), and the glands have a higher thyrocalcitonin content (Care, Duncan, and Webster, 1966). Our studies showed no difference in the response of patients with thyrotoxicosis, who had antithyroid drugs, and patients with non-toxic goitres or those who had no thyroid disorders. Our patients did not have high doses of antithyroid drugs, whereas the pigs had relatively large doses, resulting in considerable gland hyperplasia and hypothyroidism. The latter can produce an abnormal response to a calcium load. Parallel studies of thyroid tissue from patients treated preoperatively with antithyroid drugs in doses sufficient to control their symptoms have not shown any increase in the thyrocalcitonin content of these glands compared with tissue from patients with non-toxic goitres and necropsy thyroid tissue (Laljee *et al.*, 1967). It seems unlikely, therefore, that thyrocalcitonin release was inhibited by the doses of antithyroid drugs given to our patients, and this medication would still be effective two to three days after the operation.

Radioiodine therapy damages thyroid tissue extensively, leading to progressive loss of function due to impairment of cell division. Experience has shown that in many patients hypothyroidism develops insidiously many years after radioiodine therapy (Beling and Einhorn, 1961; Green and Wilson, 1964; Dunn and Chapman, 1964; Nofal, Beierwaltes, and Patno, 1966). Thyrocalcitonin production may similarly fail after thyroid irradiation, and our results suggest that this is also time-dependent. The defective response was independent of the age of the patient.

It is probable that thyrocalcitonin production is deficient in some patients after thyroid surgery or radioiodine therapy owing to factors which are similar to those that result in hypothyroidism. The evidence presented suggests that thyrocalcitonin deficiency can be demonstrated by challenging the thyroid with a calcium load before hypothyroidism is manifest. Furthermore, in patients treated with radioiodine thyrocalcitonin deficiency is time-dependent, but it may precede or follow the onset of hypothyroidism.

Summary

Intravenous calcium infusions were administered to patients treated by surgery or radioiodine for thyroid disorders in order

to assess whether these radical procedures had resulted in a deficiency of thyrocalcitonin.

A defective response to a calcium load was observed in three out of nine patients after thyroid surgery; they had suffered extensive removal of thyroid tissue. In 24 patients treated for thyrotoxicosis by radioiodine a progressive decrease was demonstrated in the response to a calcium load with the passage of time after irradiation. The failure to handle the calcium load efficiently in these patients who have had extensive removal of or damage to the thyroid tissue has been interpreted as evidence of thyrocalcitonin deficiency.

This work was supported by the United Sheffield Hospitals Endowment Fund, by a University Research Fund Grant (R.N.S.), and a Boots Research Grant (H.C.K.L.). The advice and encouragement of Professor G. M. Wilson and Professor D. S. Munro were invaluable. We are grateful for the co-operation of Mr. C. H. Talbot, who performed the operations, and of Mr. A. Young, Dr. K. H. Hardy, and Dr. A. J. Smith, who gave us the opportunity to include patients under their care. We wish to thank Miss Sandra Taylor for her technical assistance and our house-physicians, who have kindly taken the evening blood samples on many occasions.

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Long-term Trial of Local Guanethidine in Treatment of Eye Signs of Thyroid Dysfunction and Idiopathic Lid Retraction

A. L. CROMBIE,* M.B., CH.B., F.R.C.S.ED.; A. A. H. LAWSON,† M.B., CH.B., M.R.C.P.ED.

Brit. med. J., 1967, 4, 592-595

The advent of adrenergic blocking agents has provided a new tool in the treatment of the eye signs of thyroid dysfunction and idiopathic lid retraction. The increasing availability of local ophthalmic preparations of these drugs has resulted in the trial of some of them in the treatment of these distressing eye conditions. For example, Lee, Morimoto, Bronsky, and Waldstein (1961) described the therapeutic use of local phentolamine, and Sneddon and Turner (1966) and Gay and Wolkstein (1966), in almost simultaneous communications, reported favourably on the short-term use of local guanethidine (Ismelin). Sneddon and Turner (1966) also reported on the effects of conjunctival administration of the β -adrenergic blocking agent propranolol, and Gay, Salmon, and Wolkstein (1967) have suggested that local bethanidine may also be of value.

In a short-term study, comparison between the effect of local guanethidine and propranolol eye-drops on thyrotoxic lid retraction and lid lag was made by Sneddon and Turner (1966). They concluded that local guanethidine was the more effective drug for this purpose. A similar conclusion regarding the value of guanethidine was reached by us (Crombie and Lawson, 1967) in a double-blind cross-over trial which compared the effects of bretylium, bethanidine, guanethidine, propranolol, and debrisoquine. In short-term use guanethidine was also least likely to cause significant side-effects.

A long-term trial of local guanethidine in the treatment of the eye signs of thyroid dysfunction and idiopathic lid retraction is reported here.

Patients and Methods

Twenty patients were studied, four males and 16 females (Table I). The thyroid status of all these patients was assessed by clinical examination, estimation of the serum protein-bound

TABLE I.—Thyroid Status of Patients During Period of Study

Primary Diagnosis	Thyroid Status During Study	Patients		Current Treatment		Previous Treatment ¹³¹ I
		M.	F.	Carbimazole	Thyroxine	
Thyrotoxicosis	Euthyroid	4	10	8	4	6
	Mild thyrotoxicosis		2	2		
Hypothyroidism	Euthyroid		1		1	
Idiopathic lid retraction	"		3			

iodine, and a four-hour uptake of ¹³¹I. Thyroid function in each case was maintained at a stable level throughout the period of study. Sixteen patients were known to have been thyrotoxic previously, and 14 of these remained euthyroid throughout this study on the treatment indicated (Table I). Four of these 14 patients were controlled on thyroxine because of hypothyroidism after ¹³¹I treatment. Two patients remained mildly thyrotoxic in spite of carbimazole therapy. Of the remaining four patients

one was euthyroid while on treatment with thyroxine for primary hypothyroidism and three, classified as cases of idiopathic lid retraction, showed no evidence of thyroid dysfunction at any time. All of the patients had eye signs of thyroid disorder to a greater or less degree, and these had been present for periods of up to four years (Table II).

TABLE II.—Eye Signs Present Before Treatment

Case No.	Conjunctival Injection		Exophthalmos		Lid Retraction		Periorbital Oedema		Duration of Eye Signs
	R.	L.	R.	L.	R.	L.	R.	L.	
Males:									
1	+	+	+	+	+	+			2 years
2	+	+	+	+	+	+			1 year
3	+	+	+	+	+	+			2 years
4	+	+	+	+	+	+			3 months
Females:									
5	+	+	+	+			+	+	1 year
6			+	+			+	+	3 months
7					+	±	+	+	2 years
8			+	+			+	+	1 year
9			+	+			+	+	3 years
10	+	+	+	+			+	+	4 years
11	+	+	+	+	+				1 year
12	+	+	+	+	+	+	+	+	6 months
13			+	+					1 year
14	+		+		+	+			1 year
15				+		+			2 years
16	+	+	+	+					1 year
17			+		+				2 years
18			+		+				2 years
19	+	+	+		+				1 year
20	+	+			+	+	+	+	1 year

Each patient was examined at weekly intervals to begin with and then at longer intervals, depending on the presence or absence of side-effects. The average duration of the trial was 16 weeks, with a range from 6 to 26 weeks. At each visit subjective symptoms, including the subjective effects noted on instilling the preparation, were recorded; systemic blood pressure was measured in the erect and supine positions, and examination of the eye, which included external examination, with particular reference to the conjunctiva, cornea, and eye movements, was performed. The ocular fundi were studied and visual acuity and refraction measured. Exophthalmometry (Hertel) was undertaken and an estimation was made of the pupil diameter, palpebral aperture, and, in 11 of the subjects, intraocular pressure by means of both Schiötz and Goldman's applanation tonometers. Both the pupil diameters and the palpebral apertures were measured directly under constant illumination in the mid-palpebral line, with the patient fixing on a point source of light 6 metres distant. The eyes were photographed before starting treatment and after six weeks of continuous treatment. Guanethidine sulphate 10% eye-drops in a buffered solution of methylcellulose were used, one drop in each affected eye twice daily being the standardized dosage.

Results

Results are shown in Table III.

Subjective Symptoms.—With the exception of two patients (Cases 15 and 19) all of the subjects felt that guanethidine had

* Senior Registrar, Professorial Unit, Eye Department, Royal Infirmary, Edinburgh.

† Lecturer, University Department of Medicine, Western General Hospital, Edinburgh.

been of benefit to their eyes. One of these two patients (Case 15) developed an acute local sensitivity to guanethidine six weeks after starting the drug and treatment had to be stopped. Before treatment 10 patients complained of a feeling of grittiness in their eyes, and on guanethidine therapy 9 of these 10 experienced either an improvement or disappearance of this symptom. No patient complained of dizziness, and in all cases measurements of systemic blood pressure both erect and supine did not change significantly from the pretreatment figures.

TABLE III.—Changes in Eye Features After Local Guanethidine Treatment

	Number of Patients			
	Total	Improved	Un- changed	Deterio- rated
Subjective symptoms	20	18	2	
Systemic blood pressure	20		20	
Conjunctival oedema	14		14	
Conjunctival injection	12	3	7	2
Periorbital oedema	6	4	2	
Ophthalmoplegia	9		9	
Lens and fundus	20		20	
Refractive error	20		20	

Conjunctival Oedema.—Guanethidine therapy did not seem to influence the presence or absence of conjunctival oedema, which was present in 14 of the patients.

Conjunctival Injection.—Twelve patients had conjunctival injection at the beginning of the trial. On guanethidine therapy no significant change was noted in seven of the patients, three improved, and two became worse. The increased hyperaemia observed in these last two patients was, however, mild and did not prevent continuation of treatment.

Periorbital Oedema.—Six patients (Table II) had considerable periorbital oedema and in four of these (Cases 5, 10, 12, and 20) a marked decrease in the amount of oedema occurred a short while after guanethidine therapy was instituted. No change in the amount or distribution of periorbital oedema was noted in the other two patients.

Ophthalmoplegia.—No improvement in the field of action of any involved extraocular muscles was noted.

Lens and Fundus.—No change was noted in the lens and fundus of any patient on guanethidine therapy.

Refractive Error.—No changes occurred in the refractive errors of any of the patients while on guanethidine therapy.

Palpebral Aperture

The results are shown in Table IV. Lid retraction was markedly relieved or abolished in all nine patients who showed a reduction in palpebral aperture greater than 20%.

TABLE IV.—Changes in Palpebral Aperture

Eye Signs Before Treatment	No. of Patients	Percentage Reduction in Palpebral Aperture			
		≤ 10	11–20	21–30	> 30
Lid retraction f Unilateral ..	6	2		2	2
present Bilateral ..	7	1	1	4	1
No lid retraction	7	3	4		

Six patients (Table II) with predominantly unilateral lid retraction were treated on the affected side only. In two (Cases 15 and 19) there was only 1 mm. (8%) reduction in the width of the palpebral aperture. Of the other four patients in this group, two (Cases 7 and 17) showed a narrowing of 3 mm. (20–24%) and two (Cases 11 and 18) of 4 mm. (31–33%). No change was noted in the untreated eye in any of these patients (Fig. 1).

In the group of seven patients with bilateral lid retraction (Table II) one patient (Case 12) showed a narrowing of the

palpebral aperture of only 1 mm. (9%) in both eyes, and another (Case 4) obtained 2 mm. (17%) reduction in each eye. The remaining five patients (Cases 1, 2, 3, 14, and 20) derived greater relief of lid retraction, the reduction in palpebral aperture ranging from 21 to 27%. This reduction in width was symmetrical in three (Cases 3, 4, and 12), greater in the right eye in two (Cases 14 and 20), and greater in the left eye in the remaining two (Cases 1 and 2). The reduction in width of the palpebral apertures was of great cosmetic value to the patients with lid retraction (Fig. 2).

The changes in lid aperture observed in the seven patients without significant lid retraction were less marked, the reduction being on the average 12.7% (range 6–18%). None of these patients developed unsightly ptosis.

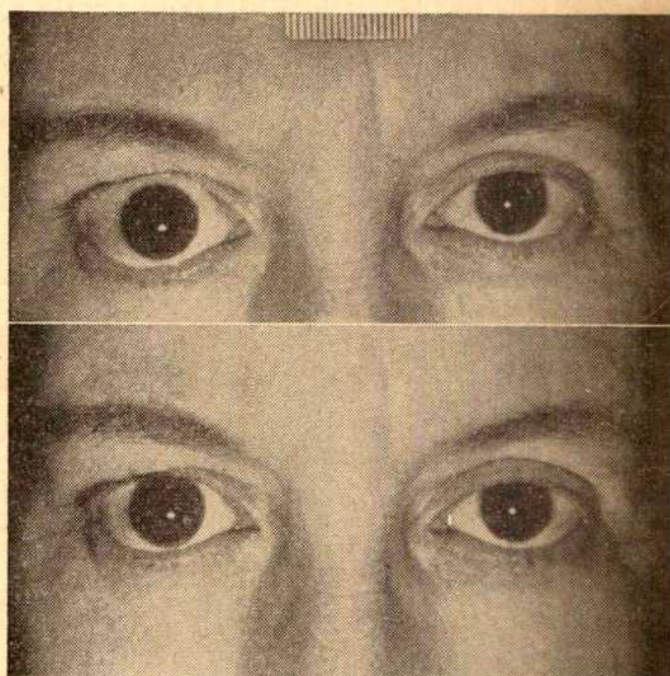


FIG. 1.—Case 18. Patient with unilateral idiopathic lid retraction. Above, before treatment. Below, after six weeks' local guanethidine (10%) to the right eye alone.

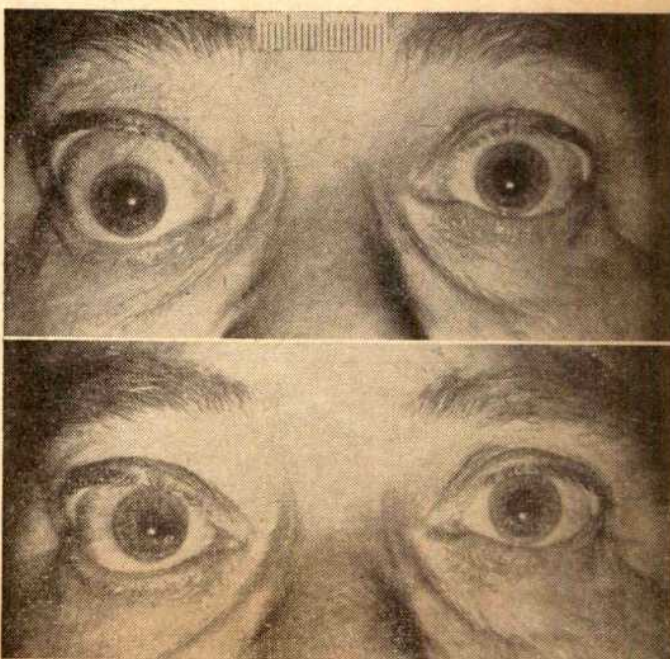


FIG. 2.—Case 14. Above, patient's appearance before treatment. Below, after six weeks' local guanethidine (10%).

Pupils

Meiosis occurred in all the treated eyes except in two patients. The pupil diameter never became less than 2 mm. and the pupil remained reactive to light and accommodation. No restriction in the field of vision was noted by any of the patients, and in 10 of the 20 patients the visual acuity improved by one line on the Snellen chart, irrespective of the refractive error present.

Exophthalmos

Bilateral exophthalmos was present in 11 of the patients. In another seven it was mainly unilateral and in the remaining two was not thought to be a significant eye sign. Exophthalmometer readings decreased by 3 mm. (14–18%) bilaterally in two patients (Cases 1 and 10) and by 4 mm. (16%) in the treated eye of a patient (Case 14) with unilateral exophthalmos (Fig. 2). In another patient (Case 2) the decrease was remarkable, being in the region of 10 mm. (25%) in each eye (Fig. 3).

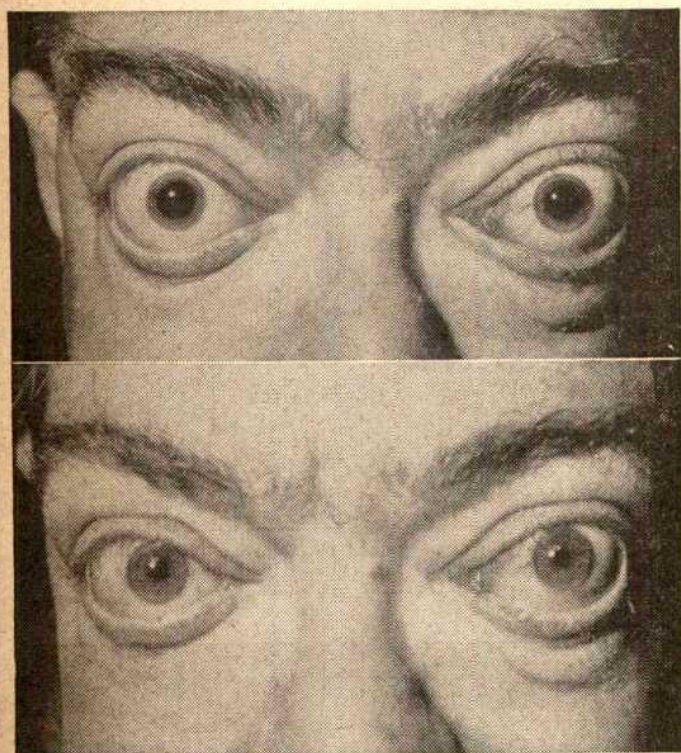


FIG. 3.—Case 2. Above, before treatment. Below, after six weeks' local guanethidine (10%).

Intraocular Pressure

The results are shown in Table V. With the exception of one patient (Case 4), all of the 11 patients in whom measurements of intraocular pressure were made were found to have reductions in pressure after guanethidine treatment. In four patients (Cases 2, 10, 12, and 20), all of whom had moderate proptosis, the intraocular pressures before guanethidine therapy were over 21 mm. Hg, measured on the Goldmann applanation tonometer, on more than one occasion. Schiøtz tonometry

TABLE V.—Changes in Intraocular Pressure in 11 Patients While on Local Guanethidine Treatment

Intraocular Pressure (I.O.P.) Before Guanethidine	No. of Patients	Percentage Increase in I.O.P. ≤ 10	Percentage Decrease in I.O.P.			
			≤ 10	11–20	21–30	> 30
≤ 21 mm. Hg	7	1	1	2	2	1
> 21 mm. Hg	4			2	1	

consistently underestimated the intraocular pressure in these cases. In the other seven patients intraocular pressures were 21 mm. Hg or below. While on guanethidine therapy the intraocular pressure fell on an average by 4 mm. Hg in the first week and did not fall thereafter. In one patient (Case 4) a rise of 2 mm. Hg occurred in both eyes on guanethidine therapy, and this slightly raised level of intraocular pressure remained unchanged while he was on treatment.

Side-effects

The toxic effects of local guanethidine are shown in Table VI. Three patients complained of mild nasal congestion while on treatment and one complained of an unpleasant metallic taste a short while after administration of the drug. One patient developed an acute local sensitivity reaction to 10% guanethidine after six weeks' therapy and the drug had to be discontinued. Ten of the patients complained of brief local irritation on instillation of the drug. These complaints of pain on instillation of the drops were mild and of little consequence in themselves, but all of these 10 patients subsequently developed a superficial punctate keratitis in their treated eyes usually affecting the lower half of the cornea. The keratitis developed after one week's treatment in four cases, after three to four weeks in another two, and after seven to eight weeks in the remaining four. The keratitis was bilateral in five cases and unilateral in five, the unilateral group including three patients who were receiving therapy to one eye only. Three cases were very mild and the keratitis did not increase in severity even though treatment was not discontinued. Treatment was discontinued in the other seven cases, and within one week the keratitis had disappeared without further treatment. When guanethidine 10% was again administered to these patients the keratitis usually reappeared within five to seven days, disappearing again when the guanethidine 10% was stopped, though the lid retraction recurred within 48 hours of discontinuation.

TABLE VI.—Side-effects of Local Guanethidine Treatment in 20 Cases

Nasal congestion	3	Local irritation on instillation ..	10
Unpleasant taste	1	Superficial punctate keratitis ..	10
Local sensitivity	1	No side-effects	10

Because of this effect of the guanethidine 10% solution, guanethidine 5% drops were substituted during the last two to four weeks of the trial. The keratitis improved markedly on this therapy; and it had disappeared in seven of the nine cases within seven days and in the other two cases within 14 days. The other effects of the 5% guanethidine drops were not as marked as when the 10% solution was used, in that on average the palpebral apertures were 1 mm. wider and the pupil diameter 0.5 mm. greater. On the other hand, the improvements in intraocular pressures were maintained, as was the subjective relief of symptoms.

Discussion

The results of this trial indicated that improvement in the eye signs associated with thyroid dysfunction after the short-term use of guanethidine reported previously (Sneddon and Turner, 1966; Gay and Wolkstein, 1966; and Crombie and Lawson, 1967) can be maintained when the drug is used for longer periods and that this therapy is also of value in cases of idiopathic lid retraction. On discontinuation of the drug a return of signs and symptoms occurred within 48 hours, irrespective of the previous duration of guanethidine therapy. In contrast to Gay and Wolkstein (1966) this study indicated (1) that in most cases treatment for one week with guan-

ethidine 10% will achieve maximum results—only 2 of the 20 patients in this trial showed any further improvement in signs and symptoms after the initial seven days' therapy; and (2) that the response to guanethidine appeared to have little relation to the thyroid status at any one time or in any one individual.

It is also of interest that, in this limited study, 4 patients out of 10 with bilateral exophthalmos for a year or more had an intraocular pressure of over 21 mm. Hg on more than one occasion. In all these cases Schiøtz tonometry gave false low readings compared with applanation tonometry. Guanethidine 10% caused a reduction in the increased intraocular pressure in these four cases, the effect being more pronounced the higher the initial intraocular pressure. Guanethidine 5% maintained this reduction in intraocular pressure in each case. No mention of side-effects was made by Gay *et al.* (1967) in relation to the long-term use of guanethidine. One patient in our trial developed an acute skin-sensitivity reaction to guanethidine after six weeks' therapy. In a separate series of 10 patients treated with guanethidine for chronic simple glaucoma, two developed this type of reaction after six and eight weeks' therapy respectively. That the reaction was due to guanethidine was not in doubt, since it occurred again when guanethidine 2.5% drops were used.

In this trial 50% of patients developed a superficial punctate keratitis after one to eight weeks' therapy, unrelated to corneal exposure and relieved by discontinuing treatment, which was done in 7 of the 10 patients involved. There seems little doubt that this complication was due to guanethidine 10%, since it reappeared on resumption of therapy with this concentration of guanethidine. No cases have been reported of punctate keratopathy due to methylcellulose, the vehicle in this case, and corneal exposure could not be implicated, since lid retraction returned on discontinuation of the therapy yet improvement in the corneal condition occurred.

In the trial mentioned above, in which guanethidine 10% was used to control chronic simple glaucoma, two identical cases of superficial punctate keratitis occurred after approximately four months' therapy. A point of speculation raised by these results is whether the cornea in patients with thyroid dysfunction is more susceptible than the normal cornea to a punctate keratitis when guanethidine 10% therapy is in use. One of the three patients, however, with idiopathic lid retraction and normal thyroid function also developed a punctate keratitis. Oosterhuis (1962) and Gay and Wolkstein (1966) reported an increase in conjunctival injection on guanethidine (10%) therapy. In our study there was no relation between conjunctival injection and the development of punctate keratitis. It seems unlikely, therefore, that the increase in conjunctival injection reported in these previous communications was associated with corneal damage. The absence of superficial punctate keratitis when using guanethidine 5% was most

striking, and this would seem to be a safer and yet equally effective concentration.

Where topical guanethidine is to be used in the treatment of lid retraction syndromes the following precautions are advisable: (1) guanethidine 5% should be used initially in all cases, and only where it is unsatisfactory should a 10% solution be considered; (2) a close watch by an ophthalmologist on the treated eyes is essential; and (3) raised intraocular pressure should be looked for in all cases of exophthalmos, since in some patients with this condition the rise in pressure may be pronounced, with danger of ultimate impairment of vision.

Summary

A long-term trial of local guanethidine in the treatment of the eye signs associated with thyroid dysfunction and idiopathic lid retraction was undertaken in 20 patients (4 males and 16 females).

Subjective benefit was obtained in 18 patients. Nine out of 10 patients who had had troublesome "grittiness" experienced great improvement in or complete disappearance of this symptom on guanethidine treatment.

Other benefits obtained included reduction in lid retraction, periorbital oedema, exophthalmos, and raised intraorbital pressure, where these abnormalities were present.

No change was found in conjunctival oedema, conjunctival injection, ophthalmoplegia, pupils, lens, fundus, and refractive error.

The main toxic effect of this treatment was the development of a superficial punctate keratitis, which occurred in 10 patients.

The therapeutic value of local guanethidine in these eye conditions was confirmed. A number of precautions are suggested for long-term maintenance therapy in the light of the toxic effects found.

We thank Dr. A. K. Pitman, of Ciba Ltd., for generous supplies of guanethidine and also Professor J. A. Strong for his helpful advice and criticism during the period of study of patients under his care and also in the preparation of this paper. We are grateful also to Mr. A. McDonald for the preparation of the illustrations.

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Preliminary Communications

Management of the Source of Pulmonary Emboli: the Value of Phlebography

[WITH SPECIAL PLATE FACING PAGE 573]

Brit. med. J., 1967, 4, 596-597

The conventional method of treating a patient who has survived a pulmonary embolus is to use anticoagulants and hope that no further emboli occur (Crane, 1957; Coon *et al.*, 1958; Barritt and Jordan, 1960). If there are further emboli most authors advocate some form of surgical blockade of the inferior vena cava (Moretz *et al.*, 1959; Spencer *et al.*, 1962; De Weese and Hunter, 1963; Miles, 1966; Lowicki, 1966). However, this type of operation has an appreciable morbidity, and if it is performed without showing either the presence or site of the peripheral thrombi it is as irrational as the blind administration of anticoagulants.

Barker and Priestley (1942), reviewing 1,665 cases of post-operative venous thrombosis, thrombophlebitis, and pulmonary embolism, found that 30% of patients who survived a pulmonary embolus had a second embolus and this was fatal in 19%. Thus after a patient has had a pulmonary embolus active treatment is urgently indicated to prevent a recurrence.

This preliminary communication describes the approach that we have developed to give patients the maximum protection from a second embolus with minimum morbidity.

METHODS

ASCENDING PHEBOGRAPHY OF THE LEGS

The patient lies on a tilting-table, the foot of the table being tilted 20 degrees downwards. A rubber tourniquet (Setoniquet, Seton Products Ltd., Oldham, Lancs.) is placed just above the ankle to distend the superficial veins of the foot. A vein on the dorsum of the foot, preferably towards the lateral side, is selected, and a small Middlesex cannula is inserted into the vein, with the use of local anaesthesia, in a distal (upstream) direction. If percutaneous puncture is not possible, a small cut-down is made.

The cannula is connected with polyethylene tubing to a 50-ml. syringe containing 40 ml. of the contrast medium Conray 280 (meglumine iothalamate) May & Baker Ltd. The foot is internally rotated to separate (radiologically) the tibia and fibula. The contrast medium is injected under television control and the tension of the tourniquet adjusted so that deep venous filling occurs. In order to fill all the calf veins it may be necessary to instruct the patient to plantar flex the foot a few times.

Split 14 by 14-in. (35.5 by 35.5-cm.) films are taken under television control during injection of the contrast medium. Films are taken of the whole venous system from the calf to the pelvis. The upper portion of the profunda vein is shown by asking the patient to perform a Valsalva manoeuvre when the common femoral vein is seen to be full of contrast medium. This technique usually shows the deep venous system from the ankle to the external iliac veins or even as high as the inferior vena cava, but if the femoral and iliac veins are not visualized percutaneous femoral vein injections are performed.

Both legs must always be examined.

If thrombosis of the iliac veins is suspected either on ascending phlebography or on clinical grounds and percutaneous

femoral puncture has not succeeded, it may be necessary to perform bilateral simultaneous peritrochanteric intraosseous pelvic phlebograms (Cockett and Lea Thomas, 1965).

After the films have been examined and regarded as satisfactory, at least 100 ml. of normal saline is injected into each leg and the legs are exercised to clear the contrast medium from the veins. This is checked by television. If the patient is not on anticoagulants 2,500 units of heparin are injected into each cannula before removal.

SURGICAL TECHNIQUES

Superficial femoral vein ligation is performed under either local or general anaesthesia. A vertical incision allows a greater length of vein to be exposed, which is of value if thrombectomy is planned.

Thrombectomy.—Thrombi are removed from the femoral and iliac veins through a venotomy in the common femoral vein by means of Fogarty venous thrombectomy catheters, suction, and a variety of forceps.

Plication of the inferior vena cava is usually performed through a right oblique flank incision, by the same retroperitoneal approach as for lumbar sympathectomy. Three or four interrupted sutures of 0000 arterial silk are passed through both walls of a flattened segment of the cava, approximately 2 mm. apart, to convert the vena cava into four or five channels (Spencer *et al.*, 1962).

ILLUSTRATIVE CASES

Seventeen cases of pulmonary embolus seen in the past year have been carefully studied by phlebography, and their management has been based on the radiological findings. The most striking feature was that the site of the thrombus, as demonstrated radiologically, often bore no relation to the site suspected clinically. Though the signs, when present, are usually associated with underlying thrombus, extensive thrombus may be demonstrated elsewhere—in the femoral or iliac veins of a leg with a tender calf or in a leg with no physical signs.

We concluded that the prevention of further emboli by surgical or medical means other than caval blockade could not be achieved without phlebography. The following three cases and their phlebograms demonstrate this point.

Case 1.—A 52-year-old woman had a simple mastectomy for carcinoma of the breast. Four days later she developed dyspnoea, pain in the chest, and haemoptysis. Anticoagulants did not prevent two further emboli. The right calf was tender and phlebography showed a small thrombus in the right common femoral vein. *The left leg was clinically normal.* Fig. 1 (Special Plate) shows that this leg contained an extensive, loose, potentially lethal thrombus. Thrombectomy and ligation of both superficial veins was performed.

Case 2.—This patient, a 32-year-old woman, developed chest pain, dyspnoea, and haemoptysis after two weeks of bed rest for low back pain. The left leg was swollen, painful, and blue. The clinical signs indicated a thrombosis of the iliofemoral segment. Peritrochanteric phlebograms (Special Plate, Fig. 2) showed an occluded iliac vein with fresh thrombus jutting into the vena cava. The cava was plicated.

Case 3.—A 45-year-old man had repeated pulmonary emboli after a femoral endarterectomy. The inferior vena cava was plicated without previous phlebography. He had a further embolus six months later. The phlebogram (Special Plate, Fig. 3) showed a double vena cava, not visible at operation—an unguarded route which could have been blocked at the first operation if its presence had been known.

PHLEBOGRAPHY

Technique.—The technique described for ascending phlebography is a modification of techniques used by many previous authors. It is simple and can be used in the very ill patient. Retrograde (upstream) injection into a lateral foot vein, foot-down tilting, the rubber tourniquet with the Velcro fastening, and the use of television are all important.

Interpretation of Results.—De Weese and Rogoff (1963) described the unequivocal diagnosis of deep vein thrombosis to be based on (1) the presence of well-defined filling defects in opacified veins, and (2) the demonstration of these defects on at least two radiographs. Recent thrombus appears as a rounded or cylindrical filling defect in a contrast-filled vein giving it a "ground-glass" appearance (Special Plate, Fig. 1). The thrombus is separated from the wall of the vein by a thin white line representing contrast medium around the thrombus. Old thrombus shows as filling defects projecting directly from the walls of the veins. The intramuscular calf veins and soleal sinusoids are difficult to fill by ascending phlebography (Cotton and Clark, 1965). Failure to fill these veins cannot be taken as evidence of occlusion, and in the absence of positive evidence of thrombus within these veins non-filling should be assumed to be a technical fault. Conversely, non-filling of the popliteal, femoral, and iliac veins has been taken as evidence of total occlusion, provided contrast medium enters the deep venous system of the calf. The internal iliac veins cannot be demonstrated by ascending phlebography and if these veins are suspected as the source of a pulmonary embolus intraosseous petrochanteric phlebography is necessary. False-positive diagnoses have not proved a problem.

TREATMENT

By defining the site and extent of the residual thrombus we have been able to apply the various methods of treatment available in a logical manner. The policy has been to "lock-in" the thrombus as low as possible.

Of our last 17 patients, five had a plication of the inferior vena cava (two of whom should have been treated by thrombectomy and superficial femoral vein ligation, on the basis of our final policy), one had plication of both external iliac veins, two had one common femoral vein and one superficial femoral vein tied, and two had their superficial femoral veins ligated. These procedures were combined with thrombectomy in six patients, in three of whom a large potentially lethal thrombus was removed.

Seven patients were treated with anticoagulants alone, though surgical treatment, particularly thrombectomy, would have been indicated in some of these if they had been seen earlier. Thus in our experience surgical blockade of the inferior vena cava which is currently so popular is necessary in only a small proportion of patients, the remainder can be treated by a more peripheral blockade.

We suggest that the management of all patients who have had a pulmonary embolus that does not require immediate embolectomy should be as follows:

- (1) Anticoagulate with heparin.
- (2) Perform emergency bilateral ascending phlebography.

(3) If no thrombus is seen in the leg veins, and the iliac veins have not been visualized, perform a pelvic phlebogram via a percutaneous femoral vein puncture or interosseous petrochanteric injection.

(4) Surgical treatment depends on the phlebograms. (a) For thrombus confined to the calf or popliteal vein, superficial femoral vein ligation only. (b) For thrombus extending into the femoral and external iliac veins, thrombectomy and superficial femoral vein ligation. If in such cases the profunda vein has not been displayed on the phlebogram it should be explored with a Fogarty catheter. If no thrombus is found, superficial femoral vein ligation is safe. If thrombus is present then the common femoral vein must be ligated or plicated. (c) For recent thrombus confined to the iliofemoral region above the junction of superficial and profunda veins, thrombectomy alone. (d) For irremovable thrombus above the formation of the common femoral vein, plication of the common iliac veins or inferior vena cava.

(5) Anticoagulants alone are indicated if the phlebogram shows a small amount of apparently old thrombus confined to the calf or popliteal veins or if no thrombus is seen and the diagnosis of pulmonary embolus is certain.

We continue the anticoagulants for six months to prevent the formation of fresh thrombus in the period when the residual thrombus is contracting, the vessel being recanalized, and new endothelium being formed.

No recurrent emboli have occurred since we adopted this regimen and we hope to present a long-term follow-up of these and other patients in a year's time.

SUMMARY

A rational approach to the prevention of a second pulmonary embolism following the first, based on bilateral leg phlebography, is described. The long-term clinical value of these suggestions is under trial.

N. L. BROWSE, M.D., F.R.C.S.,
Assistant Director, Surgical Unit.

M. LEA THOMAS, M.R.C.P., F.F.R.,
Consultant Radiologist.

M. J. SOLAN, M.B., F.R.C.S.,
Senior Surgical Registrar.

St. Thomas's Hospital,
London S.E.1.

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Medical Memoranda

Case of Late Pulmonary Embolectomy

[WITH SPECIAL PLATE FACING PAGE 573]

Brit. med. J., 1967, 4, 598-599

The recent reawakened interest in pulmonary embolectomy has chiefly directed attention to operation as a definitive, unhurried procedure, in contrast to the more tempestuous "rush and grab" of the original Trendelenburg operation. The reason for reporting this case is fourfold: (1) it illustrates the importance of diagnosis; (2) it shows that if one pulmonary artery is affected a quite simple operation suffices; (3) it shows that late operation can be successful, indeed may be obligatory; and (4) that an embolus which does not cause early death may not be removed by lysis but can remain to cause permanent harm.

CASE REPORT

A man aged 50 had a low backache for five months, followed by pain down the outside of the left leg and foot which was said to be due to prolapse of a vertebral disc. He received various treatments, including a corset.

Three weeks after this and 17 weeks before being referred for his lung condition he had pain, swelling, redness, and pitting oedema of the left leg lasting 10 days. During this time he was mobile. Three weeks later—that is, 14 weeks before being referred—he suffered the sudden onset of pain in the left side of the chest, worse on breathing and moving. Dyspnoea became severe and oxygen was needed. He also coughed up a little blood. Over the next three weeks his breathing improved and he was then comparatively well for two months.

One month before referral he had a sudden onset of dyspnoea and palpitations while in the toilet. Two weeks later he was sitting reading when he had a sudden onset of severe left-sided chest pain with palpitations, dyspnoea, coldness, and sweating. He also coughed up some blood.

He was admitted to hospital with a diagnosis of "pleurisy" and was treated with antibiotics. The pleuritic pain improved but dyspnoea remained.

On 20 December he was seen by one of us (H.N.) for the first time, and a diagnosis of pulmonary embolism was made from the story and the radiological appearance of a poor vascular pattern in the left lung. This suggested embolism of the left pulmonary artery; an angiogram taken by Dr. Chafizadeh and Dr. Massin, of Teheran, confirmed this (Special Plate, Fig. 1).

The plain radiographs of November 1966 showed evidence of bilateral pulmonary embolism. The radiographs of 26 December showed improvement in the patchy opacities previously in the right lung.

The angiogram of 29 December showed an apparent dilatation of the pulmonary trunk and of its branches. The left pulmonary artery had a gross filling defect with no evidence of contrast medium entering the left upper lobe and very little in the left lower lobe. The appearances on the right side suggested partial occlusion of some branches of the upper lobe and poor and late filling of branches of the lower lobe and perhaps the middle lobe. It appeared as if several smaller emboli had lodged in smaller branches of the right pulmonary artery.

The patient was flown to London and admitted to the Brompton Hospital on 7 January 1967. He presented the clinical features of moderate pulmonary hypertension with normal jugular venous pressure. The pulse was regular; blood pressure was 90/60 mm Hg. The E.C.G. showed P-pulmonale and QS in lead III that might

indicate an old posterior myocardial infarct. A quiet systolic murmur could be heard over the right upper lobe.

It seemed certain that the greater part of the left lung was deprived of its arterial blood flow by an old embolus. The patchy lesions on the right side did not look suitable for operation, and so it was decided to deal with the left pulmonary artery as a definitive procedure without the use of heart-lung bypass.

OPERATION

Thrombo-embolectomy of left pulmonary artery was done on 16 January, anaesthesia being conducted by Dr. Ruth Mansfield. Left posterolateral thoracotomy was made through the bed of the fifth rib. The upper lobe was densely adherent over the anterior segment and slightly adherent around this. The very adherent area corresponded with a pyramidal infarct about 4 cm. across in the anterior segment.

The left pulmonary artery was dissected from its origin down into the interlobar fissure. The appearance corresponded with that seen on angiocardiology. The first part of the artery was patent and the block was sudden and complete with extensions of thrombus or thromboembolism into the upper lobe branches.

The artery was clamped proximally and controlled distally by a rubber loop. It was opened by a longitudinal incision from above the highest upper lobe branch to the level of the apical lower branch. The obstruction consisted of old firm clot with a little recent thrombus. The extensions into the upper lobe branches were teased out with the aid of a small curette. The apical lower branch was similarly cleared and also the basal branches so far as was possible. The more distal branches still felt solid and it was not possible to secure any more thrombus by "milking" the lobe. After removal of clot the intima looked smooth and healthy; a weak heparin solution was injected into the distal branches. Previously a systemic dose of 1 mg./kg. had been given.

Sufficient back bleeding occurred from distal branches to indicate that total thrombosis had not occurred. It was presumed that distal patency had been ensured by the bronchopulmonary anastomosis.

The incision in the artery was closed, and when the clamp and snares were released very satisfactory and encouraging pulsation was present in the artery and in its branches.

Inspection of the thrombus showed almost uniform old adherent yellow clot in which it was not possible to identify any coiled embolus. Some of the portions extracted from the branches were redder and conical. Through an oversight pressures were not taken in the pulmonary arterial system.

Recovery from the operation was uneventful, and the chest radiograph showed greatly improved lung vascularity. Both objectively and subjectively he lost his dyspnoea.

An angiogram taken 14 days after operation by Dr. G. H. Miller showed a striking restoration of the arterial pattern of the left lung (Special Plate, Fig. 2), in great contrast to the preoperative state.

The improvement and well-being continued up to the time of writing. He had no signs of pulmonary hypertension.

COMMENT

This case shows several important features as were outlined in the introductory remarks. The long overlooked diagnosis was confirmed by angiocardiology. In spite of the four months that had elapsed since embolism it was still possible to perform completely successful thromboendarterectomy. The process had not caused occlusion of the distal arterial branches; these had presumably been kept patent by the minor inflow of blood from bronchopulmonary anastomotic vessels.

It is doubtless true that if death does not occur from pulmonary embolism, clots may be removed by a process of lysis and the patency of the vessels may be restored. This case shows that this cannot be relied on to happen, and if severe secondary pulmonary hypertension is to be avoided with its attendant dyspnoea and disability, removal of embolus and clot may be necessary. Presumably whether a particular embolus may be dissolved by lysis or not will depend on its

age. A recent soft embolus is more likely to be lysed than an older, rigid, and possibly partly organized one.

LORD BROCK, M.S., F.R.C.S., F.R.C.P.

Guy's Hospital and the Brompton Hospital, London

H. NABIL, M.D.

Mehr Hospital, Teheran.

R. V. GIBSON, M.B., F.R.C.P.

Brompton Hospital, London S.W.3.

Hypoglycaemic Coma Occurring during Treatment with Chlorpromazine and Orphenadrine

Brit. med. J., 1967, 4, 599-600

Hypoglycaemia may occur with several drugs in addition to those used in the treatment of diabetes. This report describes the findings in a patient presenting in hypoglycaemic coma during treatment with chlorpromazine and orphenadrine. No such association appears to have been reported previously.

CASE REPORT

A 53-year-old married woman was admitted to hospital in coma. For some years she had been under psychiatric care, and during the previous two months had been treated with chlorpromazine 100 mg. four times a day, together with trifluoperazine (Stelazine). One week before her admission the latter drug was replaced by orphenadrine (Disipal) 50 mg. three times a day. Three days later she began to have "attacks" of excessive sweating with dryness and paraesthesiae of the mouth and tongue. On the night of admission, though feeling normal on retiring to bed, she was found later to be groaning and unrousable. She was receiving no other drugs, was only a moderate smoker, and drank no alcohol.

On examination she was sweating profusely and was deeply comatose. Slow roving movements of the eyes were observed, but the pupils responded to light. There was no papilloedema or neck stiffness and Kernig's sign was negative. Both sides of the body moved slightly in response to painful stimuli; the tone of the limbs was reduced, but the tendon reflexes were all present. The plantar responses were extensor. The pulse rate was 76 and regular; the blood pressure was 150/90. Otherwise the examination showed nothing abnormal.

A clinical diagnosis of hypoglycaemic coma was made by the house-officer on duty (J. G.). The patient was given 20 ml. of glucose (25% w/v) intravenously, after which she quickly recovered consciousness. The blood sugar before treatment was 30 mg./100 ml. (potassium ferricyanide method, normal fasting level 65-100 mg./100 ml.), and after intravenous glucose was 57 mg./100 ml.

Chlorpromazine and orphenadrine treatment was continued, and the following night she had another hypoglycaemic coma, during which the blood sugar fell to 44 mg./100 ml. Recovery was rapid after 20 ml. of glucose (50% w/v) intravenously.

Investigations.—The peripheral blood count, erythrocyte sedimentation rate, urinalysis, and x-ray films of the chest and skull showed no abnormality. All tests of liver function were normal. The serum protein-bound iodine was 4.8 μ g./100 ml. The 24-hour urinary excretion of 17-ketosteroids was 10.3 (7.2) mg., of 17-ketogenic steroids 3.2 (8.2) mg., and of 17-hydroxycorticosteroids 5.9 (11.2) mg. (The values in parentheses are repeat estimations while the patient was receiving orphenadrine alone.)

CARBOHYDRATE HOMOEOSTASIS

Investigations were carried out during and after stopping treatment with the two drugs.

(a) *During Treatment with Chlorpromazine and Orphenadrine.*—The fasting blood sugar was 55-65 mg./100 ml., and the patient

had a further episode of hypoglycaemic coma (see above) at this time. After tolbutamide (1 g. intravenously) the blood glucose (glucose oxidase method) fell from 65 to 29 mg. at 45 minutes, and slowly rose to 34 and 38 mg./100 ml. at two and three hours respectively (Fig. 1). The fasting level of plasma insulin (measured by radioimmunoassay) was 9 μ U/ml. During the tolbutamide test the plasma levels of insulin were 14 μ U at 30 min., 17 μ U at 45 min., 11 μ U at 60 min., and 12 μ U at 90 min. (all levels being within normal limits). After oral glucose (50 g.) the blood glucose

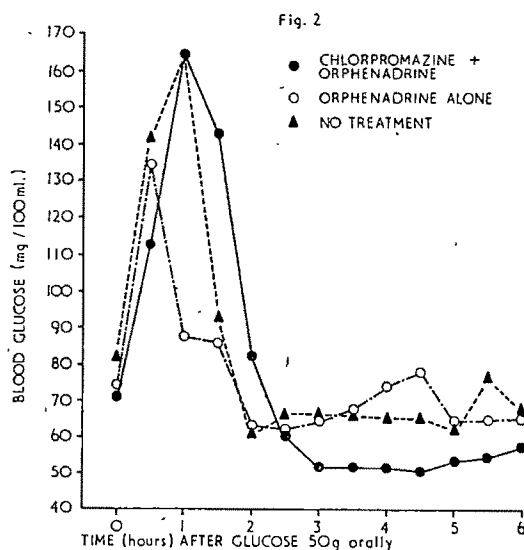
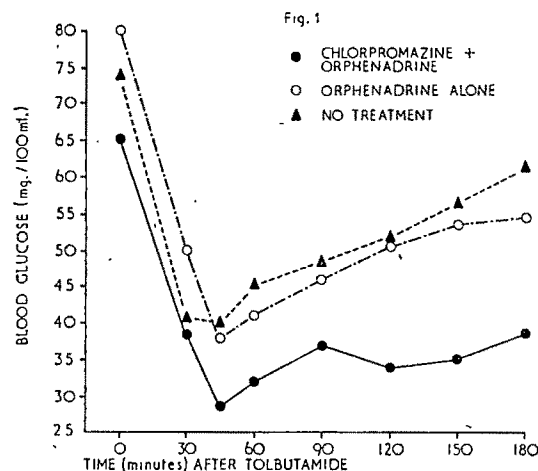


FIG. 1.—Effects of tolbutamide (1 g.) given intravenously on blood glucose levels. FIG. 2.—Six-hour glucose-tolerance tests. (Glucose estimated by the glucose oxidase methods in both instances.)

rose to 162 mg. at one hour, fell to 52 mg. at three hours, and remained below 60 mg./100 ml. for the remainder of the six-hour test (Fig. 2). The patient was starved for 72 hours, during which time the blood glucose fell to 42-44 mg./100 ml., but no hypoglycaemic symptoms developed. The response to glucagon (1 mg. intramuscularly) was normal. The blood glucose rose by 35 mg./100 ml. during the first 30 minutes, and thereafter slowly fell to a minimum value of 50 mg./100 ml. at four hours.

(b) *During Treatment with Orphenadrine Alone.*—One week after stopping chlorpromazine the fasting blood sugar had risen to 77–88 mg./100 ml. After tolbutamide the blood glucose fell to 38 mg./100 ml. at 45 minutes, but reached two-thirds the fasting value at two and a half hours (Fig. 1). The six-hour glucose-tolerance curve showed a normal pattern (Fig. 2).

(c) *No Treatment.*—Repeat studies one week later showed a normal fasting blood sugar, while the tolbutamide test (Fig. 1) and the six-hour glucose-tolerance test (Fig. 2) were both normal. It was therefore not felt justified to subject the patient to a further 72 hours of starvation.

No hypoglycaemic episodes or other abnormalities have emerged during surveillance for the past 18 months, and fasting blood sugars have been normal.

COMMENT

The patient's symptoms and two comas occurred in the postabsorptive state, responded quickly to glucose, and ceased when treatment was stopped.

Studies of chlorpromazine on carbohydrate metabolism have yielded conflicting results. Some reports have shown hyperglycaemia and decreased glucose tolerance (Courvoisier *et al.*, 1953; Dobkin *et al.*, 1954; Charatan and Bartlett, 1955), while other studies have found no effect on blood sugar and an increased tolerance (Donegani *et al.*, 1959; Bonaccorsi *et al.*, 1964).

Orphenadrine is a substituted derivative of diphenhydramine. None of this group of antihistamines has any known effect on carbohydrate metabolism, though some of the ethylene diamine group (such as antazoline) may cause asymptomatic reduction of blood sugar when given in high dosage (Goldner and Jauregui, 1954).

After tolbutamide the absolute fall in blood glucose was greater, and the rate of return towards normal was slower during treatment with both chlorpromazine and orphenadrine than with the latter alone, normality being achieved only when both were stopped. The normal circulating insulin levels, both fasting and during tolbutamide-stimulation, suggest that the drugs did not stimulate its secretion; they also, along with the absence of further attacks of hypoglycaemia during the past 18 months, make it unlikely that the patient's symptoms were due to an insulinoma or to an undetected extrapancreatic tumour.

The therapy may have increased the effectiveness of action of normal quantities of secreted insulin. Another possibility is an increased tissue uptake of glucose due to a direct effect of the drugs, for orphenadrine inhibits aerobic metabolism (de Waart, 1958; Lewis and Van Petten, 1963).

There could have been an interference with humoral mechanisms normally maintaining the blood sugar. Chlorpromazine inhibits many of the peripheral actions of adrenaline, but is without effect on its hyperglycaemic action (Courvoisier *et al.*, 1953). Impairment of the secretion of glucagon could contribute to hypoglycaemia, especially during fasting. But the normal response to glucagon in this patient excluded any

significant impairment of glycogenolysis caused by interference with phosphorylase activity.

Growth hormone and A.C.T.H. play a part in maintaining the blood sugar, and both are under hypothalamic control (Reichlin, 1963). Chlorpromazine depresses the hypothalamus (Goodman and Gilman, 1965) and interferes with the release of several pituitary hormones (Christy *et al.*, 1957); it could thereby interfere with carbohydrate homeostasis. During the combined therapy the 24-hour excretion of 17-ketosteroids and 17-hydroxycorticosteroids was depressed, but after stopping chlorpromazine there was a rise in their excretion, suggesting an inhibitory effect of chlorpromazine on hypothalamic-pituitary mechanisms.

Investigation suggested that chlorpromazine had the greater hypoglycaemic effect. Yet carbohydrate homeostasis became normal only when orphenadrine was also stopped, and the patient had been symptom-free initially on chlorpromazine alone. This, with their structural similarity, suggests a summative effect between the two drugs. Both share the group— $\text{CH}_2\text{—CH}_2\text{—N—}$ —with the ethylene diamines, but this alone is unlikely to be responsible. It is possible that summation of a direct peripheral effect of orphenadrine together with the central hypothalamic-pituitary effect of chlorpromazine may be sufficient to cause manifest hypoglycaemia.

Chlorpromazine and orphenadrine individually are commonly prescribed, but when used together the possibility of hypoglycaemia should be considered.

Our thanks are due to Dr. K. O. Black, under whose care this patient was admitted, for allowing us to publish details of the case. We also wish to thank Dr. K. W. Taylor for kindly performing the insulin radioimmunoassay determinations, and Dr. A. B. Anderson for the glucose oxidase determinations.

RICHARD M. BUCKLE, M.A., M.D., M.R.C.P.,
Senior Registrar.

JOHN GUILLEBAUD, M.A., M.B., B.CHIR.,
House-physician.

Department of Medicine, St. Bartholomew's Hospital, London E.C.1.

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Case of Cronkhite-Canada Syndrome with Associated Jejunal Diverticulosis

Brit. med. J., 1967, 4, 601-602

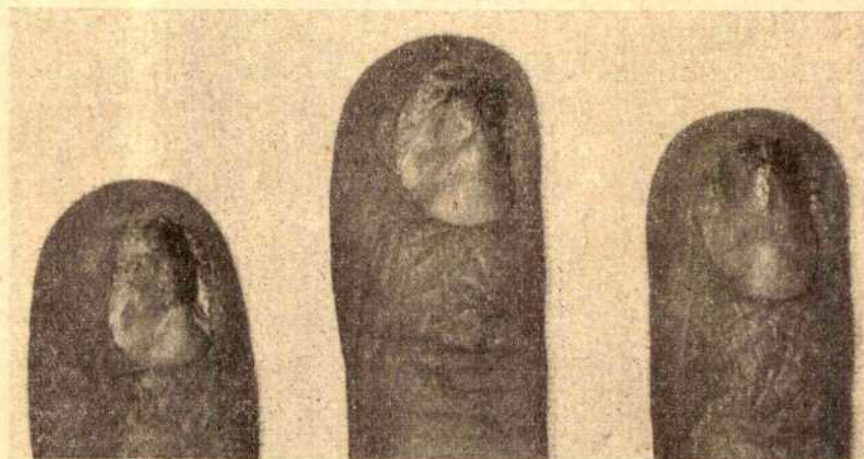
The association of gastrointestinal polypi with diffuse alopecia and nail dystrophy was first recorded by Cronkhite and Canada (1955). This paper records the ninth patient with this syndrome.

CASE REPORT

The patient was a schoolmaster aged 60. In 1957 diffuse alopecia and "unusual nails" were noted during investigations for dyspepsia. Laparotomy revealed a nodular pancreas, and chronic pancreatitis

these were polypi was confirmed by gastroscopy and gastric biopsy. The investigations indicated the presence of hypomagnesaemia, hypocalcaemia, and hypokalaemia, presumably secondary to jejunal diverticulosis. At this time there was no conclusive evidence of more generalized intestinal malabsorption. Oral replacement therapy with magnesium hydroxide, vitamin D, calcium gluconate, and potassium citrate produced an improvement in his general condition, but between 1963 and 1966 he complained of intermittent upper abdominal discomfort, vomiting, and anorexia. His weight fluctuated considerably and on two occasions he was admitted to hospital for blood transfusion because of occult gastrointestinal bleeding. A string test suggested bleeding from the jejunum.

Investigations of intestinal function in 1967 revealed more generalized malabsorption (see Table). The presence of excess urinary indican, together with an excellent response to antibiotic therapy (ampicillin 250 mg. q.i.d.), suggested that a change in bacterial flora may have been responsible for the enteropathy.



Finger-nails showing gross changes.

was suspected. The following year a gastroenterostomy was performed, but at neither operation was any abnormality of stomach or small bowel reported. In 1962 an epileptic fit necessitated a further hospital admission. His general health was good, though paraesthesiae in the hands had been noted for two weeks. His bowel actions were normal.

On examination no abnormal pigmentation of the skin or mucous membranes was seen. He had diffuse non-scarring alopecia and the body hair was also scanty. All finger-nails and toe-nails, except for the right fourth and fifth toes, were strikingly abnormal (see Fig.). In the proximal half the normal nail was replaced by a triangular area consisting of a thin nail-plate, fleshy in colour; it felt soft and could easily be indented. This abnormal nail was continuous distally with a hard thick nail which was ridged longitudinally in the midline and obliquely to each side. This part of the nail was brown in colour and was darkest and thickest centrally. Chvostek's sign and Trousseau's sign were negative, but there was a general increase in muscle tone, with spontaneous fasciculation over the quadriceps and bilateral ankle clonus.

Investigations at this time are shown in the Table. In addition, a glucose-tolerance test and Schilling test were normal. Barium enema showed nothing abnormal. Barium-meal examination showed multiple large jejunal diverticula and multiple round filling defects on the stomach wall and to a less extent in the duodenum. That

Faecal excretion of an intravenous injection of povidone-iodine (^{131}I polyvinylpyrrolidone) was at the upper limits of normal.

His general health is better and the alopecia is a little less diffuse, but his nails, though improved, remain abnormal.

COMMENT

The association of gastrointestinal polypi, alopecia, and nail dystrophy was first reported by Cronkhite and Canada (1955). Since then eight other cases have been reported. Of the nine unrelated patients, whose ages ranged from 51 to 75 years, three were males.

In our patient the appearance of the nails was distinctive and could be explained by the formation of ventral nail in the absence of normal nail production by the matrix. This has been noticed in one other patient with the Cronkhite-Canada syndrome (Shuster, personal communication) and may be a feature of it. The nail dystrophy is not pathognomonic, as it has been reported in a patient with pustular psoriasis (Samman, 1961). Alopecia and generalized pigmentation were present in all previously reported cases, but though similar diffuse hair changes had occurred in the above patient increased pigmentation was absent.

The relation between disorders of the skin and gut have recently been classified by Shuster (1967) into four groups. One cannot yet classify the Cronkhite-Canada syndrome under any of these groups, since it is not known whether the ectodermal changes are dependent on or associated with the endodermal changes.

Though our patient had only gastroduodenal involvement, polypi may involve any site of the gastrointestinal tract. A striking feature of most cases has been the severity of the symptoms and signs, which seem to be related to the extent of the polypi. Eight of the cases had diarrhoea and the faecal fat was unequivocally increased in three of the four cases in which

Summary of Investigations

Investigations	1962	1967
Haemoglobin (g./100 ml.)	13.3	14.0
Serum iron ($\mu\text{g.}/100\text{ ml.}$)	15	245
Iron-binding capacity ($\mu\text{g.}/100\text{ ml.}$)	186	330
Serum vitamin B ₁₂ ($\mu\text{g.}/\text{ml.}$)	395	357
Serum folic acid (m $\mu\text{g.}/\text{ml.}$)	3.0	—
Serum potassium (mEq/l.)	2.7	4.7
Serum calcium (mg./100 ml.)	8.0	9.3
Serum magnesium (mg./100 ml.)	0.3 and 0.6	2.4 and 2.3
Plasma inorganic phosphate (mg./100 ml.)	2.5	2.9
Serum proteins (g./100 ml.)	6.8	6.1
Electrophoresis	Normal	Normal
Urinary magnesium* (mg./24 hours)	3.2 and 2.4	—
5 day faecal fat excretion† (g./day)	5	14
Xylose excretion test‡ (g. in 5 hours)	6.5	2.7

* Normal 70-120 mg./24 hours. † As stearic acid. ‡ After 25 g. xylose by mouth.

the estimation was performed. Jarnum and Jensen (1966) demonstrated protein-losing enteropathy in their patient.

Five of the reported cases have had a fatal outcome (Cronkhite and Canada, 1955; Martini and Dölle, 1961; Johnston, Vosburgh, Wiens, and Walsh, 1962; Jarnum and Jensen, 1966), usually within 18 months of the onset of the diarrhoea. Spontaneous clinical and biochemical remissions occurred in one patient (Kennedy and Hirson, 1961). Two were improved by removal of the polypi—one by a gastrectomy (Manousus and Webster, 1966) and the other by a hemicolectomy (Zdansky and Riederer, 1963).

Jejunal diverticulosis and pancreatic disease have not been previously reported in this condition and it is possible that these may be part of the syndrome.

Jejunal diverticulosis is a well-recognized cause of intestinal malabsorption. Booth, Babouris, Hanna, and MacIntyre (1963) drew attention to the not uncommon finding of hypomagnesaemia, which was present in 15 out of 42 cases of intestinal malabsorption of various causes reported in their series. An interesting feature in the present case is the presentation with paraesthesiae and convulsions due to hypocalcaemia and hypomagnesaemia, and the later development of more generalized malabsorption despite symptomatic improvement and weight

gain after treatment with oral supplements and broad-spectrum antibiotics.

We wish to thank Professor G. Smart, under whose care the patient was admitted, and Professor Sam Shuster for their advice and constructive criticism.

W. J. CUNLIFFE, M.B., B.Sc., M.R.C.P.,
Registrar in Dermatology.

J. ANDERSON, M.B., M.R.C.P.,
First Assistant to the Department of Medicine

University of Newcastle upon Tyne and the
Royal Victoria Infirmary, Newcastle upon Tyne.

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Haemoperitoneum Associated with a Ruptured Gall Bladder

Brit. med. J., 1967, **4**, 602

Leared (1859) was the first to recognize that the gall bladder could be the source of catastrophic intra-abdominal haemorrhage. He described finding a ruptured gall bladder and 2 quarts (2.3 litres) of blood in the abdominal cavity of a man of 22 at a post-mortem examination. Since then the condition has been reported infrequently. Raycroft and Mastrangelo (1960) were able to collect only 18 cases from the world literature.

CASE REPORT

A man of 55 was admitted to hospital on 26 January 1966. His admission was precipitated by 48 hours of severe generalized abdominal pain accompanied by abdominal distension and constipation. He gave a long history of dyspepsia—30 years previously he had had a haematemesis and since then had been subject to periodic bouts of epigastric pain relieved by food. During the year before admission he had had attacks of pain in the right lower chest and for two months had also had central abdominal colicky pains and increasing distension. A barium-meal examination shortly before admission had failed to show a cause for his dyspepsia, and six days before his admission his haemoglobin was 106%.

Examination showed an obviously ill man. He was pale and clammy and had a pulse rate of 120. The abdomen was distended and though tender all over it was particularly so in the right hypochondrium. Tenderness was also elicited on rectal examination. On auscultation bowel sounds were present. Radiographs of the abdomen showed gaseous distension of both the small and large bowel. The serum amylase was 89 Somogyi units and the haemoglobin 66%.

After preliminary intravenous fluid replacement a laparotomy was performed. One and a half litres of blood and blood clot were found in the abdomen. This clearly arose from the gall bladder, which had a 2-cm. tear across Hartmann's pouch. The cystic artery was severed and blood was continuing to spurt from the proximal end. The gall bladder contained blood clot, but both it and the common bile duct appeared to be normal otherwise. No evidence of peptic ulceration was found. Cholecystectomy was performed

and the blood was removed from the abdominal cavity. Histological examination of the gall bladder showed evidence of chronic cholecystitis. The patient's postoperative progress was entirely uneventful.

COMMENT

Severe bleeding from the biliary tract is uncommon. During recent years, however, it has been shown that in a small proportion of patients with gastrointestinal haemorrhage the biliary tract is the source of the bleeding. The diagnosis has usually been made only after repeated haemorrhages have occurred and after previous gastric surgery has been undertaken (Fitzpatrick, 1961). Haemobilia has been recorded from very varied pathological causes. Minor bleeding is not uncommon in calculous cholecystitis, especially when accompanied by stones in the common bile duct, but cholecystitis appears to be the least common cause of severe bleeding. Mailer (1939), commenting on a fatal case of spontaneous rupture of the gall bladder with intraperitoneal haemorrhage, stressed the lack of inflammation in the gall bladder. Though the gall bladder in the present case showed histological evidence of chronic cholecystitis it was not the site of acute inflammation or of ischaemic necrosis. It is therefore by no means clear why the gall bladder should have ruptured, but it does seem likely that the cause was essentially a mechanical one. If the bleeding was caused by rupture of the gall bladder, the cause of the rupture remains unexplained. It is therefore thought more likely that bleeding occurred into the gall bladder first. Blood clot may have obstructed the neck of the gall bladder, leading to a rise of tension sufficient to bring about its rupture.

I am grateful to Mr. I. W. Matheson for permission to publish this case.

PAUL ATKINS, M.B., B.S., F.R.C.S.,
Senior Registrar in Surgery, King's College Hospital,
London S.E.5, and South-east Metropolitan
Regional Hospital Board.

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Current Practice

MEDICINE IN THE TROPICS

Malnutrition in Childhood in the Tropics

C. GOPALAN,* M.D., PH.D.

Of the many causes of ill-health among children of the tropics malnutrition is undoubtedly the most important. Apart from its direct effects on health, malnutrition also exerts an indirect effect by diminishing resistance to infectious diseases.

The infant and child mortality rates in tropical countries are high. In India, according to the latest census figures, while infants and children under the age of 5 years constitute 16.5% of the total population, deaths within this age group account for 40% of the total deaths in the country. Infant and toddler mortality rates in some of the tropical countries are shown in Table I. A curious reflection of such high mortality in infancy and childhood is that in contrast with the situation in Europe the average expectation of life in tropical countries is actually higher at the age of 5 years than at birth. These data indicate the magnitude of ill-health among infants and children in tropical countries.

TABLE I.—Infant and Toddler Mortality Rates in Different Countries

Developed Countries	I.M.R.	T.M.R.	Developing Countries	I.M.R.	T.M.R.
Australia	19.1	1.0	Columbia	90.0	15.6
Belgium	25.8	1.0	El Salvador	65.5	22.7
Canada	24.7	1.1	Guatemala	91.6	42.7
France	23.4	1.2	Guinea	42.0	55.4
Japan	20.4	1.9	Mexico	66.3	14.7
Netherlands	14.8	1.1	Costa Rica	86.4	N.A.
Sweden	14.2	0.8	Honduras	50.0	13.5
U.S.A.	24.8	1.0	Venezuela	48.0	5.5
			India	81.0	12.0
			Malaya	57.0	34.0
			Philippines	67.4	8.1

I.M.R. = Infant Mortality Rate per 1,000 live births.
T.M.R. = Toddler Mortality Rate per 1,000 population.

Among poor communities in the tropics undernutrition and an unhygienic environment are inseparable factors, which tend to interplay with and aggravate each other. It is therefore difficult to decide how far these mortality figures are attributable to malnutrition and how far they are the result of insanitary and unfavourable environment. However, a careful scrutiny of the data offers some suggestive indications.

A considerable proportion of infant deaths in the tropics occurs in the neonatal period. Analysis reveals that nearly 75% of these deaths are directly attributable to "premature birth." A study of over 16,000 obstetric cases in Madras in South India¹ showed that the incidence of premature births (using the criterion of body weight of 5 lb. (2.2 kg.) as normal) was 8.1% among the poor general-ward patients as against 1.6% among the well-to-do patients admitted to the special wards. Using the international criterion of a birth weight of 5½ lb. (2.5 kg.) in full-term infants as evidence of prematurity, Varkki *et al.*² found that the incidence of prematurity among infants in Coonoor (South India) was three times as high in poor communities as in the well-to-do group. Such a high incidence of prematurity may be considered as a reflection of maternal malnutrition.

* Director, Nutrition Research Laboratories, India.

The extreme severity of the malnutrition in pregnant mothers in the poorest sections of populations in the tropics can be gauged from the results of recent surveys. In a study of the diet of pregnant women of the low socio-economic groups in South India the average daily intake of protein was 44 g. (animal protein 6 g.), of calcium 300 mg., and of iron 18 mg. The total calorie intake was 1,575.

Nutrition in Early Infancy

If the infant in the tropics manages to survive the hazards of the neonatal period he is relatively safe till the end of the first year in spite of his insanitary environment. During at least the first six months the infant receives, through his mother's milk, the nutrients which he needs in amounts which are probably not too inadequate. It is gratifying that women of the low socio-economic group in the tropics are able to breast-feed their infants successfully for prolonged periods. Instances of inability to breast-feed infants, which are frequent among the sophisticated high socio-economic groups, are extremely rare among the poor. This is surprising in the light of the diet of the nursing mothers, which provides less than 50 g. of protein daily, mainly derived from vegetable sources.

In a study among poor South Indian women it was observed³ that the daily output of breast milk varied from about 600 ml. within the first six months of lactation to about 350 ml. between the 18th and 24th months. The composition of the breast milk obtained at different stages of lactation showed that the milk was quite satisfactory with regard to the proximate principles, though not with regard to vitamins and minerals (Table II). These observations point to the need for encouraging breast-feeding by poor communities in the tropics, though it must be borne in mind that these underfed mothers are able to maintain satisfactory lactation only at the expense of their own tissues.

TABLE II.—Composition of Human Milk

Duration of Lactation	Protein g./100 ml.	Fat g./100 ml.	Lactose g./100 ml.	Vitamin A i.u./100 ml.	Vitamin B µg./100 ml.	Vitamin B ₁₂ µg./100 ml.	Vitamin C mg./100 ml.	Calcium mg./100 ml.	Phosphorus mg./100 ml.
1-6 months	1.06	3.34	7.47	79	15.3	19.0	1.9	36.3	11.7
7-12 months	1.01	3.23	7.54	66	14.5	18.1	2.5	34.1	12.0
13-18 months	1.05	3.79	7.54	65	16.5	17.2	3.2	29.8	12.6
More than 18 months	1.13	3.41	7.51	66	15.1	11.5	2.9	36.6	11.1

Growth and Development

At least for four months after birth the growth rates of Asian infants are not significantly lower than those of infants of the technically developed regions of the world. While this is true of growth rates, the actual weights of Asian infants even

within the first six months of birth are lower than those of normal infants elsewhere. In Fig. 1 the heights and weights of infants and children belonging to the poor socio-economic groups in India have been compared with those of American infants and children of corresponding ages. Among European and American infants chest circumference has been reported normally to overtake head circumference around the first year. In Asian infants of the poor socio-economic groups, however, this has been found to take place at about the third year. It is, however, interesting that no significant retardation has been observed with regard to the attainment of milestones of development in infants of the tropics.

It is the universal practice among poor communities in the tropics that infants are breast-fed for prolonged periods, often extending to two years. It is also the usual practice in many poor communities that infants are maintained solely on breast milk till the end of the first year. Supplementary foods are invariably unmodified versions of the adult diets and are almost solely cereal-based. Milk and animal protein foods figure only occasionally. Due to ignorance and prejudices green leafy vegetables and fruits are also not often included. Even such qualitatively deficient diets are often fed in quantities which are inadequate. The general impression that infants and children in the tropics are "overstuffed" with starchy foods providing adequate or more than adequate calories is not borne out by actual surveys. In view of the remarkable growth retardation the protein intake on the basis of actual body weights may appear to be only marginally deficient. However, in view of the inadequacy of calories in the diets a considerable proportion of the protein must be utilized for energy purposes. The intake of vitamins, especially of vitamin A, either preformed

or as carotene, is also low; the intake of calcium rarely exceeds 400 to 500 mg.

An elaborate account of the classical nutritional deficiency diseases affecting children will not be attempted here. Excellent descriptions of such classical syndromes as scurvy, rickets, and infantile beriberi, are available in standard textbooks. In this paper major nutritional problems affecting children of the tropics will be briefly discussed.

Protein-Calorie Malnutrition

Among the various types of malnutrition in children of the tropics protein-calorie malnutrition is the most widespread and important. Two major clinical forms have been recognized, kwashiorkor and marasmus.

Kwashiorkor

Kwashiorkor is generally seen in children between 1 and 3 years of age. The onset of the disease is insidious. Towards the latter half of the first year the child shows failure to grow and a lack of interest in the surroundings. He has frequent attacks of diarrhoea and other infections. There is often loss of appetite and increasing apathy, and the child may develop discoloration of the hair and skin and a characteristic fullness of the face. Later the ankles swell, and oedema gradually spreads upwards. It is at this stage that the child is generally brought to the hospital (Figs. 2 and 3).

Growth failure and hypoproteinaemic oedema are accepted as minimal diagnostic criteria for the disease. Oedema is maximal in the dependent parts, but ascites is uncommon. There is generally no albuminuria, and this differentiates the oedema from that of renal origin. The clinical severity of the oedema bears no relation to the ultimate prognosis or to the response of the case to treatment.

The hair can be plucked off easily and is often discoloured. The discoloration may not be present throughout the length of the hair, but only in segments, and this is termed the "flag

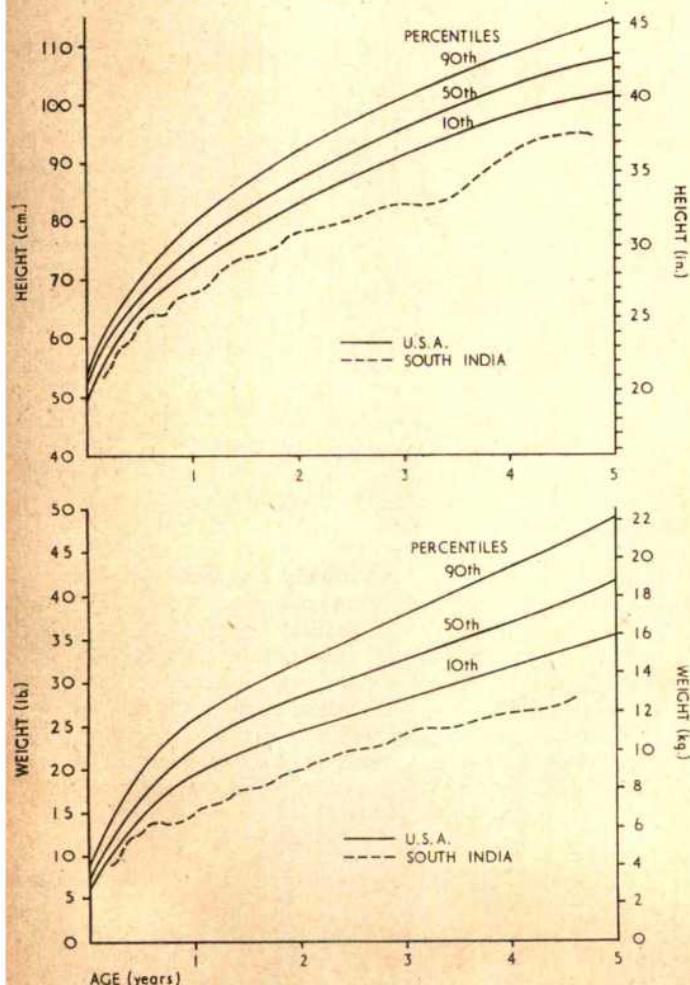


FIG. 1.—Comparison of height and weight of American and Indian children.

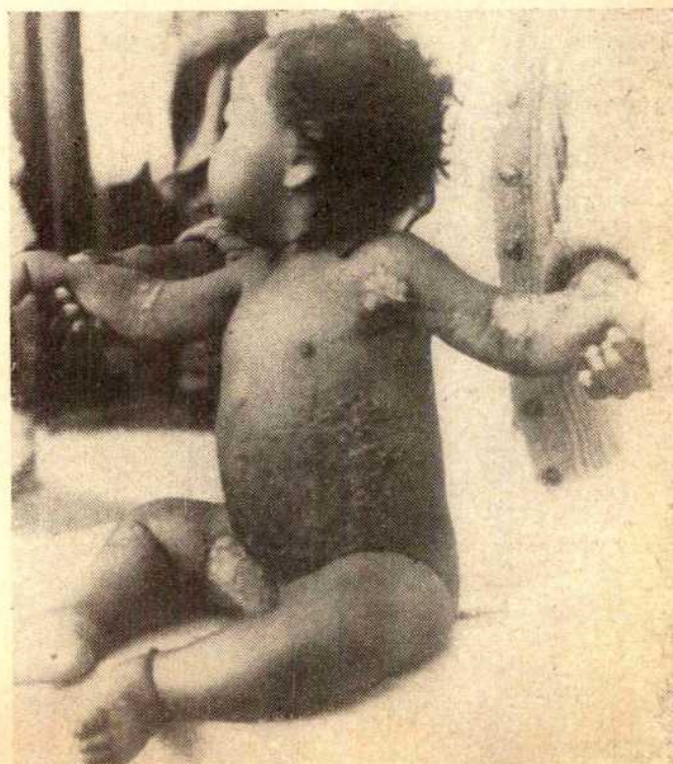


FIG. 2.—Child suffering from kwashiorkor showing oedema and skin

sign." The skin is scaly and shows characteristic changes which have been designated "crazy pavement dermatosis." The lesions start as black patches, especially over pressure points, which later exfoliate, exposing hypopigmented areas bordered by hyperpigmented zones.

Alimentary disturbances are the rule. There is marked anorexia, and diarrhoea is frequent. Pathogenic bacteria can be found in the stools in only a small percentage of the cases. However, in view of the high incidence of parasitic infestations in the tropics, ova of parasites, especially roundworm ova, are frequently seen. The faeces often show microscopic fat globules. The diarrhoea responds to high-protein therapy, and can therefore be regarded as a manifestation of protein deficiency.

The liver may or may not be enlarged. Liver biopsy invariably reveals extreme degrees of fatty infiltration, but contrary to previous belief this never leads to hepatic cirrhosis. General signs of associated vitamin deficiencies are usually present, commonly those of vitamin A and the vitamin-B complex.

There is a marked hypoproteinaemia, the reduction being greater in the albumin fraction. The serum protein and albumin levels are of the order of 4.5 and 1.9 g./100 ml. respectively. There is a reduction in many of the serum enzymes, the blood urea, and the blood cholesterol.

Anaemia is often present, and is mainly due to iron deficiency, but concomitant deficiency of other haematinic factors should also be borne in mind.

Marasmus

Marasmus is seen in a younger age group, usually between 6 and 12 months of age. These infants are usually exclusively breast-fed, and the milk available is not adequate for proper growth. There is therefore a gross calorie undernutrition. A typical case of marasmus is characterized by gross underweight, marked muscular wasting, and loss of subcutaneous fat.

TABLE III.—Differences Between Kwashiorkor and Marasmus

	Kwashiorkor	Marasmus
Age of incidence	12-36 months	6-18 months
Oedema	Invariably present	Absent
Muscle wasting	Mild to moderate	Severe
Loss of subcutaneous tissue	Mild	Marked
Hair	Discoloration; easy pluckability	Normal
Skin	Scaly; dyspigmentation; crazy pavement dermatosis	Normal
Plasma proteins	Markedly reduced	Reduced
Serum enzymes	Low	Normal
Blood urea	Low	Normal
Liver	Fatty infiltration	Normal

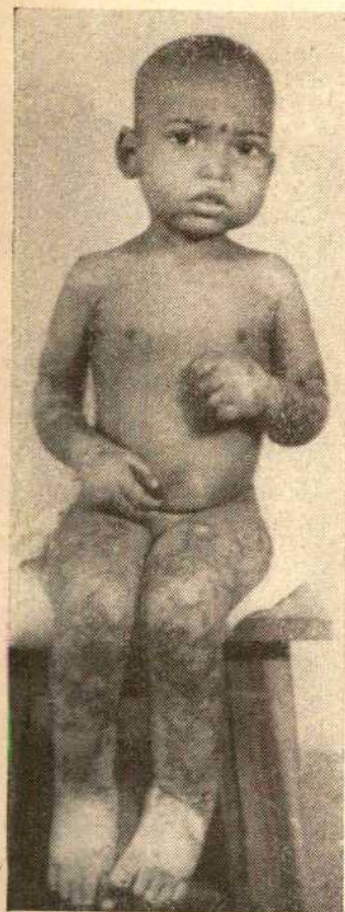


FIG. 3.—Child suffering from kwashiorkor showing oedema, skin changes, and moon-face.

Oedema is not seen in these infants, and the liver is free from fatty change. Skin and hair changes are absent.

Hypoproteinaemia is seen in marasmus, but to a lesser extent than in kwashiorkor. The serum protein and albumin concentrations are around 5 and 3.5 g./100 ml. respectively. Blood urea levels are normal, and serum enzyme activity is not much reduced. The major differences between kwashiorkor and marasmus are set out in Table III.

Marasmic Kwashiorkor

These descriptions of kwashiorkor and marasmus are of well-defined cases and may be considered to represent two ends of the spectrum of protein-calorie malnutrition. In practice there is often considerable overlap between these two clinical conditions. In India and Indonesia protein-calorie malnutrition often manifests in the clinical form designated "marasmic kwashiorkor." A picture of marasmus may precede the onset of kwashiorkor in these children. Again, after the disappearance of oedema in response to treatment the subjects may appear marasmic. The differences between kwashiorkor and marasmus are probably not so much due to differences in dietary patterns as to different "adaptation responses" to the deficient diets.

Treatment of Protein-Calorie Malnutrition

Therapy consists in feeding the children diets providing adequate protein and calories. The best protein source for these diets is milk. The therapeutic regimen described in this article is that used in the Nutrition Research Laboratories, Hyderabad.

Each child is given a diet providing 4 g. protein and 200 cal./kg. body weight, the composition of which is given in Table IV. Skimmed milk constitutes 80% of the total protein and wheat 20%. The former is diluted in a ratio of 1:6. The rest of the calories are provided by sugar, bananas, and butter. Since fat gives more calories per unit, butter helps in raising the calorie content of the diet and in keeping the bulk low. These children usually have concomitant vitamin and iron deficiencies, so they are given supplements of vitamins and iron.

TABLE IV.—Diet for Treatment of Protein-Calorie Malnutrition Based on Milk Protein

Ingredient	g./kg. body weight	cal./kg. body weight
Skimmed milk	9	36
Bread	20	70
Butter	7	63
Sugar	7	28
Bananas	2	

Though milk is the best protein for these children, it is expensive and rare in developing countries. Attempts are being made to incorporate locally available vegetable protein foods into these therapeutic diets. Groundnut (*Arachis hypogaea*), Bengal gram (*Cicer arietinum*), and cottonseed have been successfully used. However, these proteins have to be used at a level of 6 g./kg. body weight. Moreover, where possible incorporation of small quantities of skimmed milk gives better results. The composition of one such diet is given in Table V.

TABLE V.—Diet Containing Vegetable Protein Mixture

Ingredient	g./kg. body weight	cal./kg. body weight
Wheat flour	18	63
Cottonseed flour	6	24
Sugar	10	40
Ghee	7	63
Skimmed milk	3	12

The diets are well accepted by the children, though anorexia may restrict the quantities taken in the first three to four days. Clinical improvement, characterized by mental alertness, loss of oedema, and consequent loss in body weight, is evident within seven to ten days. Complete recovery occurs within three to four weeks, when there will have been a gain in body weight and the serum albumin will have returned to near normal levels. Recovery is retarded by the presence of infection, and tuberculosis should always be borne in mind. If it is present a response to therapy will be observed only after the institution of specific antituberculosis treatment. Antibody production is impaired in protein malnutrition, and a negative Mantoux reaction does not necessarily rule out tuberculosis. The practice followed in our clinic, therefore, is that all children who fail to improve with dietary therapy are treated simultaneously with antituberculosis drugs, whether or not they show evidence of the infection.

Troublesome diarrhoea is treated with binding reagents like pectin or kaolin. Where pathogenic organisms are found in the stools specific therapy is instituted. Since most of the cases have diarrhoea, potassium chloride is given routinely.

Vitamin-A Deficiency

After protein-calorie malnutrition the nutritional deficiency most widely prevalent in children of the tropics is that of vitamin A. Some 8% of the child population at any given time have ocular signs of vitamin-A deficiency.

The milder signs of vitamin-A deficiency are night-blindness, Bitot spots, and xerosis of the conjunctiva. The more severe form of vitamin-A deficiency is xerosis of the cornea, leading to keratomalacia, and eventually to blindness. The most common lesion, however, is conjunctival xerosis. Children with a history of night-blindness do not necessarily show any other ocular sign; and children with ocular lesions may not necessarily give a definite history of night-blindness.

The incidence of vitamin-A deficiency is particularly high in children suffering from kwashiorkor, for diets poor in protein are also deficient in vitamin A. Moreover, a close relationship exists between the metabolism of both nutrients. Serum vitamin-A levels are very low in these children, and nearly 65% of the children presenting with this dual deficiency suffer from the most severe form of vitamin-A deficiency, keratomalacia.

Early detection of vitamin-A deficiency, especially corneal xerosis, is vital because administration of vitamin A can reverse the ocular lesion in as short a period as 24 hours. Mild cases of xerosis are often missed owing to examination in poor light.

Treatment

Treatment depends on the severity of the lesion and on the presence of associated protein malnutrition. In children suffering from vitamin-A deficiency alone and in whom there is no corneal involvement 10,000 to 25,000 I.U. of vitamin A daily is administered orally until the lesions disappear, and this usually requires about three to four days. Smaller doses may then be given for a further seven to ten days.

Corneal lesions must be treated as a medical emergency with 50,000 to 100,000 I.U. vitamin A daily until complete disappearance of the lesion. The dose should then gradually be tapered off to 10,000 I.U. Corneal involvement is one of the last stages of vitamin-A deficiency, and the body stores of the child at this stage may be considered to be practically nil. Vitamin-A supplements should be continued for a period of six to eight months. Local application of an antibiotic is advocated until the lesions disappear.

In cases of kwashiorkor with vitamin-A deficiency, contrary to general belief, the oral route of administration is superior to the parenteral route. However, the vitamin should be given with a fat base either in the form of butter or some vegetable oil to facilitate absorption.

Doses higher than those mentioned above are not necessary. It has been found that in a number of children treated with higher doses of the vitamin signs of acute toxicity such as vomiting and bulging of the fontanelle occur. Even at a dose of 50,000 to 100,000 I.U. a small percentage of children may develop these signs, but they are likely to be transient.

Phrynoderma

Phrynoderma, or follicular hyperkeratosis, a nutritional deficiency disorder not uncommonly encountered in the children of the tropics belonging to the low income groups, is a condition generally seen in late childhood and adolescence.

The earlier belief that phrynoderma is a manifestation of vitamin-A deficiency still persists. However, this hypothesis is not substantiated by epidemiological, clinical, biochemical, or therapeutic studies. Vitamin-A deficiency is seen most commonly in the first six years of life, a period at which phrynoderma is relatively uncommon. Many children with lesions of phrynoderma have no other signs of vitamin-A deficiency, and the condition cannot be cured by vitamin-A therapy.

It has been established that phrynoderma is due to a deficiency of essential fatty acids. Vitamin-B complex deficiency also seems to have an associated role, for 60–70% of the patients manifest signs of vitamin-B deficiency.

The disease is characterized by the presence of projecting horny papules on the skin. The papules have a round or oval base and a sharp peak. The papules are generally hyperpigmented, vary in diameter from the size of a pinhead to that of a millet, are discrete, and tend to appear in groups. The lesions are distributed symmetrically, but localized lesions may also be seen occasionally. They are commonly present on the extensor surfaces, especially on the elbows (Fig. 4) and knees,

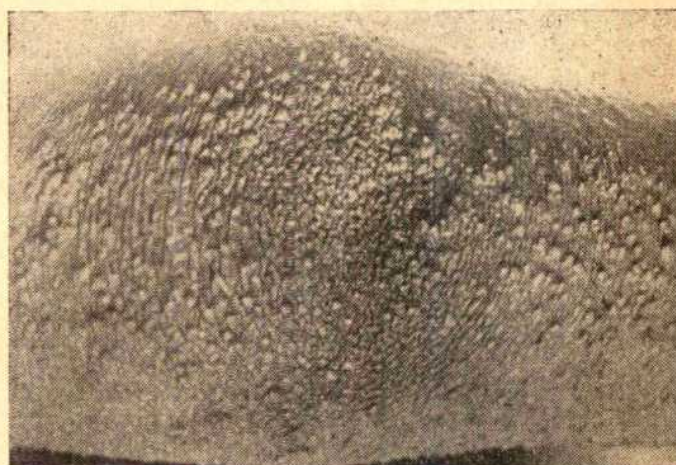


FIG. 4.—Elbow showing typical lesions of phrynoderma.

and in the gluteal region. They may also be seen on the back and on the posterior and lateral surfaces of the arms and thighs.

Nearly 60–80% of the patients also have signs of vitamin-B deficiency, such as glossitis, cheilosis, angular stomatitis, and nasolabial dyssebacea.

Histopathological examination reveals superficial hyperkeratosis of the epidermis and of the hair follicles. The sebaceous follicles are found to be dilated and plugged with dense keratotic material.

Treatment

The condition can be cured in most cases by the oral administration of fats rich in essential fatty acids. The improvement has been observed to be quicker when vitamins of the B-complex are given simultaneously. Parenteral administration of B-complex vitamins *per se* can also cure phrynoderma, but it has been found that recurrence is more frequent and quicker in such cases as compared with those treated with essential fatty acids. We have routinely employed safflower oil (linoleic acid content: 70%) in doses of 5 ml. thrice daily in combination with an oral B-complex preparation (thiamine 3 mg.; ribo-

flavine 1 mg.; pyridoxine 0.5 mg.; pantothenate 1 mg.; and niacin 30 mg.) with satisfactory results. Improvement is obvious in about two weeks, though six to eight weeks of therapy is needed for complete disappearance of the lesions. It needs to be stressed that even massive doses of vitamin A do not bring about any improvement.

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MEDICINE TODAY

Management of Parkinsonism

"*Medicine Today*" is the television series for doctors produced by the B.B.C. Advice on the preparation of the programme is given by the Association for the Study of Medical Education.

The programme on B.B.C. 2 on 5 December was on the subject of Parkinsonism. Printed below is an article prepared with the help of expert contributors to complement the television programme, which will be repeated on B.B.C. 1 on 13 December at about 11 p.m.

Many Parkinsonian patients have now been treated successfully by stereotaxic procedures, and there is considerable agreement on the indications for operation. Young patients with non-progressive and predominantly unilateral tremor often gain gratifying relief; those with marked rigidity may also respond satisfactorily. Frail patients with progressive and advanced disease do poorly, and surgery should be withheld from those with marked hypokinesia, severe disorders of gait and balance, bulbar symptoms, and evidence of intellectual deterioration. Even the most dramatic results are essentially palliative, and successfully placed lesions in selective patients do not alter the natural history of the underlying pathological process. Tremor and rigidity often recur.

Regrettably the greater number of patients are elderly and unsuitable for surgery. Every effort should be made by their doctors to encourage independence for as long as possible. Each patient poses an individual problem in management, and practical advice—from rubber-tipped walking-sticks to strategically placed aids to daily living—is greatly appreciated. Intelligent patients can often teach their doctors useful tips which can be passed on to others. Some patients with postencephalitic Parkinsonism cope remarkably well with stairs and on uneven surfaces. They should be encouraged to persist with these activities despite the anxiety often engendered in their relatives. During transient and minor illnesses patients with Parkinsonism should not spend any longer in bed than is absolutely necessary. After minor setbacks short and intensive courses of physiotherapy are often helpful, but there is little justification for sporadic visits to the clinic scattered over many months.

Drugs are generally disappointing in the treatment of Parkinsonism. Few patients gain dramatic and sustained relief, whereas undesirable side-effects are all too frequent. Though sceptics have related any amelioration of the patient's disabilities to the prescriber's enthusiasm, there can be little doubt that some patients do get useful improvement of tremor and rigidity; and a few show unequivocal relapse when anti-Parkinsonian drugs are stopped abruptly.

Most of the currently prescribed drugs are anticholine compounds, and their use stems from an early clinical observation that belladonna conferred some relief. Today naturally occurring alkaloids such as tincture of belladonna are rarely used, but a host of synthetic analogues are available. There is no convincing evidence that any one preparation is superior to the

others, and there is no rational guide to the sequence of new drugs when others have failed. The general principle is to introduce one drug at a time, beginning with a small dose thrice daily and gradually increasing the amount until optimum relief is obtained or toxic effects become intolerable. This empirical process of adjusting dosage and drug in the hope of discovering a beneficial regimen is often an exacting and frustrating task, taxing the patience and fortitude of both patient and doctor. Visual hallucinations, toxic confusional states, impaired visual accommodation, and excessive dryness of the mouth often cause patients to give up medication spontaneously before their doctor suggests this. Even in a patient who is apparently gaining satisfactory relief it is always worth while stopping treatment from time to time to ensure that the patient agrees that he is better off with his drugs.

Approved Name	Proprietary Name	Tablet (mg.)	Price/100 Tabs.
Belladonna alkaloids	Rabellon		3s. 2d.
Benzhexol	Artane	2 and 5	6s. 10d. and 13s. 8d.
Benzhexol hydrochloride	Pipanol	2 and 5	6s. 10d. and 13s. 8d.
Benztropine methanesulphonate	Cogentin	2	18s.
Biperiden	Akineton	2	11s. 6d.
Chlorphenoxamine	Clorevan	50	16s.
Diphenhydramine hydrochloride, } hyoscine hydrobromide	Benacine	25 0.325	11s. 8d.
Ethopropazine	Lysivane	50	14s.
Mephensin	Myanesin	500	12s. 8d.
Mephensin carbamate	Tolseram	500	16s.
Methixene hydrochloride	Tremonil	5	14s.
Orphenadrine hydrochloride	Disipal	50	13s. 11d.
Phenglutarimide	Aturbane	5	13s. 4d.
Procyclidine hydrochloride	Kemadrin	5	15s. 4d.
Tigloidine hydrobromide	Tiglyssin	250	47s. 6d.

Benzhexol 2 mg. t.d.s., orphenadrine 50 mg. t.d.s., benztropine 0.5 mg. t.d.s., and ethopropazine 50 mg. t.d.s. are approximately equivalent initiating doses of commonly used drugs. Some physicians favour combinations of drugs at sub-toxic levels, but there is no agreement on optimum combinations and certainly little justification for giving more than two drugs at the same time. When increments are made gradually many Parkinsonian patients may tolerate remarkably large doses of anticholine drugs, but it is important to ensure that such heroic measures are desirable and justifiable.

There is little to choose between the various synthetic anticholine drugs, and there is very little mystique in the use of these preparations. Few other useful drugs are available. Dextroamphetamine (5 to 10 mg. twice daily) is occasionally helpful to hypokinetic patients, and antidepressant drugs are often indicated in the management of their chronic and often refractory diseases. Beta-adrenergic blocking agents and dopamine derivatives are still in the experimental stage of assessment, and their safety and place in routine clinical problems has yet to be accepted. Finally, it must be recalled that reserpine, phenothiazines and methyl dopa may cause Parkinsonian syndromes—and these drugs should not be given to patients suffering from disorders of the basal ganglia.

TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Griseofulvin

This drug is marketed by Glaxo Laboratories under the name Grisovin and by I.C.I. Ltd. under the name Fulcin-Forte.

History

Griseofulvin, a metabolic product of a mould, was discovered in 1939 in England by Oxford, Raistrick, and Simonart.¹ In 1947 Brian² and Grove and McGowan³ showed it was responsible for a curling action on certain fungi, and it was found to be effective in protecting plants from fungal infection. After another 10 years Gentles⁴ showed that oral griseofulvin was effective in the treatment of experimental ringworm infections in guinea-pigs, and Williams, Marten, and Sarkany⁵ reported its successful use in superficial fungus infection in man. Griseofulvin has since become very widely used and has represented a major breakthrough in the management of various types of ringworm infection. More and more information about its action and use is being learnt, and it is useful at this stage to reassess its value.

Pharmacology

The molecular formula is $C_{17}H_{17}O_6Cl$. The drug is insoluble in water but slightly soluble in various organic solvents. Its fluorescent properties are utilized in quantitative measurements.

In vitro, griseofulvin is active against all ringworm fungi, but it has little or no effect on bacteria, candida, *Malassezia furfur*, aspergilli, and other fungi included in the group of deep mycoses. Its action is to impair the normal development of terminal hyphae, producing distortion and curling.⁶ Although fungicidal, its main effect is fungistatic.⁷ Griseofulvin does not diffuse through the stratum corneum but moves out with the cells from the prickly layer. Fungus can no longer grow on keratin which has developed while the patient is on an adequate dose of griseofulvin. As the drug does not destroy fungus growing in the outer layers of keratin, cure is obtained only when the particular keratin structure infected has completely grown out. Thus the treatment time will be 3 to 4 weeks for skin, 6 to 8 weeks for hair, and 6 to 18 months for nails. Resistance of various fungi to griseofulvin has been demonstrated, but it is very uncommon and usually not complete.⁸

Griseofulvin is absorbed from the gastrointestinal tract, and the blood levels in patients have shown considerable variation after a standard dose. When the drug has been administered after a meal with a high fat content the serum levels may be double those obtained with controls.⁹ In recent years it has been shown that barbiturates administered at the same time reduce considerably the effect of griseofulvin,¹⁰ possibly because the barbiturate stimulates destructive chemical processes in the liver which are also active against griseofulvin. This is an important consideration, as barbiturates may well be given to patients on prolonged courses of griseofulvin, when the effect of the drug will be reduced. The fine particle preparation is absorbed more readily and allows the required dosage to be halved. Although the fine particle preparation has superseded the older form of griseofulvin, the latter is still available as tablets of 250 mg., and confusion has arisen. Unless otherwise stated in a prescription the fine particle preparation is dispensed. Divided doses maintain higher blood levels, and for adults the common dose scheduled is 250 mg. (two tablets) twice per day. Some authorities recommend twice the dose, and this

could certainly be used in the treatment of severe ringworm, or when there is a possibility of partial resistance or poor absorption. The relative amount of griseofulvin required for children is higher, and 125 mg. (one tablet) twice per day is required in most cases. A number of special dosage schemes have been tried. A single large dose such as 2 to 3 g. in children has been successfully used in microsporum infections of the scalp,¹¹ and a once-weekly dose has also been found to be effective. However, it seems that a more certain response is obtained by the usual twice-daily administration.

There have been a number of trials of griseofulvin and its newer analogues applied topically, but these have shown that it has little or no value in the treatment of human ringworm.¹²

Side-effects and Toxic Reactions

Remarkably few side-effects have been reported. Urticarial, morbilliform, and other rashes occasionally occur, but most of these disappear despite continued therapy. A photosensitizing action with subsequent eruption in light-exposed areas has been reported.¹³ Headache, gastrointestinal upsets, thirst, and other minor symptoms may occur, but are rarely severe enough to demand stopping treatment. A curious feeling of distension and fullness in the epigastrium, neck, and face has also been recorded.

Griseofulvin may have some effect on porphyrin metabolism, and Rimington *et al.*¹⁴ demonstrated an abnormality in porphyrins in 21 out of 50 patients on treatment. This, however, seems to be of little practical significance, and does not give rise to any symptoms.

It has recently been shown¹⁵ that griseofulvin has an anti-inflammatory effect, which is in the region of one-third to one-tenth of that of cortisone acetate. This may account for some of the effects which have been claimed on diseases other than ringworm infections.

Clinical Applications

As griseofulvin will act on all ringworm fungi the clinical use can best be considered according to the site involved.

Scalp.—Treatment of scalp ringworm has been revolutionized and x-ray epilation has become a thing of the past. A period of six to eight weeks' treatment is often required, and in small-spore ringworm the hair distal to that laid down while on griseofulvin can still be seen to fluoresce under Wood's light. The cutting off of this distal hair over the infected patches may well stop cross-infection. The natural course of cattle ringworm causing the kerion reaction is to clear after two to three months, but with griseofulvin the treatment time and the severity of the reaction are greatly reduced.

Skin.—Small patches and large areas of infected skin respond to topical fungicides, but griseofulvin will greatly shorten the period of treatment, and perhaps the most dramatic cases treated are where *Trichophyton rubrum* infection has involved large patches, including the hands and feet. However, this is the type of case which often responds to topical fungicides, and recently Davies *et al.*¹⁶ have questioned the use of griseofulvin in smooth skin infections.

Toe-web.—Ringworm involving the skin of the toe-webs is often not cleared by griseofulvin, and in many cases after months of treatment the fungus can still be cultured from the sites. It would seem, therefore, that it should not be used to treat ringworm which has remained localized to the toe-webs.

Nails.—Finger-nails infected with ringworm will take about six months to clear, or longer in older patients. To prevent relapse it is important to treat coincidental ringworm of the

toe-webs with topical fungicides at the same time. Toe-nails will often require one to two years to clear completely, and even after such a period of treatment many are still infected or relapse when treatment is stopped. Particularly in older patients with dystrophic toe-nails it is probably inadvisable to attempt treatment with griseofulvin. Nails infected with *T. mentagrophytes* do not respond quite as well as those infected with *T. rubrum*.¹⁶

Failure of Treatment

Perhaps the commonest cause of failure is the treatment of conditions other than ringworm infection. The differential diagnosis of ringworm from some cases of eczema and psoriasis may be difficult, and mycological examination of scrapings is very important before treatment with griseofulvin is started.

Similarly, fungi known not to respond to griseofulvin may be treated, and in particular candida infection associated with chronic paronychia and *Malassezia furfur* infections (*Tinea versicolor*) are not affected.

The tablets may not have been taken regularly or the drug may not have been sufficiently absorbed. It is worth while stressing the importance of fat increasing the absorption, and the tablets should always be taken after meals. The simultaneous use of other drugs, particularly barbiturates, will reduce the effect of griseofulvin, and this may well have accounted for some reports of failure of treatment.

Resistance of ringworm fungus to griseofulvin is a very unlikely cause of lack of response.

Other Uses

Griseofulvin has been reported to be of value in gout, shoulder-hand syndrome, angina pectoris, psoriasis of the nails, and other conditions. The effect is often slight or unproved, and there does not appear to be any clear clinical application other than in ringworm infections.

The basic N.H.S. cost of 100 tablets of 125 mg. is 26s. 3d.

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Susceptibility to Infectious Hepatitis

Q.—Is a recent attack of tonsillitis likely to make a girl who is to work in a nursery school where there is an outbreak of infectious hepatitis among the staff more open to infection? Is it possible to predict an individual person's proneness to contract infectious hepatitis, and are there any factors which, if taken into account, might make it possible to predict the severity of the illness?

A.—Infectious hepatitis is an acute disease ascribed to one or more viruses whose biological characters have not been precisely determined. The evidence so far is that they are enteroviruses with mainly faecal excretion of variable duration. The mode of infection is the faecal-oral route, and there is a probability that a proportion of those infected do not show overt disease. Children suffer less from the disease in this way than adults, though they may constitute the main source of continuing infection.¹

The number of unknown factors makes it impossible to say whether a recent attack of tonsillitis renders a person more open to infection. This would surely depend more on close contact with persons excreting the virus at the time and on the actual infecting dose of virus transmitted. Contact with school staff and children and the handling and use of common objects, including crockery, would provide opportunities for infection.

There is no way of predicting nonspecific resistance to infectious hepatitis, and, at

present, no suitable laboratory method for measuring specific immunity arising from past infection, inapparent or overt.

In some outbreaks it has been noted that the illness is more severe when there is initial high pyrexia before jaundice develops and when the interval between this pyrexial stage and the appearance of jaundice is short.

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Booster Doses of Rabies Vaccine

Q.—A child who was bitten by a rabid dog has completed a therapeutic course of rabies vaccine. Should subsequent booster doses be given, and, if so, how often?

A.—A child who has been bitten by a rabid dog and has completed a therapeutic course of rabies vaccine will not as a rule require any subsequent booster dose. Exceptions to this are when the bite has been caused by a wild animal or when the bites have been severe. In these cases booster doses should be given on the 10th and 20th day after the completion of a full course of vaccine. Vaccines of non-nervous tissue origin, if available, should be used in booster doses.¹

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Tests for Connective Tissue Diseases

Q.—What is the relative value of the antinuclear-factor, L.E.-cell, and L.E.-latex tests in the diagnosis of systemic lupus erythematosus and other diseases of connective tissue? What proportion of false-positive and false-negative reactions are obtained when these tests are used for diagnosis of these diseases?

A.—The antinuclear-factor (A.N.F.) test is positive in many forms of connective tissue disease other than systemic lupus erythematosus, and is therefore of little value in the positive identification of that condition. The L.E.-cell test, on the contrary, is highly specific for systemic lupus erythematosus (S.L.E.), with few false-positive reactions apart from certain cases of drug hypersensitivity and of liver disease. Casals, Friou, and Teague² have, however, described a form of nuclear staining characterized by diffuse irregular fluorescence spreading out from the nuclear margin which is much more closely correlated with S.L.E.

The sera from many cases of S.L.E. give precipitin or complement-fixing reactions with D.N.A. and D.N.A.-protein. The L.E.-latex test detects these sera because the latex particles used are coated with D.N.A.-protein. The results with this reagent are more specific for S.L.E. than is the A.N.F. test, but its lack of sensitivity³ makes it unsuitable as a substitute for either the A.N.F. or L.E.-cell test.

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Book Reviews

Drugs in the Management of Human Disease

International Encyclopedia of Pharmacology and Therapeutics. Section 6. Clinical Pharmacology. Edited by L. Lasagna. (Vol. 1: pp. 373+xiii, 80s. Vol. 2: pp. 377-667+xiii+index, 63s.) Oxford: Pergamon, 1966.

International Encyclopedia of Pharmacology and Therapeutics. Section 12. Ganglionic Blocking and Stimulating Agents. Vol. 1. Muscarinic and Nicotinic Stimulant Actions at Autonomic Ganglia. By R. L. Volle. (Pp. 110+vii; illustrated, 30s.) Oxford: Pergamon, 1966.

This comprehensive encyclopaedia is at present being published as the various volumes become available and it will undoubtedly become an essential requirement for pharmacologists, clinical pharmacologists, and in fact for all physicians interested in the action of drugs in the management of human disease.

Section 6 deals in two volumes, under the editorial guidance of Dr. Louis Lasagna, with predominantly the methodology of sensible drug usage in man. The editor selected topics in which methodology is stressed, and authors whose views reflect sound principles and who are not dogmatic about transient fashions in drugs in current use. Accordingly, by and large, individual drugs are not dealt with in detail unless their importance contributes to the discussion of the relevant principles. As a result, these two volumes together form a companion of inestimable value to any clinical investigator, and Professor Max Hamilton's chapter on psychotropic drugs should be compulsory reading for all psychiatrists. Lasagna himself discusses with sense and moderation the problems inherent in the assessment of the efficacy of analgesics, and reviews by Professor G. M. Wilson and Dr. A. F. Lant on the evaluation of diuretics and by Dr. William Wilson on hypotensive drugs are excellent.

On the other hand, the chapter on diabetes deviates from the editorial guideline, and rival details are discussed, and, considering their lack of importance in 1967, there is a section on anorexigenics which is inordinately long. In the United Kingdom and else-

where surveys and studies are showing that an appreciable number of people, both at home and in hospital, suffer the consequences of drug treatment, always a legitimate hazard if benefit is likely to accrue from drug use. The Committee on Safety of Drugs in Britain, and the divisions of the Food and Drug Administration in the U.S.A., are increasingly concerned with the detection of adverse reactions, the mechanisms of their causation, and estimates of their true incidence in relation to the extent of drug usage. Only a meagre 12 pages in the 667 pages of these two volumes cover this very large field.

These small criticisms should nevertheless in no way detract from the great value of these two volumes, primarily designed for the clinically orientated medically qualified investigator. In contrast, the first volume of Section 12 is primarily intended for the academic pharmacologist concerned with elucidating precise mechanisms of physiological, biochemical, and pharmacological processes. This volume provides a modern account of the pharmacology of the autonomic ganglion with particular reference to stimulant drugs. As explained in his historical introduction, Professor R. L. Volle seeks to emphasize the gaps and logical weaknesses in the theoretical understanding of mechanisms of ganglionic transmission. Although the basic concept of acetylcholine as the essential mediator in synaptic transmission in ganglia is almost too firmly established to be challenged, the heterogeneity of the cholinceptive sites and the possible role of other transmitters present in the sympathetic

ganglion still require to be clarified. The precise mode of action of acetylcholine itself is still not defined particularly in its relationship to transcellular movements of ions such as calcium.

A quarter of this monograph is devoted to a detailed description of the basic chemistry, pharmacology, and toxicology of nicotine and related compounds, but the section on the clinical treatment of acute nicotine poisoning is out of place in this volume, where it will not be found by those requiring to consult it. Two chapters are concerned with the possible involvement of 5-HT, histamine, the catecholamines, and polypeptides such as angiotensin and substance P in ganglionic transmission. Professor Volle's account of his subject is concisely and clearly written, and he concludes with a plea for further investigations using microelectrode recording techniques to clarify the role of ionic mechanisms in ganglionic transmission.

These three volumes together, for the clinical and laboratory pharmacologists, deal with subjects which should bind closer the two types of individuals interested in drug action. Too often the clinician tends to be empirical and pragmatic without understanding the mechanisms involved in the use of the agents he employs. He will gain immeasurably by consultation with the contributions in Section 6, and his understanding will increase by perusal of Section 12, particularly if it is read in conjunction with Dr. W. Wilson's chapter in Section 6. On the other hand, the laboratory-confined academic and basic pharmacologist, by whom Professor Volle's monograph will be enthusiastically welcomed, will, by a perusal of the two volumes of Section 6 edited by Dr. Lasagna, see with greater clarity the ultimate objective of his work—the development and application of compounds which will prevent or alleviate disease processes in man.

A. G. MACGREGOR.

Genetic and Psychosocial Aspects of Asthma

Bronchial Asthma. A Genetic, Population, and Psychiatric Study. By Denis Leigh, B.Sc., M.D., F.R.C.P., and Edward Marlev, M.A., M.D., F.R.C.P.Ed., D.P.M. (Pp. 192+vii, 63s.) Oxford: Pergamon, 1967.

This fascinating epidemiological study of asthma in the community, carried out on a population drawn from general practice, was conducted by two physicians and a social worker based on a psychiatric hospital. In a world of specialization where boundaries are often jealously guarded this catholic approach is most welcome and this is an interesting and worth-while study planned and documented with great care. The authors have made extensive reviews of relevant literature and drawn attention to serious

deficiencies in some previous studies which now hold a hallowed place in psychosomatic mythology.

The study reminds us that asthma and related conditions are common disorders with a considerable morbidity, carrying a grave risk of superadded chronic respiratory disease. The relationship of asthma to hay-fever, vasomotor rhinitis, childhood asthma, and urticaria is well demonstrated, and the significance of hereditary factors is closely examined. The authors favour a genetic hypothesis and postulate a dominant inheritance with weakened penetrance or a multifactorial inheritance to explain their findings. They found that first-degree relatives of asthma probands had a 43% likelihood of developing asthma.

In some ways the psycho-social aspects of the study are disappointing. A project of this kind must be concerned primarily with the prevalence of defined disorders, and con-

sequently the psychiatric conditions examined were in terms of gross syndromes. It is of some interest that overt psychiatric illness was no more common among adult asthmatics than in the control group, though childhood psychological disturbance was significantly more frequent among the asthma probands, both reported as prevailing in those subjects under the age of 12 years, and as reported retrospectively in older patients. There was a significantly greater incidence of neurosis in the first-degree relatives of the asthmatic group, with females more frequently affected.

While this book is intended for the specialist rather than for the general reader, the details of design and execution of the study, the review of the literature, and the wealth of factual data ensure that it will be read with interest by workers in diverse fields.

S. BRANDON.



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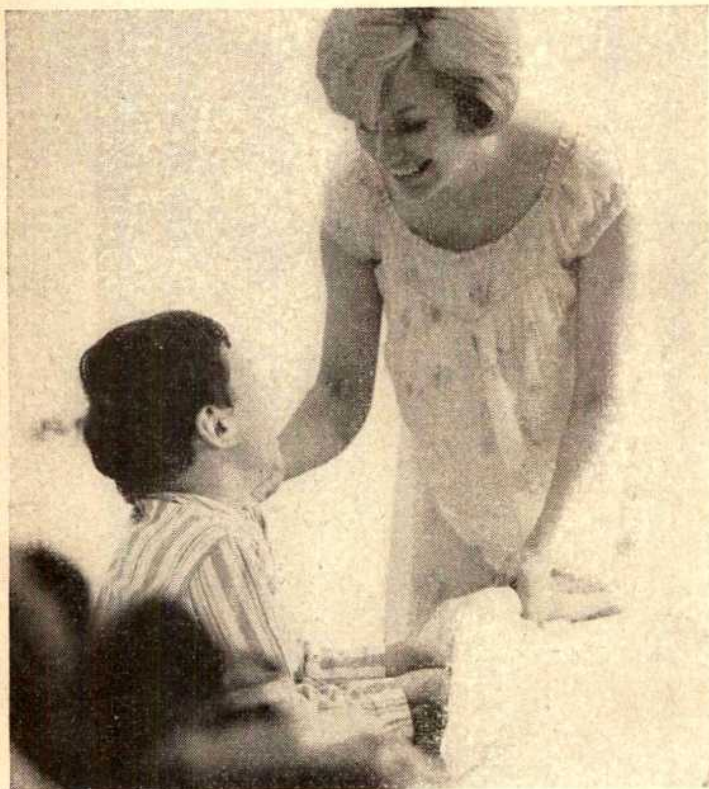
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Doctors Versus the Government

The New Zealand Doctor and the Welfare State. By J. B. Lovell-Smith. (Pp. 222; illustrated. 32s. 6d.) Auckland, New Zealand: Blackwood & Janet Paul. 1966.

This is a sober account of a fierce controversy which raged for over a decade between the New Zealand Branch of the B.M.A. and the Socialist Government of that country, and the story is of interest to those in this country who were, or are, engaged in a similar conflict with Government here. The author is a general practitioner in Auckland, and the hero, to whose memory the book is dedicated, is J. P. S. Jamieson, M.D., F.R.A.C.S., who in 1950 was a B.M.A. gold medallist and who placed all his files at the author's disposal.

A Bill to establish a compulsory national insurance scheme had been introduced in the New Zealand Parliament as early as 1883 but had been rejected; in 1900 New Zealand was the first country in the world to establish a ministry of health. The first medical problem it tackled was that of the hospitals, which had developed erratically, mainly with Government subsidies; however, by 1938 the system of public hospitals was deemed to be "of high quality." In 1935 the first Labour Government was elected, and in the same year a departmental committee was appointed to consider the question of a national health insurance scheme, together with the reports on the matter previously prepared by the Combined Hospital Boards and the New Zealand Branch of the B.M.A. The Branch gave evidence to the effect that a national health insurance scheme could not be expected to reduce the volume of illness and that the need was for proposals to prevent ill-health. The dedicated Socialists pressed for a salaried medical service and the abolition of private practice.

The battle raged fast and furious for many years. Dr. Guy Dain, as he then was, and Sir Henry Brackenbury visited New Zealand. The Government gradually shed the more objectionable items of its policy and became reconciled to payment per item of service, which was fixed in 1941 at 7s. 6d. The main dispute revolved round whether the State should contract with the doctor or with the patient. The final outcome was that the doctor claimed on the Social Security Fund for his 7s. 6d. but was not precluded from making an additional charge to the patient, who, however, had the safeguard that the doctor must send a detailed account. If the patient thought that this was excessive he could send it to a local investigating committee, who were empowered to reduce it. In 1941 the supplement paid by the patient was generally 3s., but by the time the book was written it had grown to about 7s. 6d. for a surgery attendance and 10s. for a home visit. In the early days, when many doctors charged the patients their ordinary fee and the patients made their own claim for a part refund from Social Security, the administrative cost of each refund was 1s. 6d. The whole basis of professional reward was altered; the general practitioner earned more than the specialist, and by comparison the earnings of those on salaries were "ridiculous." The author admits that the system "can rightly be regarded as open to abuse" and that abuses did occur in the early days.

During the past decade the population has increased by 12% but the number of practising doctors by 55%. Every general practitioner has free access to radiology and to laboratories for pathological examinations.

The book has a good index, but none of the 28 chapters has a heading and the exact chronology of events is hard to follow. However, the Labour Party lost the general election of 1944, since when there seems to have been peace.

ALLEN DALEY.

Comprehensive Review of Pituitary Function

The Pituitary Gland. Edited by G. W. Harris, M.A., Sc.D., M.D., D.M., F.R.S., and B. T. Donovan, B.Sc., Ph.D. (Vol. 1. Anterior Pituitary. Pp. 586+xiv; illustrated. Vol. 2. Anterior Pituitary. Pp. 670+xiv; illustrated. Vol. 3. Pars Intermedia and Neurohypophysis. Pp. 678+xiv; illustrated. Set of 3 volumes £26 5s.) London: Butterworth, 1966.

This is an opportune moment for this book to appear. Most of the pituitary hormones are defined and some have been synthesized. Many can be measured by immunoassay in body fluids, so that their role in physiology and in disease is being specified. The control of the endocrine system by hypothalamic neurosecretion is also now being defined. In these three volumes recent findings are set in perspective against the well-established data. It should provide a reference book for teachers and research workers of lasting value, though unfortunately the price may exclude this book from many private collections. It is, moreover, readable and well supplied with illustrations and charts.

Each chapter offers a readable and concise review of its field up to about 1964. The authors for the chapters are authorities from U.S.A., New Zealand, France, Italy, Sweden, Denmark, as well as the United Kingdom. Some chapters are wordy and sometimes one joint chapter might have been better than two or three separate ones. The three volumes are: Volume 1, Anterior pituitary (anatomy and biochemistry), Volume 2, Anterior pituitary (mainly its control), and Volume 3, Pars neuralis and intermedia. This book aims to cater for electron-microscopists and biochemists, as well as for clinicians.

Fortier gives an excellent and concise review of the control of A.C.T.H. secretion suitable for the clinician; other chapters review the physiology, the chemistry, and the non-endocrine actions of A.C.T.H. The chapter on the physiology and chemistry of growth hormone reviews also its relation to diabetes mellitus, acromegaly, its assay in body fluids, and also its use in the treatment of dwarfs. The physiology and chemistry of T.S.H. is fully covered, including its assay in plasma and the problem of exophthalmos. The gonadotrophins and mammatrophin or prolactin are extensively reviewed, though more in relation to animals than patients. Excellent reviews are included of the neurohypophysis in relation to kidney function and to vascular reactions, as well as the chemistry of vasopressin, and syndromes of inappropriate A.D.H. activity. Other chapters review hypophysectomy in man and in animals,

clinical tests of pituitary function, pituitary tumours in man as well as their experimental production in animals, and also the question of pituitary regeneration.

Several chapters will appeal more to research workers. A comprehensive review on the cytology of the adenohypophysis achieves a synthesis of this still unsettled field. The regulation of gonadotrophins in various species is extensively reviewed, though unfortunately in two separate chapters. The several chapters on the neurohypophysis unfold interesting details of the neurosecretion of vasopressin and oxytocin, their synthesis in the supraoptic nucleus their binding to the carrier protein neurophysin, and their propulsion down the axons to feet lying on the capillary walls in the posterior pituitary. A good introduction is offered to the hypothalamic releasing factors and their portal control of pituitary function, which is a field likely to have increasing relevance to medicine.

RUSSELL FRASER.

Revised "Hamilton Bailey"

Hamilton Bailey's Emergency Surgery. 8th edition. Edited by T. J. McNair, M.D., F.R.C.S.(Edin.), F.R.C.S.(Eng.). (Pp. 1026+xv; illustrated. £8 8s.) Bristol: John Wright, 1967.

Deplorable though it may be, much of the emergency surgery throughout the world today is carried out by junior men under less than ideal circumstances and without the direct supervision of an experienced surgeon. Moreover, more than the fair share of these cases seem to occur in the middle of the night, when the surgeon is already tired from his day's work and has little assistance from the now closed laboratory or x-ray department. It was for these humble, unsung, but essential young men, as well as for the benefit of their emergency cases, that the late Hamilton Bailey produced the first edition of *Emergency Surgery* in 1930. It was an immediate and well-deserved success, but lapsed after its seventh edition in 1958 with the unfortunate death of its author, sadly enough following an emergency operation.

Mr. McNair and his team of assistant authors must be complimented on a very fine revised edition. It combines the three essentials which the emergency surgeon requires in a reference book: succinct descriptions of disease (often with helpful case reports), clear indications of when and when not to operate, and detailed accounts of the operative procedures to employ. The illustrations are an important feature, and, as befits the late author, are of a very high standard.

As in every major textbook which has gone through many editions, here and there one detects somewhat outmoded features. One would like to see a description of the Fogarty catheter technique for peripheral embolism, for example, and few surgeons nowadays would stress the high Fowler position. These are minor comments on what is a really valuable major textbook. It will continue to prove of immense comfort to the surgical registrar, and will be read with profit and enjoyment by his chief.

HAROLD ELLIS.

International Population Trends

Proceedings of the World Population Conference, 1965. Vol. 2. Fertility, Family Planning, Mortality. (Pp. 510+xiii. \$7.50.) New York: United Nations Department of Economic and Social Affairs. 1967.

Representatives from 88 countries attended the World Population Conference held in Belgrade in 1965, and over 500 scientific and technical papers were given. The proceedings were published in four volumes. Volume 2, published this year, comprises 103 papers and 75 short summaries of other papers which had been presented. The proceedings reported in this volume have been arranged under eight headings: (i) Future population trends and prospects; (ii) Fertility; (iii) Factors and patterns of fertility in areas where fertility is relatively high; (iv) Factors and patterns of fertility in areas where fertility is relatively low; (v) Studies relevant to family planning; (vi) Mortality; (vii) Mortality, morbidity, and causes of death; and (viii) Population genetics.

The topics under discussion allowed for a great deal of speculation and the views presented were those of the authors. Some of the views, perhaps because of the limited space allowed for the article, appear to be unsubstantiated. Some of the opinions expressed on future population trends were undoubtedly biased either because of ideological beliefs or by national outlook. The consensus of opinion seems to be that birth control must play an important part in any population policy. One Russian worker thinks that a possible population of 5,000 million by the year 2000 could be well fed if the people were equipped by the methods of modern science and technology. Another worker suggests that the world area under cultivation can be increased by $2\frac{1}{2}$ to 3 times its present size. If the capitalistic theories of production did not stand in the way there would be no need of birth control, and using the methods of western Europe it would be possible to feed over 30,000 million people. In the speculations on the amount by which food production can be increased the need for living space seems to have been minimized. In Western countries the area available for food production is diminished

each year by the pressure of the population for increased living space. Ironically sites on which it is easiest to build new towns, reservoirs, motor ways, aerodromes, etc., are the best farm lands.

The papers on fertility are interesting but not very informative, because of their shortness. Some papers are accounts of pilot surveys based on rather small numbers in a very limited area of a country. Whether the results of these surveys can be extrapolated for the whole country is a matter of opinion, but large-scale inquiries will be necessary to establish trends. Economics, religion, and tradition are the major factors affecting fertility, but the environment of the people is an important factor that affects the differences between countries, especially developing countries.

Mortality and morbidity are influenced to a very large extent by the standard of living of the population and by the standard of medical care that it can afford. The section on mortality and morbidity is mainly concerned with the position within individual countries, and although international comparisons are attempted these are affected by the differences in the methods of registration and the classification of the causes between countries. In a large area of the world the care of the sick is undertaken by non-medically qualified persons—e.g., herbal doctors, witch doctors, etc. This section of the volume gives an interesting account of the large increase in medical care that has occurred in the U.S.S.R. The number of physicians, including Army medical officers, rose from 28,000 in 1913 to 501,000 in 1963.

The last section of the book deals with some of the aspects of population genetics. The difficulties inherent in this study are outlined in the various papers.

The multiplicity of books in recent years make it necessary to ask whether a new book fills any particular need. It can be assumed that the object of the World Population Conference, to provide an opportunity for workers in the same field to make each other's acquaintance and discuss mutual interests, was achieved. This volume suffers from the same defect as most accounts of symposia. It is a record of the proceedings, but whether the papers make any new contribution to knowledge is, perhaps, open to doubt, since in general the papers are short summaries of

work that has been published elsewhere. If the United Nations Organization thought it desirable to publish an account of the present state of knowledge on population subjects it should not have been beyond its powers to produce a coherent statement.

W. J. MARTIN.

Use of E.E.G.

The E.E.G. in Clinical Practice. By John Laidlaw, M.B., Ch.B., F.R.C.P.Ed., and J. B. Stanton, M.A., M.B., F.R.C.P.Ed., F.R.C.P., D.P.M. (Pp. 128; illustrated. 40s.) Edinburgh and London: E. & S. Livingstone. 1966.

This is a well produced and clearly written introductory account of the clinical uses of the simplest types of standard electroencephalographic techniques. After a good description of techniques and artefacts, the bulk of the book is occupied by what the authors call "clinical situations," that is, common clinical conditions in which the E.E.G. might be expected to help. The illustrations are excellent and the comments pertinent, particularly the authors' insistence on the value of the E.E.G. being enhanced if clear and appropriate questions are asked rather than diffuse requests for " ? epilepsy."

There is a short chapter at the end entitled "The Future of the E.E.G. in Clinical Practice," which refers particularly to the use of sleep records in temporal lobe epilepsy, and serial recordings in hepatic encephalopathy. One would have thought that both these situations were very much of today rather than the future. The whole book, in fact, is disappointingly conservative. There is no reference whatever to any underlying neurophysiology, so that the techniques are presented like a sort of static photograph of that little bit of cerebral activity which current electronic amplification apparatus can produce for us.

As a crammer book for those neurologists and psychiatrists who want to have a passing acquaintance with the E.E.G., the volume may have some value, but unfortunately it is only too likely to confirm such readers and others in a jaundiced view of clinical neurophysiology that is increasingly out of date.

D. A. POND.

Books Received

Review is not precluded by notice here of books recently received.

Les Soins à Domicile. Vers une Nouvelle Institution Médico-Sociale. By Jacques Massion. (Pp. 155. No price given.) Brussels: École de Santé Publique. 1967.

The Patient's Progress. Edited by Felix Marti-Ibanez, M.D. (Pp. 148. \$5.95.) New York: MD Publications. 1967.

The Guilty Mind. Psychiatry and the Law of Homicide. By John Biggs, jun. (Pp. 236. 18s.) London: Oxford University Press. 1967.

Anatomy and Surgery of Hernia. 2nd edition. By Leo M. Zimmerman, M.D., and Barry J. Anson, Ph.D.(Med.Sc.). (Pp. 368+ix; illustrated. £6 18s.) Edinburgh and London: E. & S. Livingstone. 1967.

Carcinogenesis. A Broad Critique Collection of Papers presented at 20th Annual Symposium on Fundamental Cancer Research, 1966. Published for the University of Texas, M. D. Anderson Hospital, and Tumor Institute, Houston, Texas. (Pp. 774; illustrated. \$16.00.) Baltimore: Williams & Wilkins. 1967.

Cerebral Palsy. A Clinical and Neuropathological Study. Clinics in Developmental Medicine No. 25. By Erna Christensen and Johannes C. Melchior. (Pp. 134; illustrated. 28s.) London: Spastics Society Medical Education and Information Unit in Association with William Heinemann. 1967.

The Id and the Regulatory Principles of Mental Functioning. By Max Schur, M.D. (Pp. 220. 42s.) London: Hogarth Press. Institute of Psycho-Analysis. 1967.

Renal Disease. 2nd edition. Edited by D. A. K. Black. (Pp. 798+xii; illustrated. £6 6s.) Oxford: Blackwell. 1967.

The Technique and Practice of Psycho-Analysis. Vol. 1. By Ralph P. Greenson. (Pp. 452+xv. 84s.) London: Hogarth Press. Institute of Psycho-Analysis. 1967.

The Limits of Man. An Enquiry into the Scientific Basis of Human Population. By Hugh Nicol. (Pp. 283. 35s.) London: Constable. 1967.

Applied Audiology for Children. 2nd edition. By D. M. C. Dale, Dip.Ed.(N.Z.), Ph.D.(Manchester). (Pp. 159+xiv; illustrated. \$7.75.) Springfield, Illinois: Charles C. Thomas. 1967.

The Growth of Medicine. Compiled and edited by Frederick Stenn, M.D. (Pp. 199+xvii. \$9.50.) Springfield, Illinois: Charles C. Thomas. 1967.

Advances in Enzyme Regulation. Vol. 5. Proceedings of Symposium. Edited by George Weber. (Pp. 469+xiv; illustrated. £6 10s.) Oxford: Pergamon. 1967.

Middle Articles

MEDICAL EDUCATION

Postgraduate Medical Education

A report¹ published this week calls for an overall plan of action for postgraduate medical education in Britain. Even twenty years after 1948, it states, there is no real co-ordination of effort or objective, particularly in vocational training, and today this is still the key question. "The formation of the Scottish Postgraduate Medical Association in 1962 was a promising step, but with only powers of persuasion and no money, how effective has it proved in helping to solve the major problems of the day? In 1967 the initial objectives of the Central Committee [for Postgraduate Medical Education] gave no hint of crisis or emergency."

According to the report the whole question of postgraduate education has been bedevilled by the way in which specialist status has become continuous with consultant rank in the National Health Service. "Particular specialties doubtless require particular qualities of mind and will, but a career structure should not imply a competition in which some succeed and are trained and some fail and drop out." In the report's view three main elements are missing at present in the arrangements for postgraduate education: a structure, both for postgraduate and continuing education; adequate finance; and a mechanism for co-ordination.

Need for Structure

The report was commissioned by the Nuffield Provincial Hospitals Trust to explore the responsibilities of the various bodies concerned in postgraduate medical education. Discussing the lack of a structure for vocational training in the National Health Service, it emphasizes that sufficient training posts for the various specialties must be provided. So far there has been little effective supervision of training posts as a whole, even though, in the case of senior registrars, the universities work closely with the regional hospital authorities. Hence, the report suggests, there must be an independent authoritative central body, both to demonstrate the need for a training structure and to approve and supervise training posts.

The report continues by saying that, though at present the Ministry of Health has the paramount influence on postgraduate training, there is no evidence that there is an overall plan of action. The Ministry has already outlined the regional postgraduate organization it considers necessary, but, the report says, it is not clear what part the universities and colleges are to play in this, and regional hospital boards must be given a

clear lead. Furthermore, the particular sum spent on postgraduate education by a particular regional board has to be decided according to its other commitments; hence there are considerable differences in the provision of postgraduate schemes among the various regions. In the report's view, moreover, there is one notable outstanding anomaly—namely that, in contrast with their counterparts in teaching hospitals, few consultants in regional hospitals have any teaching element recognized in their contracts.

At present the Central Committee for Postgraduate Medical Education is intended only to be advisory, but the report questions whether it can continue this role if it is to perform a useful function. If it is to start influencing events it needs quickly to enlarge its aim beyond the one already outlined (a review of preregistration posts). On the other hand, the report emphasizes that the committee's potential influence is very great, and its support of the Fellowship Scheme for advanced clinical studies may have been a factor in the prompt approval given by the Ministry for a substantial grant. The report expresses surprise that the constitution of the committee does not include representatives from the Ministry, as the Minister is ultimately responsible for the standards of medical care. "The Ministry of Health appears to have been holding back from the assumption of too much authority in this field in the hope that the gap will be filled in another way; but it is inevitable—and proper—that it will be forced into greater intervention if the vacuum is not filled."

Specific responsibilities suggested for the Central Committee might include implementing the standards for specialist registration, if these are laid down by the General Medical Council; co-ordinating the efforts of the service and educational authorities in postgraduate training; and commenting judiciously on the effectiveness of the career structure for the specialties. The Central Committee could delegate the approval and supervision of training posts and the form and content of training to the colleges; while the responsibility for service matters could be delegated to the regional postgraduate medical committees.

Finance

The report says that the future financing of the Central Committee will require special consideration, and it is a weakness that as long as the committee consists only of educational members—as at present—it

can hardly look for continuing support outside the universities and colleges. Substantial funds will be needed to carry out the functions suggested above and to enable the committee persistently to inquire into the content and method of postgraduate medical education. Nevertheless, in relation to postgraduate medical education as a whole the amount of money needed for its long-term stability and security is said not to be very great, provided the vast potential of the universities, the colleges, and the regional postgraduate committees is exploited through delegated powers. It would seem desirable, the report considers, to look more optimistically to the Ministry of Health as the prime source of funds rather than to the University Grants Committee, and it cites the Ministry's financing of a nursing research unit (see p. 628) as a precedent.

Role of Central Committee

Discussing the role of the Central Committee, the report says that this can really gain in authority only if it were to become the key adviser to the Ministry on postgraduate medical education. It might be in the nation's best interests that the committee should be seen to be independent and should be made responsible for monitoring all matters concerning postgraduate medical education in the National Health Service. Nevertheless, there must be provision for dialogue with the Ministry and its satellites.

Concluding, the report says that the Central Committee is at present the best focus that exists or is likely to exist for some time. Its first real test will be how it faces up to deciding what is necessary to bring some order to the chaos of the immediate post-registration phase. "Finally it is not too optimistic to believe that to fulfil its potential, the Committee need not depend on being granted statutory powers of direction or sanction. There is already a miscellany of bodies wielding a wide range of powers in the field of postgraduate medical education, which derive from statute or long tradition. Indeed, what is now required is possibly the influence and authority that stems from the cool considered views of an intellectual élite, suggesting the form of a society rather than a board of management. Perhaps the Central Committee is indeed the start of a British Academy of Medicine."

REFERENCE

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CONFERENCES AND MEETINGS

Tropical Splenomegaly Syndrome

[FROM A SPECIAL CORRESPONDENT]

A one-day symposium was held at the Royal Postgraduate Medical School in London on 17 November. The participants comprised experts in tropical medicine, parasitology, pathology, immunology, and haematology, most of whom had had personal experience with splenomegaly in the tropics. They met to review the present state of knowledge and to define those areas where further research was likely to be fruitful.

Splenomegaly is common in tropical countries, and well-recognized causes include portal hypertension due to hepatic cirrhosis, haemoglobinopathy, leishmaniasis, and schistosomiasis. In some areas there exists a form of massive splenomegaly found mostly in adults in which the above causes can be excluded. This type of splenomegaly has been termed idiopathic splenomegaly, tropical splenomegaly, "big spleen" disease, cryptogenetic splenomegaly, Bengal splenomegaly, and African macroglobulinaemia. The disorder is found in regions where malaria is endemic, and it has been customary to consider malaria a causative factor, although the evidence in favour is largely circumstantial. Many interesting features have been described as a result of studies by workers in Uganda, Nigeria, New Guinea, and elsewhere using modern techniques.

The majority of participants favoured a noncommittal title of tropical splenomegaly syndrome, at least for the time being. It was pointed out that a syndrome only has been described, which may not, in fact, be a homogeneous entity in all areas studied. A more definite title should wait until further work has produced a clearer understanding of the causal mechanisms.

Role of Malaria

Much of the time was spent discussing the evidence in favour of malaria being the cause. Massive splenomegaly has become less common in Calcutta and Algeria since the control of malaria in these regions. In Uganda this form of splenomegaly is not found in areas free of malaria but is common in other parts.

There are pockets of high incidence of the disorder in valleys at an altitude of 3,000 feet (914 metres) and above in New Guinea, where the pattern of malaria transmission is likely to be unstable. Affected persons in Uganda show high titres of fluorescent malarial antibody in the serum, though it was pointed out that the interpretation of this type of test is difficult and that high titres do not necessarily indicate a state of immunity to malaria.

The most conclusive evidence that malaria is implicated in the aetiology of the syndrome was provided by a group of workers in Ibadan, who have obtained beneficial results with continuous antimalarial therapy. Proguanil was the drug chosen, and it was given in a daily dose of 100 mg. There was a slow but progressive diminution in the size of the spleen (over a matter of months) associated with correction of anaemia and an improvement in general health. This occurred despite the fact that malarial parasites could not be found in the blood of these patients before treatment. It was emphasized that in some cases therapy had to be continued for more than a year before maximum reduction in spleen size was achieved, in many cases the spleen becoming palpable. Cessation of therapy caused the spleen to enlarge once more, full relapse taking about three months. It was the opinion of the meeting that lifelong anti-malarial therapy was likely to benefit patients with the tropical splenomegaly syndrome provided that medical surveillance was possible. Chemotherapy probably decreased acquired immunity to malaria and should not be used for long periods without recognition of this effect. Splenectomy was not indicated, since the risks of bacterial infections and fatal attacks of malaria in subjects after splenectomy were considerable.

An Abnormal Immunological Response?

Massive splenomegaly in adults is not the usual reaction of immunity in areas where malaria is endemic and transmission stable,

and it is likely that some special factor or factors operate to produce the syndrome in susceptible people. Affected subjects show few or no malarial parasites in peripheral blood films and there is lack of malarial pigment in the reticulo-endothelial cells in biopsy material—both features usually being associated with immunity. There is no real evidence that poor nutrition is a contributory factor. Perhaps infection with a combination of species of malarial parasites or an unusual frequency of challenge may produce an abnormal immunological response, resulting in massive splenomegaly.

Anaemia is a usual finding in the tropical splenomegaly syndrome, and recent isotope studies have shown the causes to include pooling of red cells in the enlarged spleen, increased rates of red cell destruction, and expansion of the plasma volume. The mechanism of hypervolaemia is obscure. Another interesting feature of the disorder is an abnormality in serum-immunoglobulin concentrations. There is an increased amount of the immunoglobulin IgM in the serum, this finding in general being more marked in those patients with the larger spleens.

The descriptions of the syndrome from different regions of the tropics showed some variable features. In Nigeria peripheral blood and marrow lymphocytosis might be found, and it was suggested that lymphoproliferative disorders might be more common in such patients. This lymphocytosis was not seen in New Guinea or Uganda. Splenic histology in New Guinea patients was reported to show more dilatation of sinuses and less lymphoid proliferation in the pulp than was observed in Africa. Splenomegaly was more frequent in the Rwanda than in the Baganda tribe, living in the same area of Uganda. There was some evidence from Nigeria that possession of the sickle-cell gene might give some protection from the development of massive splenomegaly. The disorder was more common in women than in men in both Africa and New Guinea. Finally, the relationship of the tropical splenomegaly syndrome to cryptogenetic splenomegaly in Hong Kong—which is often associated with hepatic cirrhosis—was unknown.

Aspects of Anxiety

[FROM A SPECIAL CORRESPONDENT]

Any discussion of anxiety must begin with a definition of the term, and a variety of definitions were put forward by participants in the World Psychiatric Association's symposium on "Aspects of Anxiety" held at the Royal College of Physicians in London from 13 to 15 November. Professor MAX HAMILTON (Leeds) distinguished three uses of the word in the senses of a normal reaction to danger, a pathological mood, and a disorder or syndrome—anxiety state or anxiety neurosis. Dr. LOPEZ IBOR (Madrid),

President of the W.P.A., reminded the audience that the present time had been referred to as an age of anxiety, perhaps because of the rapid changes in society, but that anxiety was presumably a feature of the human condition which had always existed. He felt that pathological anxiety differed from normal anxiety in its intensity. "If one *troubles*, the other *disturbs*." The amount of anxiety reached a pathological degree when it transcended the subject's ability to bear it; either the flow of painful stimuli was

overwhelming or the total lack of stimuli, as in sensory deprivation, was frightening.

Measurement of Anxiety

Professor H. J. EYSENCK (London) showed how experimental psychologists had constructed a model of anxiety with respect to its origin, its behavioural effects, and its differences in different persons. This model had a certain amount of coherence and experimental support and might be helpful to

psychiatry. In terms of modern learning theory the primary drive for anxiety was pain; neural stimuli associated with pain caused fear responses which resulted in a secondary drive stimulus of anxiety.

Dr. M. H. LADER (London) pointed out that from the standpoint of psychophysiology there were two approaches to the investigation of anxiety. Attempts might be made to induce anxiety in normal subjects or psychiatric patients by various stimuli, or differences might be sought between patients complaining of anxiety and normal subjects. Several physiological values could be used for study of anxiety, mostly in the realm of the autonomic nervous system—such as blood pressure, heart rate, finger pulse volume, or skin conductance. A reciprocal relationship existed between anxiety and depersonalization; thus values such as skin resistance underwent great change in anxious patients with episodes of depersonalization.

Dr. J. SMYTHIES (Edinburgh) dealt with the central brain mechanisms involved in anxiety. Fear reactions seemed to be controlled in general by a complex system, including the limbic structures and in particular the amygdala, hypothalamus, and reticular formation. Swedish workers had related these mechanisms to chemical findings, for they had shown that, whereas the cortex mainly runs on acetylcholine, the limbic system, hypothalamus, and reticular formation contained large quantities of noradrenaline and serotonin, and there were actually different neurons with specific chemical transmitters—noradrenaline, serotonin, and dopamine. He had also been able to relate the action of the hallucinogen mescaline—an analogue of adrenaline—to the anxiety level in the subject; terrors and psychosis tended to be induced in people with a high resting level of anxiety or those who became frightened during the experimental use of the drug.

Dr. M. VARTANIAN (Moscow) had shown that intravenous injection of serum from anxious patients into rabbits led to a rise in noradrenaline content of the hypothalamus, quite apart from the usual stress reaction due to injection of foreign serum. He had also demonstrated autoimmune reactions in persons under intense stress, for the serum of patients in acute psychotic states frequently contained antibodies to brain proteins, as did that of 40–50% of normal subjects under intense stress.

Dr. J. BOWLBY (London) said that the cause of the separation anxiety in children deprived of their mother was something of a puzzle, but recent work on affectional bonds in birds and mammals might hold the clue. The bonding and attachment behaviour of animals presumably served the purpose of protection from predators and was probably not related primarily to food or sex, as had been suggested in the past. Just as the bonded animal temporarily separated from its mate would search for the latter and exhibit distress until it was found, so the human adult who had lost a spouse would for a while after bereavement go through a period of behaviour which could be interpreted as a search for the lost object, as Dr. C. MURRAY PARKES (London) showed from his studies of widows.

Separation anxiety could also be manifested as a result of separation off by a political system, and Dr. W. VON BAEYER (Freiburg) discussed his studies of the victims of political persecution in the Third Reich, at least one-third of whom retained appreciable lasting psychiatric effects of their experiences.

Genetic and Environmental Factors

Studies on twins by Dr. ELIOT SLATER and Dr. J. SHIELDS (London) had shown that inherited factors played a part in predisposing to anxiety. Nevertheless, the environmental factor might often be the dominant one.

The President of the Symposium, Dr. W. SARGANT (London), devoted much of his presidential address to his conviction that drug treatment of anxiety was of paramount importance, after pointing out to his hearers that anxiety was perhaps the major psychiatric problem of the day, as shown by the 43 million prescriptions for psychotropic drugs issued by practitioners in the National Health Service in a recent three-year period, mostly for anxiety and tension. He reiterated his

faith in the monoamine oxidase inhibitor group of antidepressants in the management of phobic anxiety states in persons of good previous personality, and in the usefulness of antidepressant drugs in general, perhaps combined with electroplexy, in depressive tension and anguish. He felt that there was still a place for frontal leucotomy in patients without response to drugs or electroplexy.

Dr. M. GELDER (London) was concerned with the efficacy of specific desensitization in the treatment of anxious patients with isolated phobias. He considered this treatment superior to either group or individual psychotherapy, but only as regards removal of the phobia. Desensitization did not lower the level of general anxiety.

A specialist in physical medicine, Dr. F. COOKSEY (London), drew attention to the frequent failure of doctors to take into account and assess the degree of anxiety accompanying physical disabilities, as exemplified by the patient with low back pain or a stroke. Ideally any department concerned with rehabilitation should have a psychiatrist working in it, and he should be consulted early and not as a last resource.

NEW APPLIANCES

Grooved Probe Dilator: Aid to Vascular Anastomosis

Mr. D. G. A. EADIE, senior lecturer in surgery, the London Hospital, writes: An instrument has been designed to facilitate the anastomosis of small blood vessels where accurate insertion of the corner suture is

The probe dilator (Fig. 2) is constructed of polished stainless steel to prevent injury to the vessel endothelium. The head is detachable from a malleable copper rod to permit thorough cleaning. Four different-



FIG. 1



FIG. 2

essential to achieve a perfect technical result. It has a threefold function: firstly, the groove allows the needle to be placed and recovered with ease—that is, at the corner of the vessel to be sutured (Fig. 1); secondly, the probe itself acts as a dilator; and, finally, once the probe is in position it acts to steady the vessel, thus eliminating the need to grasp the vessel with dissecting forceps.

sized heads are available, ranging from 4 to 7 mm. in diameter.

This instrument is available from the Genito-Urinary Manufacturing Company Limited, 28a Devonshire Street, London W.1. The prototype was made by Mr. F. H. Watson, of the London Hospital instrument department.

Correspondence

Letters to the Editor should not exceed 500 words.

Medical Science: Master or Servant?

SIR,—It is refreshing in these days of diminished personal responsibility in public affairs to read Lord Platt's Harveian Oration (25 November, p. 439), for, in case some innocent readers might not suspect it, he was a professor of medicine during a period when he might have been supposed to exert some influence. Despite the number of chairs in medicine and therapeutics, which he considers large, expansion is a very recent one, so that, for example, ten years ago only about half of the London teaching hospitals had such chairs, and it is perhaps not surprising that the departments concerned were, and still are, particularly interested in studying the phenomena and causation of disease, since this provided the first challenge in caring for patients.

Unlike Lord Platt, I think that in this country this represents a considerable advance within the last twenty years, and it might put matters into slightly better perspective if the often markedly limited physical and financial conditions of many of these university medical units were looked at realistically. There is no substitute, however, for the first-class idea which can be brought to fruition in even the most unpromising conditions, but the environment and attitude towards many university medical units has left much to be desired. He also fails to point out that the "therapeutic explosion" was occurring at precisely this time also, and while there is no doubt that university medical departments played little direct part in this, apart from the reasons given, I think a major cause is the previous lack of biochemical and pharmacological tradition in the training of doctors. This situation is being remedied quickly. How is it possible within the framework of the present organization of medical research to bring more first-class ideas to fruition unless departments of medicine are expanded? Many can see as clearly as Lord Platt that the study and development of the action of drugs or of psychological factors in disease are pressing problems, but in order to create a new post in my own school with the sort of person I hoped would produce such ideas I was compelled to turn for financial support to the pharmaceutical industry in the hope that ultimately the university could take over the enterprise. Since the university works on a quinquennial basis, it may readily be seen that speedy action is difficult. I am sure that most of the current professors of medicine can see the problems clearly enough, and I am sure that they would find it considerably easier to help in the advances and changes in direction of scientific and medical effort if it was as easy to translate thoughts into action in the current university setting as Lord Platt seems to find it in retrospect. Since I believe there are people with first-class ideas in university departments of medicine, I

would like to suggest that one of the ways to give them opportunities for the developments that many would like is to change the concept of departments of medicine as they currently exist in this country.

Despite his strictures on the American approach to the problem, I believe that a university hospital should have a large all-embracing department of medicine in which it is as easy to employ a physicist as a physician who, without ever doing any research work, demonstrates the highest of skills in the care of patients. The error of the American approach has been its emphasis on research of any standard to the exclusion of clinical skills in giving positions in university departments, and this is something which I am sure we can avoid. Nevertheless, the atmosphere of co-operation and enthusiasm with high-class work which characterizes many of these departments is something I would dearly like to see reproduced more widely here. It seems to me that our most pressing problem is how to bring about this transition quickly in our current financial and intellectual situation. Our so-called university hospital system is inelastic and still overmuch attached to separatism within the clinical sphere.

The main revolution that has to occur is in the mind as well as in the organization of medicine, and I think that Lord Platt is grievously wrong in contrasting the understanding of patients and their needs with the scientific aims of medicine. We can keep out the dangerous fools attached to machines as long as we can let in the wise men. This is where we need the real leadership in our profession which will bring about a synthesis and understanding and not the continuation of old divisions.—I am, etc.,

St. Mary's Hospital,
London W.2.

W. S. PEART.

SIR,—In congratulating Lord Platt (25 November, p. 439) on his brilliant account of the misdirected efforts now wasted on certain types of clinical research, may I offer statistical confirmation of two of the points he makes?

His statement "that sex education was taboo until quite recently" I can confirm by the research I did on the types of sex education medical students received in the universities of this country.¹ From 47 medical schools questioned 36 replies were received, 24 from Britain and 12 from abroad. Less than half of the students at these medical schools entered their professional life with any adequate equipment to deal with these problems, and I have reason to believe that the position is not very different today.

I can also confirm Lord Platt's statement of the almost complete neglect of psychological factors in my own subject of infertility,

where so often the treatment of her (and occasionally his) genital organ is all that the sterile couple receives. That 25% of all cases presenting at my clinic have infertility of emotional origin² is statistical confirmation of Lord Platt's thesis that "scant attention has been given to the ills of the mind of man and woman and the study of their behaviour in health and disease and in society."—I am, etc.,

Cheadle,
Cheshire.

BERNARD SANDLER.

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- ² ———, *J. Obstet. Gynaec. Brit. Comm.*, 1961, **68**, 809.

Hospital Boards

SIR,—If my friend Mr. R. G. Macbeth's description (25 November, p. 482) of the struggle for power is a true reflection of the state of the Health Service in most of the regions in England I can only be thankful that so much of my medical life has been spent in Scotland.

Yet, even north of the border, Mr. Macbeth seems to consider that at least half the teaching hospitals exist in a state of frustration and annoyance owing to the interposition of the regional hospital board between them and the Scottish Home and Health Department. On what authority he bases this assumption is not stated, but, as a former clinician who has had the experience of serving on all the bodies mentioned in his letter, in addition to occupying at the present time the post of a temporary medical administrator, I feel I am in a position to correct some of his statements.

It has always appeared to me from conversations I have had with my colleagues in England that the retention of the boards of governors of teaching hospitals as a separate body fostered a state of internecine warfare between boards of governors of teaching hospitals, regional hospital boards, and the university faculty, and that the two primary objectives for which these bodies existed—namely, the welfare of the patient and the education of the student—were liable to suffer. Mr. Macbeth's solution is to abolish the regional hospital board, but might not the better plan be to do away with the boards of governors of teaching hospitals as such and replace them by group boards of management as in Scotland?

No one would pretend that there is never any area of disagreement between regional hospital boards and boards of management in Scotland, but this is seldom serious, and, if necessary, an appeal can be made to the Scottish Home and Health Department by a board of management. In general, I believe boards of management and the university recognize that the regional hospital board has a useful and specific function in formulating policy and determining priorities. Provided communications are good, this will eventually operate to the advantage of all, and in my opinion since the Health Service started

there has been very considerable progress in the improved interrelationship and harmony between the university, boards of management, and regional hospital board. Mr. Macbeth's solution seems to be for the Ministry of Health to allocate to smaller area boards than the regional hospital board a block grant, the exact slice of the financial cake being determined by the Ministry as it thought fit. In other words, there would be no body of local opinion to guide the overall distribution of financial resources. I very much doubt if one can designate such a policy as being one of devolution, and I venture to think that under Mr. Macbeth's scheme the smaller areas would be likely to receive a less equitable share than they do at present, since there would be a greater tendency for the Ministry to place most of their goods in the show-rooms of the teaching hospitals for political purposes.

The second part of Mr. Macbeth's letter deals with the composition of the boards of governors of the teaching hospitals, and here I think there is probably room for reorganization, but in Scotland this is more likely to be concerned in the first instance with the recommendations of the Brotherston working party contained in their recently issued report on the Organization of Medical Work in the Hospital Service in Scotland,¹ which, if they are adopted, will certainly involve the medical staff in a greater share in the organization of the teaching hospital than is the case at present.

Finally, I feel it is a mistake for Mr. Macbeth to leave even the faintest implication that the boards of governors of the teaching hospitals have a monopoly of integrity and service in the Health Service.—I am, etc.,

Aberdeen.

E. G. COLLINS.

REFERENCE

- ¹ *Organization of Medical Work in the Hospital Service in Scotland, 1967.* H.M.S.O.

Managing the Hospitals

SIR,—In recent months the management structure of hospitals has been the subject of many investigations with the expressed view of improving efficiency at all levels and making the most of the available resources. These investigations have given rise to a spate of reports—for example, Farquharson Lang (Scotland),¹ Hawnt (Northern Ireland),² and the most recently published King's Fund (London) report.³ It is now quite obvious that these important reports are receiving scant attention from hospital doctors, because they have not been made aware of their content and are thus unable to investigate them fully and assess their eventual effect.

It is suggested that there is now a case for all levels of hospital medical staff to examine and assess their individual roles in the hospital structure of the future, and consider if any benefit is to be derived from the application of recognized managerial principles in their own work. These principles are based on an analysis of business and commercial efficiency. Their acceptance, in part or *in toto*, without critical examination and recognition of the unique structure and function of a hospital could prove disastrous to the efficiency of hospital medical practice. The medical profession can be proud of the

standard of efficiency in the majority of our hospitals, and should recognize that if industry, the Civil Service, and other administrators had matched this in their own spheres then much of the stagnation of our present-day economy would never have occurred. The fact that continued and steady progress has been made in the hospital service where levels of authority are difficult to define, and where variations occur from region to region, is an argument in itself for retaining the existing flexibility. The same considerations weigh heavily against the introduction of "super managers," which most of these reports favour.

It is significant that the idea of a "super manager," who would in most cases be a lay administrator, originated from committees and working parties composed almost entirely of hospital secretaries and other laymen, who are completely unqualified to investigate the subjects under review. It would not be uncharitable to suggest that a "Charter for Hospital Secretaries" would be an apt title for their various recommendations. In most cases these working parties have decided their own terms of reference and do not appear to have gathered the detailed and impartial evidence on which their opinions should have been based.

The influence of the Institute of Hospital Administrators can be seen clearly in the recommendations contained in these reports. Their views were made clear when asked by the Ministry of Health for their comments⁴ on the Salmon Report on Nursing⁵: "Today hospital administration can no longer be viewed in the simple terms of comprising a partnership of medical, nursing, and lay administration. In the complex of the modern hospital medicine and nursing are only two of a wide range of essential services." They declare that the Bradbeer concept of tripartite administration "has become regarded as wholly outmoded by both hospital administrators and by others concerned with the management of the hospital service."

It is imperative that the medical profession realize that these reports carry implications as great as did the original introduction of the National Health Service. They should not allow less important preoccupations to detract from the recognition of the magnitude, the scope, and the far-reaching effects of these reports. The lay take-over of hospital administration by all-powerful general managers, most of whom would be "lay," would eventually reduce the status of medical staff to the level of all other groups of hospital workers. These reports infer that the medical profession can play no worthwhile part in the running of the hospital service. The interference with professional freedom and the doctor-patient relationship which would eventually follow the introduction of such systems would unquestionably ruin our hospital service for all time, and would make hospital medical practice an unattractive and unrewarding career.

The present reorganization of the general-practitioner service will eventually locate most general practitioners in group-practice centres owned by local authorities. It does not require a great stretch of the imagination to see this branch of the profession eventually fall under the thumb of lay administrative managers.

All doctors should unite now to face this great challenge to our profession and its freedom. The British Medical Association should ensure that the maximum amount of

publicity is given to the implications contained in these reports. The response to your leading article (4 November, p. 252) indicates a lack of interest by the profession, who do not appear to be aware of the gravity of the situation which is now facing them, and unopposed implementation of these reports through lack of interest is very likely to occur. The medical profession and the British Medical Association should ensure that "medical administration" is added to the curriculum of undergraduate and post-graduate medical training as a matter of the utmost priority to ensure that a supply of top-quality medically qualified administrators will be available to fill the managerial breaches now being artificially created.—We are, etc.,

JAMES BLUNDELL.

J. LOWRY.

North Armagh
Hospital Management Committee,
Lurgan, Co. Armagh.

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² Report of a Joint Working Party (unpublished).
³ *The Shape of Hospital Management in 1980, 1967.* King Edward's Hospital Fund for London. See also *Brit. med. j.*, 1967, 4, 187.
⁴ *Hospital*, 1966, 62, 589.
⁵ *Report of the Committee on Senior Nursing Staff Structure, 1966.* H.M.S.O. See also *Brit. med. j.*, 1966, 1, 1375.

Clomiphene for Ovulation

SIR,—Your leading article (25 November, p. 434) states that "to determine whether a woman responded at all to clomiphene and when she ovulated requires nearly continuous 24-hour collections of urine for steroid assays over two to three weeks." But surely all the non-ovulating infertile woman wants is to conceive and the only test that interests her is a pregnancy test.

How many busy housewives or working women can collect 24-hour specimens daily for three weeks? How many laboratory units in how many hospitals can do the necessary estimations and do them daily for three weeks on a considerable number of women without getting literally inundated with urine? Your leading article cites this as "an example of a situation where the skilful use of laboratory resources can be of great benefit to a few people while a failure to use them can do harm to a larger number." What harm? Your leading article states that the untoward side-effects of clomiphene are slight, so even if it is given to many women who do not need it, as it undoubtedly will be, or do not respond to it, it will not do them any harm. It is obviously waste of time and clomiphene to give it to women with regular ovulatory cycles, because its only therapeutic function is to induce ovulation. Most of our cases, however, have been patients with long-standing secondary amenorrhoea or oligomenorrhoea with only two or three cycles a year, in whom ovulation obviously does not occur or occurs only very seldom.

It is of course important to select suitable cases so far as possible, and urinary gonadotrophin or oestrone estimations are helpful for this purpose. It is also important to weed out those cases that do not respond to clomiphene at all, for it becomes inappropriate to go on treating them for more than three or four courses, though some women who do not respond to the first course may do so to the second or third course. But to

weed the non-reactors out it is quite unnecessary to make them collect all their urine for three weeks. The induction of uterine bleeding 10 days to a fortnight after the treatment shows that there has been some response. Basal temperature recording will show in the majority of cases whether ovulation has taken place and may indeed be the earliest indication that conception has taken place. Serial vaginal cytology (vaginal smears taken daily or on alternate days) will give an accurate indication of the oestrogenic response, the induction of ovulation, and the post-ovulatory progesterogenic response. Women of even moderate mental capacity can be taught to take their own smears, and they can bring them up to the clinic once a week, once a fortnight, or even once a month. All that is needed is a vaginal cytology unit to interpret them. At present there are very few. There should be more. If there were a great deal of unnecessary routine steroid hormone estimations on 24-hour urine specimens would be avoided and steroid chemists would be able to get on with their research work.—I am, etc.,

PETER BISHOP.

Chelsea Hospital for Women,
London S.W.3.

Neutropenia Caused by Methyldopa

SIR,—So far as we are aware only two cases of neutropenia caused by methyldopa (Aldomet) have been recorded,^{1,2} and therefore we think it worth while to report a third.

A Persian doctor's wife aged 43 consulted us because of pain in the back. This was found to be due to osteoarthritis. In the course of routine examination she was found to have a blood pressure of 200/120 mm. Hg. The urine was normal in all respects. An intravenous pyelogram and a renal arteriogram showed nothing abnormal. Methyldopa and a low-calorie diet were prescribed. Her blood pressure fell satisfactorily. After 10 days her temperature rose to 102° F. (38.9° C.) and a white cell count showed a total of 2,000 with 800 neutrophils. Methyldopa was discontinued and ampicillin prescribed. Three days later the leucocytes were still 2,000, and the neutrophils had fallen to 460 per cu. mm. A marrow examination by Dr. M. J. L. Patterson showed the following results—Cellularity: reduced. Erythropoiesis: normoblastic and somewhat depressed. Granulopoiesis: markedly depressed. Megakaryocytes present and appear normal. Reticulum cells infrequent. Plasma cells normal. Mitoses reduced. Iron present in normal amounts.

Thereafter the white cell count improved. After a further five days the total leucocytes numbered 3,000 per cu. mm. with 1,290 neutrophils. By the end of three weeks the leucocyte count had risen to 4,000 and the neutrophil count to 2,160.

One difference between this case and Dr. K. G. A. Clark's¹ is that, whereas his showed active granulopoiesis to the metamyelocyte stage, in ours granulopoiesis was much depressed. There was no evidence of autoimmune haemolysis which methyldopa occasionally causes: the red cell osmotic fragility was normal, the serum bilirubin 0.4 mg./100 ml., and the direct antiglobulin test negative.—We are, etc.,

RAYMOND GREENE.
A. W. SPENCE.

London W.1.

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Low Back Pain

SIR,—Although it is now commonly believed that defects in the neural arch (spondylolysis) are stress fractures rather than congenital in origin,^{1,2} it is quite misleading to suggest that such stress fractures of the pars interarticularis are common findings in patients with low back pain ("Medicine Today: Low Back Pain," 11 November, p. 341). Furthermore, it is rare to find a defect in the pars interarticularis which can be shown on serial x-rays to go on to unite. Perhaps this is because the forces acting on the lower lumbar vertebrae tend to separate the fracture surfaces.

Defects of the neural arch, with or without an associated forward slip (spondylolisthesis), are more commonly found in association with chronic low back pain, and 7.9% of a total of 4,411 patients from four series quoted by Rowe and Roche had defects demonstrable on x-ray. When symptoms occur they are the result of the mechanical weakness or lumbar instability³ resulting from the defect, and are the same as those seen in lumbar instability from any other cause, such as degenerative disease of the lumbar spine.⁴ When conservative treatment fails the logical treatment is spinal fusion⁴ to stabilize the unstable segment, a form of treatment not mentioned in your article.—I am, etc.,

A. W. F. LETTIN.

Orthopaedic Department,
St. Bartholomew's Hospital,
London E.C.1.

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SIR,—As I presume your "refresher" column on back troubles (11 November, p. 341) is intended to help general practitioners, I think it should be remarked that the clinical picture as described differs somewhat from that seen in general or industrial practice, where loss of the ankle jerk in sciatica occurs in a comparatively small minority of cases, and muscular weakness or wasting are excessively rare except following surgical intervention.

Further, the observed natural history of the syndrome leaves one in no doubt of the common origin of lumbago and sciatica, from intervertebral disc lesions, without the need for aetiological differentiation.

Lumbago is usually a mild condition, and, while one cannot doubt the wisdom of strict bed rest for a first attack in the slender hope that full healing may take place, when the condition becomes recurrent, with an admitted frequency of about two attacks a year, this advice is not only overcautious but quite impractical. In fact the majority of cases of lumbago improve most quickly with the earliest possible mobilization, and in what must be thousands of cases in industrial practice I have never once seen the threatened sequelae of urinary or other sinister complication.—I am, etc.,

W. I. D. SCOTT.

Chester.

Congenital Dislocation of the Hip

SIR,—Your leading article (18 November, p. 371) on the admirable study of hip-dislocation by Dr. H. V. L. Finlay and his colleagues (same issue, p. 377) raises a point which perhaps needs a brief comment. You state that congenital dislocation of the hip is congenital but is "not a genetic defect in the same class as the developmental errors like harelip, cleft palate, and absent or supernumerary fingers." In fact none of these conditions are entirely genetically determined, but there is an important degree of genetic predisposition for all of them. The evidence for this in twin and family studies is as good for congenital dislocation of the hip as for cleft lip and palate, and rather better than for most instances of absent or supernumerary fingers.¹ On the other hand, if you are using "genetic" not in the sense of determined by genes but in the older sense of developmental (timing and the class of morphological abnormality involved) your statement is of course valid.

The familial aggregation of congenital dislocation of the hip is of some practical importance. Even where all babies are screened for the condition it is worth, for example, examining a baby girl whose brother or father had congenital dislocation of the hip with special care; just as it is worth examining a little girl who is first-born and breech-born with special care.—I am, etc.,

M.R.C. Clinical Genetics Research Unit,
Institute of Child Health,
London W.C.1. C. O. CARTER.

REFERENCE

- Carter, C. O., in *Progress in Medical Genetics*, 1965, Vol. IV, ed. A. G. Steinberg and A. G. Bearn. New York.

SIR,—Dr. H. V. L. Finlay and others are to be congratulated on their study of congenital dislocation of the hip in the newborn infant (18 November, p. 377). They give a valuable description of Barlow's tests and rightly emphasize the importance of direct palpation of the head of the femur. Unfortunately your leading article tends to blur the distinction between the Barlow and Ortolani tests. The distinction between these tests is of vital importance.

In Ortolani's test¹ the knee is held with the hip flexed and the hip is then slowly abducted. In the dislocated hip reduction of the joint will occur with a palpable "jerk" or "jolt," which is usually visible. ("Click" is not a good translation of the Italian "sbalzo" and "scatto"). Ortolani emphasized that his test was practically identical with the Lorenz manoeuvre for reduction of congenital dislocation of the hip. It is therefore effective only if the hip is actually dislocated. For this reason it will not always detect congenital dislocation of the hip in the early stages when the hip is merely unstable or where the hip slides in and out of the acetabulum without a jerk or jolt. Ortolani did not in fact recommend the test in the first three months of life.

Barlow's test,² on the other hand, is designed specifically for use in the newborn and the first three months of life. The hip is held in a pincer grip between the thumb in front and the middle finger behind. In this way when the flexed hip is abducted pressure

of the middle finger will reduce a dislocated hip and pressure of the thumb will dislocate an unstable hip. The essential feature of Barlow's test is that the hip joint is palpated directly by the hand, and slipping the head of the femur in or out of the acetabulum is appreciated by direct digital palpation. Barlow's test is therefore not only more sensitive it is also more accurate than Ortolani's. It detects the unstable hip in the early stages; it also eliminates the clicks which can occur in the absence of any hip instability. Expressed in other words, Barlow's test demonstrates very early "slips," whereas Ortolani's test demonstrates somewhat later "jerks."

The confusion which has arisen between these two tests is perhaps due in part to Mr. Barlow's modesty in describing his own test as a modification of Ortolani's. It is in fact based on different principles. Ortolani's test (like the old "telescoping" test) is an indirect examination in which an attempt is made to assess the hip by manipulating the shaft of the femur. Barlow's test, on the other hand, as Dr. Finlay and his colleagues rightly emphasize, does not involve any manipulation of the shaft of the femur; the examining hand goes straight for the hip joint. I do not think that Barlow's test will ever be adequately understood until we cease to speak of it as a "modified Ortolani" test and until we get rid of the idea that we are looking for a "click."—I am, etc.,

A. W. FOWLER.

Bridgend General Hospital,
Bridgend.

REFERENCES

- ¹ Ortolani, M., *Pediatrics (Napoli)*, 1937, 45, 129.
² Barlow, T. G., *J. Bone Jt Surg.*, 1962, 44B, 292.

Mushroom-worker's Lung

SIR,—Dr. C. T. B. Adams (18 November, p. 421), referring to my paper on mushroom-worker's lung (16 September, p. 708), describes a solitary case of a mushroom worker with general and respiratory symptoms, radiological pulmonary nodulation, negative serum precipitin test, and a scalene lymph node showing sarcoid features, and concludes that his patient is suffering from sarcoidosis and not from mushroom-worker's lung as I have described it.

Assuming that Dr. Adams's patient was in fact suffering from sarcoidosis, this does not rule out the possibility that he was in addition suffering from mushroom-worker's lung. In a proportion of cases of farmers' lung the serum precipitin test is negative. Only if the patient were re-exposed at the mushroom farm and his reactions observed could one be certain that he was not suffering from mushroom-worker's lung.

However, the demonstration of sarcoid histology in one lymph node does not justify a diagnosis of sarcoidosis unless there is good supportive evidence, which should include due consideration of possible environmental hazards. I would suggest that two other explanations are possible in Dr. Adams's case. Firstly, the patient might have been suffering from a "non-sarcoid" condition of the lungs, and the sarcoid histology of the scalene lymph node represented merely a local sarcoid reaction. Such local sarcoid reaction in lymph nodes draining, for example, pulmonary neoplasms are well

recognized.^{1,2} Secondly, the patient might have been suffering from mushroom-worker's lung, but the so-called sarcoid histology of the scalene lymph node represented a lymphatic spread from the pulmonary lesions. The histology of farmer's lung at an early stage shows a granulomatous appearance similar to sarcoidosis. Although there has been no previous report of such a case, Dr. Adams's patient could be the first to have shown this phenomenon.

Dr. Adams speculates about the possibility of precipitins in the blood of my Cases 1 and 2 having persisted from previous farming jobs. A careful occupational history was taken, and neither of them had any other farming experience before commencing work at the mushroom farms.

The patients described in my paper showed such a clear-cut relationship between the development of their clinical and radiological features and their exposure at the mushroom farm that there could be little doubt that their condition was a variety of extrinsic allergic alveolitis, and quite distinct from sarcoidosis.—I am, etc.,

Redhill General Hospital,
Surrey.

ALEX SAKULA.

REFERENCES

- ¹ Sakula, A., *Brit. J. Cancer*, 1963, 17, 206.
² — *Lancet*, 1963, 2, 363.

Institutional Care of the Mentally
Subnormal

SIR,—I have been following with considerable interest the recent article by Professor T. McKeown and Dr. I. Leck (2 September, p. 573) and subsequent correspondence (11 November, p. 355) on the care of the mentally retarded in England and Wales. What puzzles me is why a better defined policy for their care has not emerged before now, since provision has been under way since 1913. All that appears to be happening is a process of hair-splitting between what is or is not a medical-nursing concern, what is deemed skilled and unskilled care, and an attempt to farm out certain types of mentally retarded children, and I assume adults, too, between health and education authorities. Those who work closely with the mentally subnormal cannot but hold the view that theirs is usually a lifelong need, from the cradle to the grave, and so continuity of care is essential. A piecemeal project is both wasteful and frustrating. Integration of the services dealing with them is advocated in recent reports.

In Northern Ireland since 1949 there has been operating a service for the mentally subnormal which avoids dichotomy of responsibility.² Here the care of the mentally subnormal, who are legally designated "persons requiring special care" by the Mental Health Act (Northern Ireland), 1948/61 is vested in one authority—namely, the Northern Ireland Hospitals Authority—as part of the hospital and specialized services. The authority is responsible both for the community care and the hospital or residential needs of all those found to be persons requiring special care. The authority has designated the day-to-day administration of this duty to three special-care management committees. Each regional committee carries out ascertainment, the provision of care in the community, including junior and senior schools (training centres), sheltered workshops, hostels, clubs, etc., and hospital and residential accommodation as is required. This arrangement facilitates the

change of care from community to hospital as circumstances dictate.

Such a unified control has enabled the needs of the subnormal to be assessed and provided for, subject of course to financial control, with that single-mindedness of purpose essential to obtaining speedy results. This is reflected in that from starting in 1949 some 1,283 places have since been created in day special-care schools or centres and hospital accommodation for some 1,363 patients. As well, hostels for 26 girls and 20 boys have been opened. A total of 5,624 are on the special care registers out of a population of some 1,458,000.³

The training of both nursing and teaching staff is undertaken within the hospital precincts. Psychological services are engaged in diagnostic and research projects in association with other disciplines such as speech therapy, physiotherapy, and social work. An active employment service also functions for trained boys and girls. In all of this close liaison is maintained with other agencies such as education, health, and welfare authorities, general practitioners, and the general hospitals. The parents and friends of the mentally handicapped not only contribute generously towards our free funds for the patients but also take an active interest in the standards of care and training extended to those in need. In return, counselling advice is offered regarding problems of the mentally retarded and their management.

It is suggested that co-ordination of the services for the subnormal is the most sensible approach.—I am, etc.,

T. W. H. WEIR.

Muckamore Abbey Hospital,
Muckamore,
Co. Antrim.

REFERENCES

- ¹ *Stress in Families with a Mentally Handicapped Child*, Report of a Working Party set up by the National Society for Handicapped Children, 1967, London.
² Scally, B. G., and MacKay, D. N., *Irish J. med. Sci.*, 1964, p. 267.
³ *Northern Ireland Hospitals Authority Nineteenth Annual Report for 1966, 1967*, Belfast.

Deaths from Tuberculosis

SIR,—Dr. A. Pines (18 November, p. 416) rightly draws attention to one aspect (drug-resistance) of the problem of deaths from tuberculosis. In England and Wales the total deaths in 1966 from tuberculosis were 2,354, and no fewer than 525 were persons not notified before death as suffering from tuberculosis.¹

The Research Committee of the British Tuberculosis Association, with the help of the Ministry of Health and General Register Office, is to conduct a national inquiry into tuberculosis mortality. A letter is shortly to be sent to all chest physicians inviting their co-operation. They will be asked to give details of the circumstances of every death attributed to tuberculosis in their own districts between 1 February and 30 April, 1968.

The main purpose of this inquiry is to determine the nature of any avoidable factors, both clinical and administrative, which contributed to a death ascribed to tuberculosis and whether the death can be strictly attributed to active tuberculous disease or its treatment and was therefore preventable.

The comparable inquiries into maternal mortality carried out by the Ministry of Health have contributed significantly to the

reduction of deaths in that field. We hope to publish our findings in a similar way.—I am, etc.,

PETER DAVIES,
Research Committee,
British Tuberculosis Association.

London W.1.

REFERENCE

¹ *Annual Report of the Chief Medical Officer of the Ministry of Health, 1966, 1967.* H.M.S.O.

Tongue Pain and Giant Cell Arteritis

SIR,—Dr. A. H. Henderson (11 November, p. 337) draws attention to the importance of pain in the tongue as a feature in giant cell arteritis. We have found glossitis in 12.6% of a series of 87 cases of temporal arteritis.^{1,2} The glossitis varied from gangrene of the anterior two-thirds of the tongue to a sensation of burning. Commonly the tongue was raw-beef red and sore. There were also examples of blistering and bruising, and this, together with the pathogenesis of other skin lesions in giant cell arteritis, has led us to suppose that in vascular areas such as the tongue, scalp, and face necrosis is due to haemorrhage rather than occlusion.³

We agree with Dr. Henderson that the tongue should be examined in every case where giant cell arteritis is suspected, as it may present important confirmatory evidence.—We are, etc.,

P. D. C. KINMONT.
D. I. MCCALLUM.

Derby.

REFERENCES

- ¹ Kinmont, P. D. C., and McCallum, D. I., *Brit. J. Derm.*, 1965, **77**, 193.
- ² ———, *Dermat. Digest*, 1966, **5**, No. 8, 51.
- ³ ———, *Brit. J. Derm.*, 1964, **76**, 299.

Cross-infection in a Surgical Unit

SIR,—Dr. J. E. Tinne and others (11 November, p. 313) acknowledge that the addition of colistin to the routine post-operative drip may be essential in combating the type of infection reported. They do, however, caution, "... its nephrotoxicity must be borne in mind."

To date no positive histopathological evidence has been offered to support the claim that colistin is nephrotoxic. The evidence from animal studies¹ is that when massive doses (19.2 mg./kg./day intraperitoneally) are given to rats and mice only very slight congestion with tubular necrosis can be detected; at levels of 9.6 mg./kg./day no such changes are seen. For such effects to appear in man, therefore, a dose of about 1,152 mg./day would be required, which is some 4½ times the recommended dose. In humans no histological evidence of damage was found in 11 renal biopsies² following therapeutic doses of colistin, although Katz,⁴ using an excessive dose (15.4 mg./kg./day), believed that in one patient nephrotoxicity was apparent, but the findings suggest that the lesion was regressing.

The question of nephrotoxicity must therefore be discussed in the light of reports of elevated blood urea nitrogen and plasma creatinine levels in patients receiving colistin for urinary infections⁵ or in healthy volunteers.⁷ A fall in blood urea nitrogen during therapy has also been found,⁶ and the effect on renal function is clearly dose-dependent.^{8,9} Even so, doses of up to 720 mg./day have been used without affecting blood urea

nitrogen,¹⁰ and in conditions of elevated levels prior to therapy (>50 mg./100 ml.) no further change has been attributable to colistin.¹¹ The reason for these variable transient and reversible changes in blood urea and creatinine in some cases is not clear. It has been suggested³ that colistin may be vaso-active, reducing renal blood flow and glomerular filtration rate, although this has been challenged⁴ on the basis of one case.

Clearly, so far as we are aware, no irreversible damage to the kidney has been demonstrated, and, whatever the significance of the observed blood changes, it is still held^{3,6} that the administration of colistin is of such therapeutic benefit as to allow its controlled use even where renal dysfunction is proved. As has rightly been pointed out by Dr. Tinne and his colleagues, there is an increasing hazard from Gram-negative infections in hospitals, especially due to *Ps. aeruginosa*, which may be located in the sputum of staff members. A recent paper¹² describes successful management of patients with positive sputum culture by combined intramuscular and aerosol colistin. This regimen resulted in therapeutically effective blood levels without involvement of the kidney.—We are, etc.,

P. A. P. POMPA,
Medical Adviser.
A. D. S. CALDWELL,
Medical Information Officer.

Pharmax Limited,
Medical and Research Department,
Dartford, Kent.

REFERENCES

- ¹ Wright, W. W., and Welch, H., *Antibiot. Ann.*, 1960, **7**, 61.
- ² Yow, E. M., Tan, E., Shanc, L., Schonfeld, S., and Abu-Nassar, H., *Arch. intern. Med.*, 1961, **108**, 664.
- ³ Fekety, F. R., Norman, P. S., and Cluff, L. E., *Ann. intern. Med.*, 1962, **57**, 214.
- ⁴ Katz, R., *Med. Ann. D.C.*, 1963, **32**, 408.
- ⁵ Wolinsky, E., and Hines, J. D., *New Engl. J. Med.*, 1962, **266**, 759.
- ⁶ Petersdorf, R. G., and Plorde, J. J., *J. Amer. med. Ass.*, 1963, **183**, 123.
- ⁷ Brumfit, W., Black, M., and Williams, J. D., *Brit. J. Urol.*, 1966, **38**, 495.
- ⁸ Roberts, C. B., and Kirby, W. M. M., *Antimicrobial Agents Annual*, 1960, p. 409.
- ⁹ Ross, S., Puig, J. R., and Zaremba, E. A., *Antibiot. Ann.*, 1960, **7**, 89.
- ¹⁰ Edgar, W. M., and Dickinson, K. M., *Lancet*, 1962, **2**, 739.
- ¹¹ McCabe, W. R., and Jackson, G. G., *Amer. J. med. Sci.*, 1960, **240**, 754.
- ¹² Halliday, N. P., *Clin. Trials J.*, 1967, **4**, 771.

Which Stethoscope?

SIR,—On the basis that some 3% of adults are sufficiently hard of hearing to need hearing-aids there are several hundreds of general practitioners and others in this country for whom the article by Drs. C. S. Hampton and A. Chaloner (18 November, p. 388) is merely of academic interest, since they would hear practically nothing through even the most efficient stethoscope. Many

practitioners, although deriving benefit from their hearing-aids in their private lives, are prevented from using them in their professional work because of the difficulties involved in the concurrent use of an aid and the traditional binaural stethoscope.

So long as the hearing-aid has a microphone cut-out switch, however, there is no reason why a transistorized stethoscope should not be used with the ear-insert in situ. The essential components of a home-made (or do-it-yourself) transistorized stethoscope may be found in any hearing-aid repair department. The minor modifications in wiring of the components are well within the scope of anyone with a minimum of electronic know-how and take only a few minutes. The photograph illustrates the compactness of the gadget and the ease with which it is used. Almost its only disadvantage is that it is a two-handed instrument; when used with a sphygmomanometer the chest-piece has to be tucked under the cuff or else held in position by the patient. I shall be pleased to supply details of the electrical modifications to anyone interested.—I am, etc.,

91 Embankment Road,
Plymouth, Devon.

BERNARD PECK.

SIR,—Congratulations on the article "Which Stethoscope?" (18 November, p. 388). Can we have some more on the same lines? For example, "Which Ophthalmoscope?"—I am, etc.,

Oxford.

R. P. RYAN.

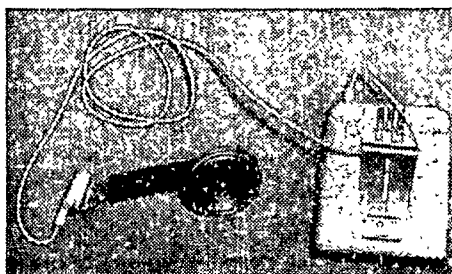
Cardiac Involvement in Psittacosis

SIR,—We have noted with interest the account of a case of psittacosis myocarditis by Dr. R. Coll and Dr. I. Horner (7 October, p. 35). We wish to report a similar case.

Our patient was a boy aged 13. He was small and obese, and had not attained puberty. When admitted to hospital (30 September 1967) he gave a history of dyspnoea, cough, and expectoration of about three weeks' duration. At first his sputum had been mucoid, but later it became purulent and was finally blood-stained. He had also suffered from nausea, retching, upper abdominal discomfort, and diarrhoea. On examination there was moderate overfilling of the jugular veins, and the liver was enlarged about 2 cm. There were crepitations throughout the lung fields. The heart rate was 140 per minute, and the pulse was thready in character; the blood pressure was 95/60 mm. Hg. The apex beat was heaving and was 2 cm. to the left of the mid-clavicular line in the fifth left intercostal space. Radiological examination revealed moderate generalized cardiac enlargement, and suggested the presence of a small pericardial effusion. The electrocardiogram showed a general low voltage pattern.

Digoxin, frusemide, and tetracycline were given. At first there was some reduction of dyspnoea, but the heart rate was unaffected, and nausea and retching persisted. Four weeks after admission he developed a pleural effusion and soon after this he died suddenly. Necropsy confirmed the diagnosis of myocarditis and the presence of a pulmonary embolus. These findings were considered to provide an adequate explanation of the patient's sudden death.

During the illness specimens of serum had been sent to the Regional Virus Laboratory, Ruchill Hospital, Glasgow. The only abnormal finding was the presence of anti-



body to the psittacosis group of organisms in titres of 1/1024 (3 October), 1/256 (12 October), and 1/64 (23 October). When the serological reports were received inquiry revealed that the patient had recently been in contact with budgerigars which were kept as domestic pets.

The history, the clinical picture, and the serological and post-mortem findings seem to warrant a diagnosis of psittacosis with cardiac and pulmonary signs. The persistent nausea and retching have not yet been explained. When further necropsy reports are available and the results of virus isolation studies have been completed we intend to publish a more detailed account of this case.—We are, etc.,

W. J. MACLENNAN.

I. W. DYMOCK.

Department of Materia Medica
and Therapeutics,
University of Glasgow
and Stobhill General Hospital,
Glasgow N.1.

CONSTANCE A. C. ROSS.

Regional Virus Laboratory,
Ruchill Hospital,
Glasgow N.W.

Deaths from Exposure

SIR,—The annual winter toll of deaths from exposure begins this year with the loss of two African officer cadets on Dartmoor.¹

Wide publicity has been given to the dangers of wet and cold by the mountaineering societies.² The necessity of extra food and clothing, the importance of the early recognition of signs of fatigue, and the suicidal folly of travelling light appear to be widely known except perhaps in Army circles.

What is apparently not so well understood is that judgement is impaired by bad conditions before physical signs of exhaustion develop. Young men whose judgement has already been impaired by the necessity to show determination, drive, and enthusiasm, and who may in addition fear failing the course if they show prudence, are particularly likely to make wrong decisions. The inexperienced will tend to press on, and bring severe trouble upon themselves or other people.

Imperative instructions to abandon the operation in the event of deterioration of weather or the physical condition of the participants ought to be part of the briefing for this sort of training by ordeal. Without this it is likely to be unnecessarily costly.—I am, etc.,

FRANCES MARGARET ULYATT.

London S.E.27.

REFERENCES

- ¹ *The Times*, 3 and 4 November 1967.
- ² *Safety on Mountains*, 1966, 6th ed. London.
- ³ *Exposure, Notes on Recognition of Symptoms and Treatment*, 1964, Pamphlet 380. London.

Varicose Ulcers and Use of Topical Corticosteroids

SIR,—I have read with great interest the letter on the above subject by Dr. C. D. Evans and others (25 November, p. 482).

As a general practitioner with considerable interest in dermatology I am well aware that current thinking certainly appears to suggest that the use of corticosteroid ointments, either with or without antibiotics, leads to the rapid extension of stasis or varicose ulcers. This

point was particularly emphasized by Dr. R. P. Warin in his excellent article on "Advances in Treatment of Skin Diseases" in last October's *Practitioner*.¹ Unfortunately this does not always seem to be borne out in practice from a general-practitioner point of view. I can think of numerous cases where the use of such an ointment has stimulated healing.

I am at present treating a case of a very large varicose ulcer of the right leg of some weeks' duration. In spite of the usual methods of treatment, including pressure bandaging, etc., this ulcer failed to heal, and eventually disintegrated into a dirty sloughing sore involving a large area in the lower third of the leg. As the patient refused to attend a dermatological clinic I eventually (in desperation) used an ointment containing oxytetracycline hydrochloride B.P. and hydrocortisone B.P. After one week there was dramatic improvement in the ulcer and after two weeks (two days ago) there was considerably more improvement, the ulcer now being half the size in width and depth, perfectly clean, with no evidence of secondary infection present.

If the use of corticosteroid increases the extension of the ulcer, one would expect to be confronted with a perfectly clean, dry lesion (due to the action of the antibiotic on secondary infection) but with a more penetrating ulcer due to the cortisone. Does the fact that this is not always so depend on the amount of time for which the corticosteroid has been applied or perhaps on some other factor like the pH of the lesion? Might there not be some synergistic action between steroid and antibiotic in certain cases? On the other hand, is this just a case of the dermatologist seeing only the general-practitioner failures and not their successes?

I should be grateful for your readers' views.—I am, etc.,

Glasgow S.3.

GERALD M. JESNER.

REFERENCE

- ¹ Warin, R. P., *Practitioner*, 1967, 199, 446.

Abortion and Conscience

SIR,—Dr. Myre Sim (4 November, p. 297) exhorts those of us without religious objections to abortion to heed our medical consciences. He is so convinced of the rightness of his views that he brands any doctor who acts differently as lacking in conscience. I do not agree with this assumption. Many highly conscientious doctors favour abortion on social grounds. In the present state of knowledge it is still open to question whether in a particular family the addition of an unwanted child will endanger the health of the other children. We recognize the strong association which criminality and psychiatric disorder have with emotional and material deprivation in childhood, but these associations are not invariable nor can accurate predictions be made in the individual case. Many of us, while supporting Dr. Sim's call for more research, feel that available evidence is strong enough to warrant action.

The history of medicine abounds with instances where far-sighted action brought advances which, had they had to await incontestable evidence, would have been long delayed. John Snow removed the handle of the Broad Street pump 30 years before the cholera vibrio was isolated. For most of us it takes courage to recommend or to perform

an abortion. It is an operation from which we shrink with a natural abhorrence. How much easier it is to do nothing, especially if inaction can be condoned by invoking "medical conscience."—I am, etc.,

London W.2.

ALAN SANDERSON.

Housing and Health

SIR,—Wing-Commander D. M. Fanning (18 November, p. 382) in his masterly analysis of the effect of flat-dwelling on health draws attention to the increasing incidence of neurotic illness in flat-dwellers.

Is it not possible to lay this lamentable consequence fairly and squarely at the doors of the architects? It appalls me, on visiting patients who live in flats, to find perhaps 100 people living in one building, all in separate rooms with absolutely no common meeting-ground apart from the entrance hall. The appalling loneliness of flat-dwellers is accentuated many times over by the enforced juxtaposition of others in the same condition.

The provision of a common dining/sitting/recreation-room where free-and-easy contacts could be encouraged would of course not solve the problem entirely. It would, however, be a step of the utmost importance from the point of view of psychological hygiene. It is time the medical profession insisted on such a provision in the construction of all future multi-storey flats.—I am, etc.,

Huddersfield,
Yorks.

S. L. HENDERSON SMITH.

"Big Spleen" Disease

SIR,—In preliminary studies we have shown that in some patients with "big spleen" disease abnormal splenic uptake of ⁵⁹Fe in labelled red cells in vivo is reduced following antimalarial therapy. This effect was not seen in patients with hypersplenism due to other causes.

These early observations lend experimental support to the recommendation by Drs. E. J. Watson-Williams, N. C. Allan, and A. F. Fleming (18 November, p. 416) that antimalarial therapy should be given an extended trial in the treatment of suspected "big spleen" disease.—We are, etc.,

W. C. WATSON.

J. C. FERGUSON.

J. RUNCIE.

Department of Medicine,
Nairobi Medical School,
Kenya.

Carcinogenicity of Tobacco and Tobacco Smoke

SIR,—Dr. H. P. Beckett's view (2 September, p. 614) that the carcinogenic factor(s) seems to be contained only in the smoke inhaled from the superheated area of the cigarette is, to say the least, doubtful.

Laboratory animals do not smoke, and it is the same yellow-brown condensate, tobacco tar, that stains the fingers of man that is painted on their skins. That carcinogens are present is therefore equally certain. As the available epidemiological and experimental data are not adequate to fix a safe dosage

of chemical carcinogens below which there will be no response in man,¹ the absence of papilloma and carcinoma in the stained fingers of man to date is surely significant.

The naive histological demonstration of Dr. F. J. C. Roe and Mr. A. L. Levene (2 September, p. 615) does not have adequate relevance either. Had they demonstrated unchanged epidermal thickness in the stained fingers of heavy cigarette smokers (20 and more per day for 20 years and more) and non-smokers of comparable age, sex, and occupation in addition, they would have a leg to stand on. Nor did I ask if tobacco smoke is a carcinogen for man either. What I asked was (5 August, p. 373) whether the absence of "cigarette-smoker's finger," and the fact that not all heavy cigarette smokers develop lung cancer, did not argue for some other essential factor, in addition to cigarette smoke, for the evolution of malignant disease in any particular heavy cigarette smoker. To date I have had no answer.—I am, etc.,

Medical Centre,
Cape Town,
Republic of South Africa.

M. GLASS

REFERENCE

- ¹ *Smoking and Health*, Report of the Advisory Committee to the Surgeon General of the Public Health Service, Publication No. 1103, 1964, p. 143. Washington.

Dose of Phenoperidine

SIR,—My attention has been called to a typographical error in the recently published tenth edition of *Recent Advances in Anaesthesia*, published by J. & A. Churchill Ltd., London.

On page 48, line three the dose of phenoperidine is given as 0.5 mg./kg. instead of 0.05 mg./kg. The publishers have already arranged for an erratum slip to be pasted into this page, but some copies had previously been put into circulation. I would be grateful if you would kindly print this letter so that readers of the book can make the necessary alteration if it has not already been done, and thus avoid any risk of possible overdosage.—I am, etc.,

London N.6.

C. LANGTON HEWER.

Crime and Sex Chromosome Anomalies

SIR,—Recent studies^{1,2} have shown a relatively high incidence of chromosome anomalies among mentally disordered patients, a large proportion of whom were mentally subnormal, requiring treatment under special security owing to dangerous violent or criminal propensities. It has been suggested that an association exists between the possession of an extra Y chromosome, increased stature, and a tendency to criminal behaviour.

We are therefore undertaking a chromosomal survey among prisoners received into H.M. Prison, Wandsworth. The two groups being examined are (a) consenting accessible prisoners of height 6 ft. (1.8 m.) or over and (b) consenting accessible randomly selected prisoners admitted during the same period.

Leucocytes were cultured from peripheral blood employing the method of Moorhead *et al.*³ Results so far obtained are as follows: (a) of 34 subjects examined 31 were normal, 2 were 47 XYY, and 1 47 XXY; (b) of 33 subjects 32

were normal and one a possible balanced translocation with 45 chromosomes (16/21-22?). In group (a) there were two subjects with very long Y chromosomes (defined as twice the length of the G group chromosomes). One of these was an XYY subject.

The numbers concerned are too small to allow statistical analysis, but enlargement of the present samples may enable us to examine a number of variables connected with sex chromosome anomalies.

J. Z. has been the recipient of a grant from the Mental Health Research Fund.

—We are, etc.,

A. W. GRIFFITHS.

H.M. Prison, Wandsworth,
London S.W.18.

J. ZAREMBA.

St. Lawrence's Hospital,
Caterham, Surrey.

REFERENCES

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Major Accident Procedure

SIR,—Many of us will recall the tragedy of the 1957 Lewisham train crash, and the haphazard manner in which the various accident services operated. As a direct result of experience gained at that time, major accident procedures were developed covering the whole country. Recently we have experienced another train crash near by, at Hither Green, but on this occasion the accident services worked well, being highly organized in their operations.

As a consequence, the planners of major accident procedures are no doubt resting content, presuming that such efficiency would have pertained elsewhere. However, in my opinion the sole reason why efficiency prevailed the other week at Hither Green was due to the fact that the same teams of personnel were involved as in 1957, having resolved that they personally would never again provide an inefficient major accident service.

Outside the Lewisham area the plans for major accidents are undoubtedly highly organized, but I for one am sceptical that these are anything but paper plans. Having worked as a casualty officer in six hospitals in the North-east Metropolitan Region in the past few years, at only one have I been made aware of the existence of the major accident procedure. As one who is deeply interested in the provision of accident services, I hope that all concerned will review their plans following the Hither Green tragedy, and make certain that the personnel involved are kept fully informed.—I am, etc.,

London E.15.

CHRISTOPHER BOLT.

Computers in Medicine

SIR,—Do you think that our profession has seen what is in this Pandora's box (4 November, p. 250)? The lid is open and cannot be closed—but shall we be servants or masters of its contents?

Every technical advance of our era has, through our own folly, brought more harm than benefit. Need one give instances? The telephone has destroyed the privacy of thousands; the internal combustion engine the civilization of our cities; the television the freedom and originality of our minds; pharmaceutical advance has given us the practical certainty of world starvation; and nuclear fission the high probability of the destruction of life itself. It is a solemn warning we are generally afraid to heed.

There are ominous signs that the computer is already becoming an instrument of depersonalization and intimidation. It could be a source of new knowledge and power for the good of our strange race, but we shall have to rule it with a determination commensurate with its potentialities.—I am, etc.,

Exmouth, Devon.

RICHARD HARDY.

Doctors for Industry

SIR,—I would like to follow the lead given by Drs. G. A. Lawrenson and M. E. M. Herford (7 October, p. 52) in commenting on the leading article "Doctors for Industry" (16 September, p. 692).

As a doctor in medical charge of an Army training regiment over the past five and a half years, I have seen approximately 5,000 young men of 17 to 18 years of age coming into the Army after upwards of two years spent in mostly industrial occupations, and have carried out several brief examinations on the majority of them, which have been of great value in supervising their physical well-being and assessing their physique and state of nutrition.¹ All these have been young men without specific handicaps, and, as Dr. Herford comments, would be abandoned by the Factory Medical Inspectorate of the future as needing no medical care other than the treatment of illness, in spite of much poor but partly remediable physique on the one hand, and considerable obesity on the other.

I join him in challenging this proposed change, and am in agreement with his general conception of planning the medical care of the "whole man" during the vital youthful years in industry. In the Army we have to devote considerable attention to physical requirements in order to bring our recruits up to our own modest standards of physical efficiency and nutritional well-being, and, for the most part, among those who make the grade and stay with us, we succeed very well. In consequence, lack of stamina and many other accompaniments of poor physique are remedied, as well as obesity reduced, and in addition we see little of the problems of abnormal behaviour and aggressiveness which are characteristic of this age group today. Our regimen does seem to possess something helpful for growth into maturity which is lacking in much of what society today offers young people. We do in fact provide that "whole man" care which Dr. Herford advocates.

Judging from this experience it seems to me that a medical service to young people in industry must include among other things provision for a number of routine medical examinations designed to assess growth, physique, and nutrition, so that appropriate advice or treatment may be given. In putting forward this proposal I do not intend in the least to belittle other aspects of health which

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"Price's Textbook of the Practice of Medicine"
9th Ed., p.1219, O.U. Press, London



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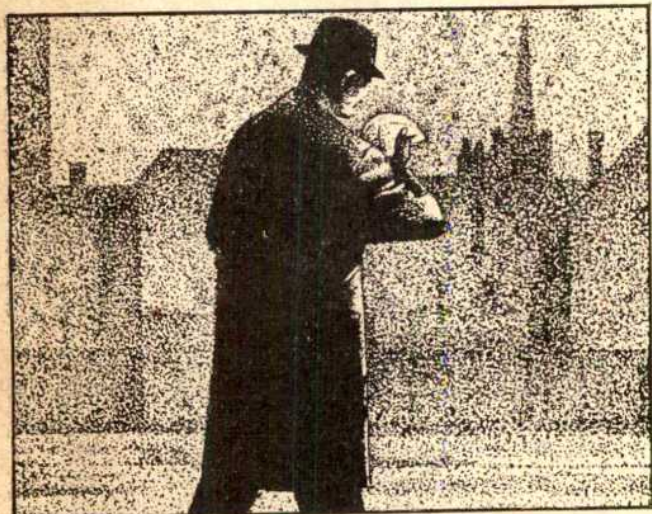
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Dr. Herford has in mind,² upon which I cannot comment because I see little of them in my own work. Supplementing these examinations there should be facilities for remedial exercises, where indicated, and for proper midday feeding for all in this age group. In order to test out such ideas, would it not be possible to run some pilot schemes in which the results in all-round well-being after two years could be compared with those of areas where matters are allowed to proceed as at present?—I am, etc.,

R. Y. TAYLOR.

Yeovil,
Somerset.

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Consultant Distinction Awards

SIR,—Dr. T. Manners (4 November, p. 298) highlights one of the greatest problems facing the hospital service today. The tendency of the present Review Body to extend the scope of the distinction award system inevitably means that it is regarded as part of the consultant's essential salary structure. This also means that the very substantial number of consultants who will never receive an award, many of whom have little or no private practice today, will, unless some considerable changes are made, remain with few exceptions the lowest paid of all senior doctors both in the hospital service and in general practice.

This state of affairs creates two fundamental problems. It ensures that the consultant who works hard to provide the best possible National Health service to his patients goes unrewarded, whereas his colleague who works less hard inevitably develops waiting-lists, and so patients, in desperation, begin to come to him privately. This in turn leads to less time being available for hospital work and more work falling on the shoulders of junior staff. Thus does the reward increase as the contribution to the National Health Service decreases. The second great problem concerns the integration of general practitioners into the hospital service. As one who for years has supported this policy in the form of clinical assistantships and the smaller cottage-type hospital I was delighted to see that the Scottish Working Party¹ advocates its extension. They foresee that the disparity between the rewards of general practice and the basic salaries of the hospital service will prevent many general practitioners from taking on hospital commitments. On the other hand, if the medical assistant salary is increased to the point where it competes with general practice, not only the registrar but also the consultant will find that his session earns him less than his assistant.

The distinction awards can never overcome these fundamental problems, and unless the Government and Review Body realize their importance and put forward definite proposals for surmounting them the next 15 years may be remembered as a period of rising waiting-lists and a constant move towards private practice, to the lasting detriment of a hospital service the great achievement of which has been to provide for the less fortunate members of our society a standard of medical care unequalled throughout the world. No Government, and least of all a

Socialist Government, should allow anything to imperil it.—I am, etc.,

Princess Margaret Hospital, K. D. CROW.
Swindon, Wilts.

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- ¹ *Organization of the Medical Work in the Hospital Service in Scotland*, 1967, H.M.S.O.

Countersigning of Forms

SIR,—After a long and distressing illness a patient of mine died last month of carcinoma of the bronchus. The appropriate form for a night visit (E.C. 81a) was sent to me by the Southern Relief Service, having been signed by their doctor but not by the patient's widow. I cannot bring myself to debase my profession by taking this form round to the house of my deceased patient at the time of his widow's grief. For this reason I am sending the form to the executive council in its present state.

I feel the larger issue of having similar forms countersigned at all is a source of deep concern and dissatisfaction to all members of the medical profession.—I am, etc.,

Wallington,
Surrey.

C. R. NUNAN.

Approval of Emergency Treatment Service

SIR,—Your correspondent Dr. A. Dowling (25 November, p. 490) attempts to defend the Emergency Treatment Service and suggests medico-political influences as the reason for its "non-starter" status in London.

I would like to question whether there is any real need of the service at all in a well-organized general-practitioner service. Surely in most towns (at least of the size where E.T.S. operates) it should be possible for doctors to organize themselves in efficient practices with four to five partners and thus ensure about one night on in four. Is that asking too much? And also are doctors really happy about State Registered Nurses answering the phone?

There is a lot of emotional talk about whole patient care and responsibility for one's patients, but if one of a group of general practitioners cannot be on call to deal with one of their patient's acute appendicitis, cardiac asthma, or simply answer a pertinent question are those doctors really providing a service in keeping with the tradition of good family doctoring? The answer is "no," and as soon as doctors do something about making their services efficient the sooner will schemes such as E.T.S. wither and patients will be much more satisfied.—I am, etc.,

London S.W.17.

PETER FITT.

Educating the Public

SIR,—The Government, we are informed,¹ has agreed to continue with the "education of the public in the use of doctors' services," for which we must be grateful. However, I am sure that this has been used as an argument between our negotiators and the Ministry.

Surely, if they really wished to improve the lot of individual doctors, it would be much more efficient if they set aside a proportion of the sum they are now making available for leaflets, posters, and news-flashes for a grant to individual practitioners, who could then compose their own "notes for the guidance of patients," which, if approved, could be included with the medical card sent out by the executive councils. This is a practice which has been carried out for many years by our own very helpful council and caters for the vast variety between different practices.—I am, etc.,

Cambridge.

GORDON SIMPSON.

REFERENCE

- ¹ *Ministry of Health Letter*, E.C.L. 90/67.

Simplifying Filing

SIR,—The world is getting rather full of paper and other records, such as radiographs. Especially in medical establishments there would seem to be a lack of system with regard to what to keep and what to throw away. As far as my experience reaches there is in practice a rather arbitrary custom of deciding that after x years documents must be discarded to make room for more recent ones. At this stage it is impracticable to sort them out as to their relative values, so they all go out together.

The following is a suggestion to allow documents to be marked when they are being dealt with in the first place in such a way that a clerk can go through them periodically and throw out those which have been marked with the relative lack of priority. As far as medical documents are concerned they seem to me to have four more or less separate values: Clinical "C"; Research "R"; Administrative "A"; and Litigious "L." The periods I suggest as being useful and not too numerous are 1, 3, 10, 30, and 100 years, combining these in a diagram or table:

	Yrs	1	3	10	30	100
Date	C					
	R					
	A					
	L					

If this diagram is stamped on relevant documents it is easy when reporting on or filing the document to tick the relevant "boxes" to indicate conspicuously that a valuable report or radiograph should not be thrown away before a less valuable one. Presumably the "C" and "R" lines would be the responsibility of the consultant and the "A" and "L" lines would be the responsibility of the hospital secretary. And the whole would give a clear indication for discarding, retaining, or reassessing.

At this stage I will not enter into a lengthy discussion; that will be more fitting when the C.R.A.L. has been tried out in practice. This is merely a preliminary notice.—I am, etc.,

Halsstead, Essex.

W. A. L. COLLIER.

Obituary Notices

M. L. HINE, M.D., F.R.C.S.

Mr. M. L. Hine, consulting ophthalmic surgeon to Charing Cross Hospital and the Royal Westminster Ophthalmic Hospital, London, died on 2 December. He was 84.

Montague Leonard Hine, son of a doctor, was born at Leytonstone, Essex, on 24 January 1883, and received his early education at Rydal Mount, Colwyn Bay. He had a



(Elliott & Fry)

distinguished academic career, obtaining an entrance scholarship to the Middlesex Hospital in 1900, and first and second year exhibitions. He qualified with the Conjoint diploma in 1905, and a year later he graduated M.B., B.S. with honours and distinction in medicine, and was designated Broderip scholar. After early resident appointments at the Middlesex Hospital he proceeded M.D. in 1907, and took the F.R.C.S. the following year. In 1909 he went to Singapore and to the Cocos Islands as medical officer to the Eastern Extension Cable Company. After returning to England he held appointments as clinical assistant and registrar at the Royal Westminster Ophthalmic Hospital (now Moorfields Eye Hospital, High Holborn) from 1912 to 1914, becoming surgeon in 1915, and dean of the medical school from 1920 to 1946.

During the first world war he served as eye specialist with the R.A.M.C. in France. After demobilization with the rank of captain he was appointed ophthalmic surgeon to the Miller General Hospital in 1919, a post he held until 1934. He was also ophthalmic specialist to the Ministry of Pensions from 1919 to 1928. In 1934 he was appointed ophthalmic surgeon to Charing Cross Hospital. He was a past president of the ophthalmic section of the Royal Society of Medicine, and editor of the 7th to 10th editions of May and Worth's *Diseases of the Eye*.

He married in 1924 Jennette M. Robertson, and they had a son and a daughter.

T. K. L. writes: With the death of Mr. Montague Hine ophthalmology has lost one of the last of the old school of ophthalmic surgeons who did an enormous amount of work in a relatively short space of time, and yet performed it with the greatest care and attention and with the maximum satisfaction to his patients. Punctually on Monday and Thursday afternoons he walked into the outpatient department ready for the fray, and worked hard seeing all the new patients at his clinic and at the same time teaching all the students around him. His house-surgeons would never dream of being a minute late. It was a pleasure to work for him, and he had at his command a large number of faithful

clinical assistants who had served him for many years. It was in the operating theatre where we house-surgeons found him of the greatest help, for he among all the honorary staff was by far the most generous in delegating operations to us. He would go to endless trouble in helping us with difficult cases, and his practical expertise was remarkable. Not that he was an exceptionally spectacular surgeon to watch, but his clinical judgement was first-rate and his technique always safe. There must be many generations of house-surgeons at the Royal Westminster Ophthalmic Hospital who have cause to be grateful to him for his valuable teaching. He was always keen to undertake new methods of treatment, and throughout life remained a keen student himself eager to try out new ideas. He was one of the first surgeons in the hospital to undertake operations on the vertical muscles in certain cases of squint.

His patients realized at once that they were in safe hands with Monty Hine. Indeed he never failed to listen to all their troubles, and to reassure them. He was as good a physician as he was a surgeon, but above all it is his excellence as a teacher by which he will long be remembered.

D. S. TORRENS, M.A., M.B., B.CH. B.A.O.

Professor D. S. Torrens, professor of physiology and former dean of the medical school at Trinity College, Dublin University, died on 24 November in a Dublin nursing-home. He was 70.

David Smyth Torrens was born in County Londonderry on 10 September 1897. He went to Trinity College as a demonstrator in physiology in 1922 from the zoology department of the Institute of Science in Dublin. He later became assistant to the professor, and during this time he decided to study medicine at Trinity College, and graduated M.B., B.Ch., B.A.O. in 1934. In 1936, on the death of Professor Pringle, he was elected to the chair of physiology and to the King's professorship of the Institutes of Medicine. He was dean of the Trinity College medical school from 1950 to 1959, and was vice-dean from 1959 to his retirement in September of this year. During his time as dean of the medical school he was a member of the General Medical Council.

David Torrens had a natural instinct for teaching and devoted his college life wholeheartedly to the interests of the students. He combined this with an inborn aptitude for physiology, and more especially histology, fascinating an audience of staff and students alike with his observations on the most simple histological specimen. For many years he was the unofficial College doctor, and—even after the inauguration of the College health service—staff and students frequently confronted him with their problems, worries, and diseases. His rooms in College were his home

for forty years and his address was familiar to many thousands of graduates, not only medical, who are now scattered throughout the world. It was in his rooms that Davy could be found at all hours of the day and night entertaining students past and present. Breakfast was served to those who came directly from the mail boat, tea was served at any hour, and late-night visitors were often treated to fried egg and bacon from midnight onwards. Nothing was too much trouble for him. No one will ever know how much money he lent to those in difficulties. Shortly before his retirement his friends were given the unique opportunity of repaying in some small way the debt they owed him. Contributions poured in from all corners of the world and to him his presentation fund became embarrassingly large. In a gesture which was typical of him he insisted on returning the largest contribution, saying that the sender's need was greater than his.

With typical modesty he never spoke of his attainments in the field of horology, yet he had pursued his interest in clocks and watches since the age of 10, and had become known among horologists as a leading authority in this specialty. His eminence in horology was recognized at a ceremony in London as recently as last September, when he was made an honorary freeman of the Worshipful Company of Clockmakers. During his lifetime he amassed a vast quantity of clockmakers' tools, and here again was evidence of his generosity, for he made a habit of purchasing the property of clockmakers after their death as a means of financially assisting the next of kin.

To those who did not know of his extreme generosity and his infinite ability to assist those in need, his popularity was difficult to understand. His manner was often sharp to the point of rudeness, and he was not a conversationalist, always preferring to listen rather than to talk. Even among his closest friends he rarely, if ever, talked about himself. No one will ever know the extent of his achievements, but one thing is certain—that he gave far, far more to this world than he ever attempted to take from it.—C. C. C. O'M.

CASIMIR FUNK, PH.D.

Dr. Casimir Funk, a pioneer in vitamin research, died in Albany, New York, on November 20, at the age of 83.

Casimir Funk was born in Warsaw on 23 February 1884, but when 16 years old went to Switzerland for his education, first at Geneva and later at the University of Berne. Trained as a chemist he gained his Ph.D. in 1904, when still only 20. He then moved to the Pasteur Institute in Paris to study under Bertrand, and two years later to the University of Berlin, where he worked under the guidance of Fischer and Aberhalden. Apart from a year at the Municipal Hospital in Wiesbaden, where he first became interested in the science of nutrition, he remained in Berlin until 1910, when he came to London.

In 1911 he entered the Lister Institute for research on experimental beriberi, and remained there for five years. After a period at the Cancer Hospital Research Institute he left in 1915 for the U.S.A., where he worked in various laboratories and attacked problems such as the synthesis of adrenaline and the extraction of vitamins from fish-liver oils on a commercial scale. In 1923 he returned to Warsaw to organize the department of biochemistry of the State School of Hygiene. 1928 found him in Paris, working mainly on sex hormones, and he remained there until 1939, when he returned to settle permanently in New York. In 1947 he organized the Funk Foundation for Medical Research, and became its president. The rest of his life was devoted mainly to cancer research.

Undoubtedly it is the word "vitamin" by which Funk will be remembered. In his attempts to isolate the factor in rice polishings that can prevent human beriberi and avian polyneuritis, which actually resulted only in the production of crude concentrates, Funk correctly concluded that the elusive substance was an organic base. It was obviously essential for life, so "vitamine"—shortened from "vital amine"—seemed a suitable name. Moreover other diseases were recognized as being due to dietary deficiencies, and it was concluded that they might be due to lack of other vitamins. Thus in June 1912, according to the *Journal of State Medicine*, he grouped together "beriberi, polyneuritis in birds, epidemic dropsy, scurvy, experimental scurvy in animals, infantile scurvy, ship beriberi, and pellagra" as deficiency diseases, and speculated that rickets could be added to the list. He was not alone, of course, in propounding this theory. He was, indeed, passed over when many years later a Nobel award was shared between Hopkins, for his proof of the existence of "accessory food factors," and Eijkman, for his pioneer work on the relationship between human beriberi and avian polyneuritis.

Eventually, as the various "vitamines" were obtained in pure enough form to allow some knowledge of their chemistry, it became clear that they were widely different substances, and that some did not contain nitrogen. The final "e" was therefore dropped, to leave "vitamin," which has no chemical implications. Funk's inspired choice of a name has been of great service to biochemists and nutritionists in helping to correlate facts and theories in a specialized field. Even since the various vitamins have been isolated, chemically identified, and given chemical names it has remained a great convenience to class them together as vitamins—a group of biologically active substances.—T. M.

E. V. MCCOLLUM, PH.D., LL.D.

Professor E. V. McCollum, who died in Baltimore, Maryland, on 15 November, aged 88, was distinguished for a long career devoted to the science of nutrition. His early research on vitamins was about contemporary with Funk's work in this field, and it is melancholy, but convenient for paying tribute to their memories, that their deaths should have occurred so close together.

Elmer Verner McCollum was born on a farm in Kansas on 3 March 1879, and was educated at the University of Kansas and at Yale, where he took his Ph.D. In 1907 he

became an instructor in agricultural biochemistry in Wisconsin University, where he stayed to become an associate professor, and eventually full professor. In 1917 he left Wisconsin to become professor of biochemistry in the School of Hygiene and Public Health in the Johns Hopkins University, Baltimore, a post from which he retired in 1946. He remained in Baltimore, and retained his interest in nutrition, for the rest of his life.

McCollum's discovery of vitamin A, on which his main claim to fame might be based, was made while he was in Wisconsin. In 1913, with M. Davis, he confirmed the finding of Hopkins and others that rats could not live for long upon a diet made from purified protein, carbohydrate, and fat. Butter and egg yolk contained a factor which would allow survival and growth if given as small supplements to this purified diet, but olive oil and lard were inactive. This substance was named by McCollum "fat-soluble A." Two years later another substance which promoted growth in rats was detected in aqueous extracts of wheat germ and egg yolk. It was named "water-soluble B," and was identified with Funk's antipolyneuritis factor. Before long Funk's and McCollum's systems of nomenclature were combined, and the recognition of vitamins A and B opened up a long and fruitful period of research throughout the world. As a further important contribution, made after going to Baltimore, McCollum in 1922 differentiated clearly between vitamins A and D. Hopkins had shown that when heated fat is aerated vitamin A is destroyed. McCollum, Simmonds, Becker, and Shipley treated cod-liver oil in this way, and found that vitamin A was lost without a corresponding loss of the antirachitic value of the oil.

During his long career McCollum also became interested in mineral metabolism. After his finding that manganese is necessary for lactation in rats, headlines appeared in the popular press to the effect that "manganese is mother love." He wrote two excellent books—*A Newer Knowledge of Nutrition* (with Nina Simmonds) in 1918, which ran through several editions, and *A History of Nutrition* in 1957. In personality he was friendly, erudite, and approachable. His unofficial title in America, "the father of nutrition," was well deserved, as also were his foreign Fellowship of the Royal Society and his honorary membership of the (British) Nutrition Society. The passing of this "grand old man" will be much regretted by all his British friends.—T. M.

S. H. WARREN, M.R.C.S., L.R.C.P. D.P.H.

Dr. S. H. Warren, a former director of the Central Public Health Laboratory at Newcastle upon Tyne, died on 31 October. He was 85.

Stanley Herbert Warren was born on 16 January 1882, and received his medical education at St. Mary's Hospital and University College Hospital, London, qualifying with the Conjoint diploma in 1905. He was trained in the Bacteriological Laboratory at St. Mary's Hospital under the late Sir Almroth Wright, and had been demonstrator in bacteriology at University College Hospital Medical School for two years before taking up an appoint-

ment as resident pathologist at the Royal Sussex County Hospital, Brighton. He took the D.P.H. in 1908, and was later awarded a Graham scholarship at University College Hospital which enabled him to undertake further research into pathology and bacteriology. The outbreak of the first world war ended his tenure of the scholarship and he joined the R.A.M.C. After demobilization with the rank of captain he went to Newcastle to join the staff of the department of bacteriology of what was then the University of Durham College of Medicine, and on Tyneside he spent the remaining 40 years and more of his life. The work of the department included not only teaching and research but also the provision of bacteriological services for local authorities and others in north-east England, and he became chiefly engaged in the latter branch of the departmental activities. Administrative rearrangements a few years later resulted in the services for the local authorities being made the responsibility of an independent Public Health Laboratory, of which he was appointed director; and, apart from a two years' absence while in charge of a wartime emergency laboratory, he was director of the Public Health Laboratory for nearly 20 years. He retired shortly after its merging in the national Public Health Laboratory Service.

E. M. D. writes: Warren was an able bacteriologist, of consummate technical skill, and experienced in laboratory organization. He supervised personally all the work of his laboratory to ensure the high standard of efficiency he demanded. He had to contend for very many years with the grievous handicap of increasing deafness, a disability which made conversation with him difficult, and he suffered much in consequence. Of a sensitive disposition, he came to be diffident about joining in company and to limit social contacts to companionship with some friendly colleague in whose presence he could relax and feel less isolated. He married in 1941, and from then until his death the relatively lonely life which had so long been his became happily transformed. He is survived by his widow and two sons.

A. WILKIE, M.B., CH.B.

Dr. A. Wilkie, a general practitioner in Droylsden, Lancashire, died in hospital on 14 November after a short illness. He was 61.

Alfred Wilkie was born on 25 March 1906, and received his medical education at Aberdeen University, graduating M.B., Ch.B. in 1928. After early appointments at Hull Royal Infirmary and the East Suffolk and Ipswich Hospital he became assistant medical officer at Heatherwood Hospital, Ascot. In 1939 he settled in general practice in Droylsden, and in his quiet unassuming manner quickly endeared himself to the people of the area. He took an active part in local affairs, and in 1962 became chairman of the Ashton-under-Lyne Division of the British Medical Association. In the same year he became the senior partner of the large practice which he had helped to build. He was severely ill in 1958, but made a good recovery and continued to lead an active life and practice.

His wife died in 1954 after a long illness, and they had no children. His loss is keenly felt by his colleagues.—A. M. G.

News and Notes

EPIDEMIOLOGY

Infectious Diseases

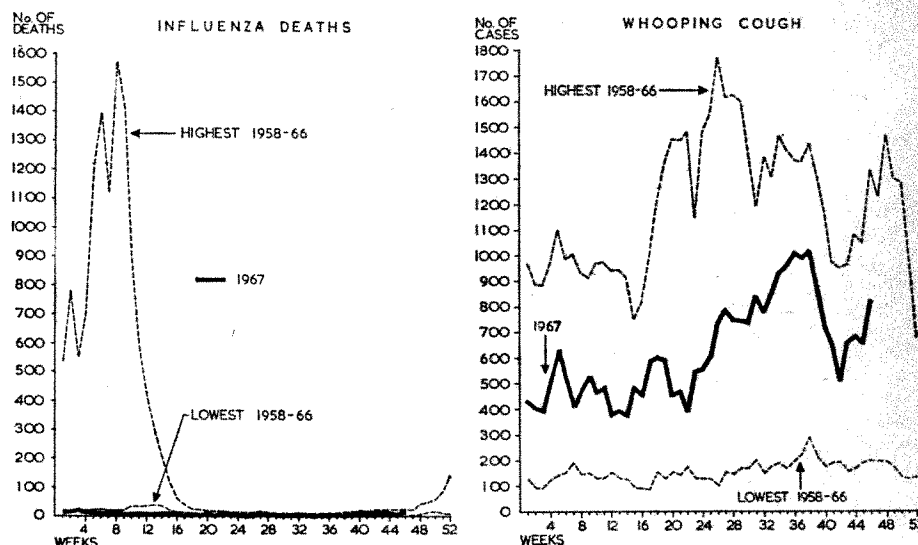
Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending	
	17 Nov.	24 Nov.
Typhoid Fever		
Birmingham C.B. ...	0	1
Diphtheria		
Manchester C.B. ...	0	1
Dysentery		
Berkshire ...	5	17
Wokingham R.D. ...	5	15
Durham ...	26	20
Stanley U.D. ...	10	12
Lancashire ...	51	55
Irlam U.D. ...	0	22
Warwickshire ...	16	101
Coventry C.B. ...	6	84
Yorkshire West Riding ...	49	60
Leeds C.B. ...	14	19
Sheffield C.B. ...	9	17
Glasgow ...	30	45

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of deaths from influenza and cases of whooping-cough in England and Wales.

Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 18 November (No. 46) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire
Diphtheria ..	1	1	0	0		0	0	1		
Dysentery ..	270	34	90	10	4	437	53	96	14	2
Encephalitis, acute ..	1	0		0		1	0		0	
Enteric fever: Typhoid ..	0	0	0	0	1	0	0	0	0	1
Paratyphoid ..	4	0	0	0	0	0	0	0	0	0
Food-poisoning	116	31	6	2		103	21	7	4	
Infective enteritis or diarrhoea under 2 years				27	48				29	43
Measles* ..	1,254	51	29	19	73	10,417	1343	430	120	137
Meningococcal infection ..	5	1	2	0		9	1	8	1	1
Ophthalmia neonatorum	16	1	0	0		14	2	0	0	
Pneumonia† ..	97	4	86	9	4	139	16	129	1	1
Poliomyelitis, acute: Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic ..	0	0	0	0		0	0	0	0	
Puerperal fever§	77	31	3	0		84	24	4	0	
Scarlet fever ..	382	70	31	4	7	479	56	31	9	10
Tuberculosis: Respiratory ..	195	43	40	5		231	63	33	7	
Non-respiratory ..	37	6	6	0		52	9	2	3	
Whooping-cough	824	115	45	7	27	543	67	86	6	8
DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd.	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0	0	0	0	0
Dysentery ..	1	0		0		0	0		0	
Encephalitis, acute ..				0						0
Enteric fever ..	0		0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5	0	2	1	0	4	1	0	1	0
Influenza ..	11	3	1	0	0	13	3	3	0	0
Measles ..	0		0	0	0		0	0	0	0
Meningococcal infection ..			0				0	0		
Pneumonia ..	706	112	15	21	11	751	103	21	16	15
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0		0	0	0	0
Tuberculosis: Respiratory ..	42	8	0	0	2	34	5	1	0	3
Non-respiratory ..	0	0	0	0	0	0	0	0	0	0
Whooping-cough	0	0	0	0	0	1	0	9	0	0
Deaths 0-1 year	288	52	19	8	9	325	58	20	11	15
Deaths (excluding stillbirths)	10,867	1758	587	151	158	10,786	1729	619	133	182
LIVE BIRTHS	14,879	2410	833	240	394	14,986	2580	855	256	402
STILLBIRTHS	202	17	13			220	38	15		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.

PARLIAMENT

Questions in the Lords

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Treatment of Drug Addicts

LORD SANDFORD asked the Government on 28 November how many drug addicts had been seen at the treatment centres set up in connexion with the Dangerous Drugs Act; how many were receiving treatment at each centre; and what treatment was being given.

LORD KENNET stated that the most recent records of the treatment of heroin addiction by National Health Service hospitals related to the quarter ended 30 September, in which 173 persons were admitted as inpatients and 171 commenced outpatient treatment. At the end of September 64 inpatients and 167 outpatients were receiving treatment at 39 hospitals.

The forms of treatment, which varied widely and were determined by clinical judgement in individual cases, included psychotherapy with individual patients or in groups, physical methods of treatment such as drugs, occupational and industrial therapy, and social support. Attention was also given to patients' physical condition.

LORD SEGAL asked on 30 November what was the Government's estimate of the number of heroin addicts likely to be notified under the Dangerous Drugs Act, and when accurate statistics were likely to become available.

LORD STONHAM, Minister of State at the Home Office, told him that the number of

known addicts in 1966 was 899, but the Home Office could not firmly estimate the number that would be notified until the regulations requiring notification were in force, which it was hoped would be early next year.

He added in answer to Lord Segal that one of the regulations would require a doctor attending a person he thought or suspected to be addicted to any drugs to notify particulars to a central authority. The other regulation would restrict the prescribing of heroin and cocaine to addicts, and that regulation was being drafted.

LORD SEGAL, emphasizing the importance of research, asked if the notification forms could include additional information such as occupation, country of origin, whether the addicts were on sickness or unemployment benefit, and other details that might be of value.

LORD STONHAM explained that the forms which would be completed under the regulations would give all the information thought necessary. The central records were being transferred from the drugs branch of the Home Office to the statistical branch, which was better equipped to maintain them. Some of the items mentioned by Lord Segal might not be required, but the Home Office would look at all of them.

Abortion Act Registrations

LORD SEGAL, commenting on the number of applications from private nursing-homes for registration under the Abortion Act [it was 100 up to 24 November] suggested in the House of Lords on 30 November that, as the demand for abortion beds might greatly exceed the supply, unoccupied beds in maternity hospitals might be made available for emergency abortion cases when the Act came into operation.

LORD KENNET, speaking for the Government, promised to bring the suggestion to the attention of the Minister of Health.

VISCOUNT BARRINGTON inquired whether, if the number of applications was regarded as low, this might be due to the widespread opinion in the medical profession—particularly as reflected in the presidential address of the President of the Royal College of Obstetricians and Gynaecologists—that doctors did not yet know where they were in this matter.

LORD KENNET said he knew of no reason for disappointment about the number of applications that had been received.

LORD SILKIN suggested that as the Act did not come into operation until April it was rather early to be putting these questions and creating doubts.

LORD KENNET agreed, pointing out that the normal process of advertising for applications, considering them, and inspecting premises was now under way.

MEDICO-LEGAL

Blood Tests and Adultery

[FROM OUR LEGAL CORRESPONDENT]

Blood tests on a husband, wife, and child were the foundation for a finding of adultery made against the wife by Mr. Justice Rees in the High Court on 6 November (*The Times*, 7 November).

The parties were married on 21 November 1959. The wife had during the marriage persistently stayed out late despite the husband's complaints. At the relevant time the wife and husband were having regular intercourse. Though they were using contraceptive procedures, it was possible that the wife might have conceived a child by the husband. The parties separated on 14 January 1961, and the child was born on 17 June 1961.

In August 1961, for the purpose of magistrates' court proceedings, the husband's solicitors asked the wife whether she was willing to provide blood samples from herself and the child for comparison with a sample from her husband. She agreed.

Dr. Alan Grant, lecturer in forensic serological medicine at Guy's Hospital, took samples from the parties and the child on 26 August, and grouped them under a num-

ber of systems, including the Rhesus system. In the child's blood he found Willis C factor, which was absent from the blood of the husband and the wife. Further samples were taken on 11 June 1966, with the same result. No further information was obtained by applying to both the earlier and later samples further grouping systems which had become available since 1961.

Dr. Grant gave his opinion that, as there was no dispute that the child was the mother's, and as neither she nor her husband had Willis C factor, the husband could not be the father. This opinion was expressed to be subject to the biological possibility that the Willis C factor might have appeared in the child's blood as a result of a mutation. Dr. Grant said that it was plain from the structure of the blood groups that in the course of evolution mutations had occurred. For over 20 years he had been "feverishly searching for evidence of a mutation" and had found none. In giving evidence before the magistrates in 1962, Dr. Grant had assessed the chances of a mutation occurring at one chance in 50,000 generations. He

now revised that assessment to about one chance in 1,000,000 generations. There was even less chance that Willis C factor could be present in the blood of the husband and wife but be so suppressed as to be not apparent on examination.

Mr. Justice Rees accepted Dr. Grant's evidence and granted a decree nisi to the husband on the ground of his wife's adultery. He also made a declaration that this child was not the husband's. Since the result of the decree was to bastardize the child, the court demanded a high standard of proof of adultery before making the decree. The court required to be satisfied of adultery beyond all reasonable doubt.

The child was represented at the hearing by counsel instructed by the Official Solicitor. The questions whether or not the Official Solicitor should consent to the child's blood sample being taken, and whether the court had power to order the sample to be taken without consent, did not arise, presumably because the mother had already given consent in 1961. Judgement of the Court of Appeal in a case raising these questions is still awaited.¹

REFERENCE

¹ *Brit. med. J.*, 1967, 2, 120.

MEDICAL NEWS

Chancellor of Cambridge University

LORD ADRIAN, O.M., F.R.S., a former Vice-Chancellor of Cambridge University, has succeeded the late LORD TEDDER as Chancellor.

A Nobel Laureate in medicine, Lord Adrian was professor of physiology at Cambridge from 1937 to 1951. He then became Master of his old College, Trinity College, Cambridge, retiring in 1965. In 1954 he was President of the British Association while also



(Douglas Glas)

President of the Royal Society. The following year he was raised to the peerage. In 1958 the British Medical Association awarded him the Association's Gold Medal for Distinguished Merit in recognition of his services to medicine, particularly his research in the physiology of the nervous system.

Royal College of Physicians of Edinburgh

At the annual meeting of the Royal College of Physicians of Edinburgh on 30 November the following officer-bearers were elected: president, Dr. C. W. CLAYSON; vice-president, Dr. J. HALLIDAY CROOM; members of council, Professor R. H. GIRDWOOD, Dr. J. LAURIE, Dr. R. F. ROBERTSON, Professor J. W. CROFTON, and Dr. E. B. FRENCH.

Chair of Psychiatry at Oxford

The W. A. Handley Charity Trust is to give Oxford University £121,000 to endow a professorship of psychiatry.

The Nuffield Committee for the Advancement of Medicine at Oxford is to allocate £5,000 a year to support the chair. The Oxford Regional Hospital Board has offered the professor accommodation and facilities as well as an annual contribution, and the United Oxford Hospitals have offered consultant status and outpatient facilities.

Care of the Elderly

Opening the first purpose-built psycho-geriatric assessment unit in this country at Barncoose Hospital, Redruth, Cornwall, on 29 November, the MINISTER OF HEALTH said that geriatrics was being increasingly accepted as a rewarding career. The number of consultant geriatricians had risen from 115 in 1964 to 156 in 1966.

Combined Unit for Cardiac Surgery

A report prepared by a joint committee of the Royal Colleges of Physicians and Surgeons describes the requirements of a combined unit for medical and surgical care of heart disease at all ages. Such a unit, the report states, must have facilities for diagnosis, treatment, and research. Facilities for training should also be available. The unit should be sited in a general hospital and be linked to diagnostic, therapeutic, and research services in other branches of medicine and surgery. It should be flexible enough to allow for expansion. Other recommendations refer to size, staffing, and work load.

Appointment to Professorship

Dr. J. H. GREEN, reader in physiology at the Middlesex Hospital Medical School, has had the title of professor of physiology conferred on him. He is 48. Dr. Green was educated at Cambridge, where he graduated M.B., B.Chir., and at the Middlesex Hospital Medical School. He has been a member of the physiology department at the school since 1951 and was appointed reader in 1960. He holds the Ph.D. (Lond.).



Dr. Green's main research interests lie in the regulation of blood pressure by baroreceptors. His other interests include the use of closed-circuit television and video-tape recording as teaching adjuncts. He is the author of the textbook *An Introduction to Human Physiology*, published in 1963.

Nurse Education and Training

The Ministry of Health is financing the establishment of a research unit at the offices of the General Nursing Council for a period, in the first place, of five years. Besides carrying out research into nurse education, the unit will co-ordinate work on experimental schemes of training. It will be staffed by a research officer (a new post) and two assistants. Miss G. E. WATTS, chairman of the council, is chairman of the joint steering committee. The unit is expected to start work early in 1968.

Flats for Married Medical Staff

Supported by a grant from King Edward's Hospital Fund, the Bromley Group Hospital Management Committee has completed a two-storey building in the grounds of Farnborough Hospital, Kent, to provide accommodation for junior medical staff. The building comprises three one-bedroom and two two-bedroom flats, each with fitted kitchen, dining-room/lounge, and bathroom. All the flats are centrally heated. The building, furnishings, and equipment have cost approximately £22,000.

Protection Against Ionizing Radiations

Proposed regulations for the protection of workers against ionizing radiations were published by the Ministry of Labour last week. They include provision for radiological and medical supervision. The employment of a person under 18 on work that requires him to be designated as a classified worker is prohibited. Any objection to the draft regulations, which are complementary to the regulations of 1961, must be sent to the Secretary, Ministry of Labour, Baynards House, 1 Chepstow Place, London W.2, by 29 December. (The Ionizing Radiations (Unsealed Radioactive Substances) Regulations. H.M.S.O., 2s. 9d. net.)

Royal Society

At the anniversary meeting of the Royal Society on 30 November Professor P. M. S. BLACKETT, O.M., F.R.S., was re-elected President of the Society. Among Fellows

newly elected to the Society's Council are Dr. J. H. HUMPHREY, head of the division of immunology and deputy director, National Institute for Medical Research, and Professor W. D. M. PATON, professor of pharmacology at Oxford University.

Journal of Medical Microbiology

This new journal, which is expected to appear in August next year, is to be established as an official publication of the Pathological Society. It proposes to publish papers on all aspects of microbiology that apply to human and veterinary medicine.

British Council

Strengthening professional contacts between Britain and other countries was an important part of the work of the British Council in 1966-7. More than 700 specialist and advisory tours were carried out under its auspices, about half being concerned with science, medicine, technology, and agriculture. During the year the Council assisted some 12,000 overseas visitors to Britain, the highest number recorded.

People in the News

► Dr. MARY D. SHERIDAN has had the Honorary Fellowship of the Society of Medical Officers of Health conferred on her.

► Dr. BERYL CORNER is undertaking post-graduate teaching courses in neonatal medicine in medical schools in India under the auspices of the World Health Organization.

News in Brief

The National Cervical Cancer Prevention Campaign has changed its name to the Women's National Cancer Control Campaign.

Grants and Awards

The Medical Research Council has made a grant of £12,663 to Professor S. D. M. COURT, department of child health, and Dr. P. S. GARDNER, department of virology, University of Newcastle upon Tyne, to aid the continuation of studies of acute respiratory infection in children jointly undertaken by the two departments.

Coming Events

Postgraduate Medicine, 1967 (T.V. Programme).—"Puberty," Scottish Television, 11 December (11.50 p.m.), repeat 13 December (1.10 p.m.).

Royal Society of Medicine.—Holiday lectures for young people (13 to 19 years), 28-29 December and 3 January. Tickets (free) in advance. Details from Assistant Secretary, R.S.M., 1 Wimpole Street, London W.1.

British Medical Association.—Conference, "Educational Technology for Continuing Medical Education," 3-5 January, University of Sussex. Fee, including meals, 10 guineas (resident), 8 guineas (non-resident). Applications to Secretary, British Medical Association, Tavistock Square, London W.C.1.

Information and Library Services for Biomedical Engineering.—Conference, organized jointly by Biological and Engineering Groups of A.S.L.I.B., Biological Engineering Society and Hospital Physicists Association,

5 January, University College, London W.C.1. Fee £2. Details from Mr. B. R. STYLES, Technical Librarian, Ministry of Public Building and Works, Chessington, Surrey.

Association of Head and Neck Oncologists of Great Britain.—Symposium, "Tumours Involving the Lower Jaw," 12 January, 10.30 a.m., Chester Beatty Research Institute, Fulham Road, London S.W.3. Applications to Mr. R. W. RAVEN, Department of Surgery, Royal Marsden Hospital, Fulham Road, London S.W.3.

Association of Physicians of India.—Joint annual conference, 23–27 January, Cuttack. Details from Dr. B. B. TRIPATHY, S.C.B. Medical College, Cuttack, Orissa, India.

Central Council for Health Education.—Annual conference, "Dependence on Drugs and Alcohol," 25 January, St. Pancras Assembly Rooms, Town Hall, Euston Road, London N.W.1. The conference fee is £1 ls. and applications should be made to the Medical Director, C.C.H.E., Tavistock House North, Tavistock Square, London W.C.1.

Institute of Religion and Medicine.—Panel discussion, "Who Tells the Patient What?" 25 January, 2.30 p.m., Friends' House, Euston Road, London N.W.1.

Royal Eye Hospital.—Refresher course for consultant ophthalmologists, 19–23 February 1968. Applications should be made to Professor D. HILL, Courage Laboratory, Royal Eye Hospital, St. George's Circus, London S.E.1.

Central Council for Health Education.—Seminar for medical officers of health, "Family Life Education," 26–28 February 1968, Conference Centre, 70 Brompton Road, London S.W.3. Details from Medical Director, C.C.H.E., Tavistock House North, Tavistock Square, London W.C.1.

2nd International Congress of Lymphology. 15–20 March, Miami, Florida, U.S.A. Details from International Society of Lymphology, Central Office, P.O. Box 128, 8028 Zurich, Switzerland.

Week-end Refresher Course for General Practitioners.—Obstetrics, 23–24 March,

Postgraduate Medical Centre, Royal Victoria Hospital, Boscombe, Bournemouth. Details from Mr. S. LUBERT, M.R.C.O.G., at the hospital.

British Occupational Hygiene Society and North Staffordshire Medical Institute.—International symposium, "Health Conditions in the Ceramic Industry," 27–29 March 1968, North Staffordshire Medical Institute, Stoke-on-Trent.

Cambridge University Institute of Criminology.—Postgraduate course in criminology 1968–9. Applications by 31 March to Institute of Criminology or to Secretary, Board of Graduate Studies, Mill Lane, Cambridge.

Association of Surgeons of Great Britain and Ireland.—Annual meeting, 4–6 April, London.

European Association of Radiology.—Symposium Ossium, 4–6 April 1968, London. Details from Dr. J. S. MACDONALD, Secretary-General, Symposium Ossium, 156 Lambeth Road, London S.E.1.

Ophthalmological Society of the United Kingdom.—Annual Congress, 1968, 17–19 April, New Arts Building, University College of South Wales and Monmouthshire, Cardiff.

M.R.C. Mineral Metabolism Research Unit in association with Department of Urology, Leeds General Infirmary.—International symposium on renal stone research, 17–20 April 1968, Leeds. Details from Dr. B. E. C. NORDIN, General Infirmary, Leeds.

Third International Meeting of Endocrinology.—"Physiopathology of Adipose Tissue," 9–12 May 1968, Marseilles. Details from Secretariat, Hôpital de la Conception, 144 Rue Saint-Pierre, Marseilles 5.

Australian College of General Practitioners.—Fourth general practitioners' convention, 17–23 May 1969, Brisbane. Details from Honorary Secretary, P.O. Box 1498 V, Brisbane, Q.4001.

World Congress on Fertility and Sterility.—Sponsored by International Fertility Association, 20–27 May 1968, Tel-Aviv, Israel.

Details from Dr. N. SOFERMAN, P.O. Box 26102, Tel-Aviv.

International Association for Accident and Traffic Medicine.—Congress on motor-vehicle and aeroplane accidents, 29 May to 3 June 1969, New York City. Details from I.A.A.T.M., 520 First Avenue, New York, N.Y. 10016.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Sunday, 10 December

BRITISH FELLOWSHIP OF THE ISRAEL MEDICAL ASSOCIATION.—At Hampstead Synagogue, 1 Dennington Park Road, London N.W.6, 3 p.m., Miss Ruth Aliav: Never the Last Road.●

Monday, 11 December

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.
HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, 7 p.m., Professor E. B. Chain, F.R.S., Dr. F. Wrigley: The Birth of a Drug
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., combined staff consultation clinical meeting.
KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. S. D. Lawler: Chromosomes and Leukemia; 6.30 p.m., Dr. D. Robertson-Smith: Nuclear Sexing ●
ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., lecture by Professor D. L. Mollin.
SCOTTISH TELEVISION LTD.—11.45 p.m., Puberty. (Sponsored by Glasgow Postgraduate Medical Board.)

Tuesday, 12 December

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Professor R. B. Woburn: Adrenal Tumours.
ROYAL SOCIETY OF HEALTH.—At Caxton Hall, London S.W.6, 6 p.m., Professor R. F. L. Logan: The Role of the Hospitals in Community Health Care Today and Tomorrow.
TUNBRIDGE WELLS POSTGRADUATE CENTRE.—At Kent and Sussex Hospital, 8.30 p.m., Mr. R. Campbell Connolly: Cerebrovascular Catastrophes.
WESTMINSTER MEDICAL SCHOOL.—At Keene Lecture Theatre, 6.45 p.m., Professor G. S. W. Organe: Anaesthesia in Russia, 1967.
WEXHAM PARK HOSPITAL, SLOUGH.—At Lecture Room, School of Nursing, 8.45 p.m., Mr. P. French: Anterior Fusion in Cervical Spondylosis.

Wednesday, 13 December

B.B.C. 1 TELEVISION—11 p.m. (approx.), Medicine Today: Parkinsonism. (Sponsored by A.S.M.E.)
CHILMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.
INSTITUTE OF CHILD HEALTH.—At Kennedy Lecture Theatre, 5.30 p.m., Professor J. J. van der Werff ten Bosch (Rotterdam): Effects of Growth-promoting Substances in Man.
INSTITUTE OF UROLOGY.—5 p.m., Dr. G. A. Rose: Calcium and the Kidney
KENNEDY INSTITUTE OF RHEUMATOLOGY.—At rear of West London Hospital, 5 p.m., Professor M. J. H. Smith: Metabolic Actions of Aspirin
MANCHESTER MEDICAL SOCIETY. SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University Medical School 5 p.m., Dr. G. Taylor: Comparative Immunology.
ROYAL COLLEGE OF OBSTETRICIANS AND GYNARCOLOGISTS.—5.30 p.m., postgraduate Museum demonstration by Dr. W. B. Robertson: Uterine Fibroids
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m. Bradshaw lecture by Professor R. Milnes Walker: Cancer in South-west England
ROYAL FREE HOSPITAL.—5.15 p.m., Dr. M. A. Epstein: Cellular Structure and Function.
ROYAL POSTGRADUATE MEDICAL SCHOOL.—2 p.m. pathology guest lecture.
SCOTTISH TELEVISION LTD.—1 p.m., Puberty. (Sponsored by Glasgow Postgraduate Medical Board.)
STOKES MANDEVILLE HOSPITAL.—6 p.m., rag class by Dr. W. Stokes

Thursday, 14 December

BROOK GENERAL HOSPITAL.—2 p.m., cardiology extended course by Dr. R. Hartley, Dr. M. Zoob.
HONYMAN GILLESPIE LECTURE.—At Surgery Lecture Theatre, Edinburgh Royal Infirmary, 5 p.m., Dr.

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

BRITISH JOURNAL OF OPHTHALMOLOGY

Contents of the December issue are as follows:

Haemorrhological Factors in the Development of Diabetic Microangiopathy. Jörn Ditzel.
Amblyopia Therapy: Results at the Giessen Clinic. J. T. Flynn and B. Verecken
Study of Late Phase Fluorescence in the Rabbit Fundus. A. W. Sollom and I. A. R. Brown.
Histological Study of Late Phase Fluorescence in the Rabbit Fundus. A. W. Sollom and I. A. R. Brown.
Misinterpretation of Sphenoidal Ridge Meningiomas. Aly Mortada
Posterior Subcapsular Cataracts and Macular Lesions after Long-term Corticotrophin Therapy. J. Williamson and T. G. Dulakos.
Corneal Hypersensitivity to Herpes Simplex. J. S. Swyers, R. N. Lausch, and H. E. Kaufman
Cytological Diagnosis of Phacolytic Glaucoma utilizing Millipore Filtration of the Aqueous. Morton F. Goldberg.
Ocular Manifestations of Vitamin A Deficiency. G. Venkataswamy.
Plastic Dermoid Cyst. B. Shukla and S. P. Srivastava
Ophthalmological Synopses. Book Review. Notes. Index, 1967.

Volume 51, No. 12. Yearly subscription (12 numbers) inland £8 8s., overseas £9. With *Ophthalmic Literature* and Index (7 numbers) inland £15, overseas £16.

Universities and Colleges

CAMBRIDGE

Sc.D.—G. A. Gresham, M.D.
Ph.D.—R. M. Clarke, M.B.
M.B.—C. J. G. Sutton, J. P. Dymond.

ABERDEEN

Appointments.—Dr. C. C. Bird (lecturer, Department of Pathology); Dr. J. E. Leng (terminable lecturer, Department of Child Health); Dr. Pierre Diomi (terminable lecturer, Department of Surgery); Dr. Audrey Sutherland (research fellow, Department of Social Medicine).

EDINBURGH

Appointment.—Dr. R. C. B. Aitken (senior lectureship, Department of Psychiatry).

LONDON

The title of reader in pathology in relation to oral disease has been conferred on Mr. T. Lehner in respect of his post at Guy's Hospital Medical School.

M.D.—Sylvia W. Davies.

Ph.D.—*In the Faculty of Medicine:* R. W. Daisley, M. M. A. Hassan, D. S. Hewick, S. A. Malcolm, E. J. Triggs, A. A. El-B. M. Wahbi, Dorothy G. T. Wells, R. M. Greenwood, S. I. Mekky, D. S. Pepper, J. R. Walton, R. St. C. Gaskin, E. M. Hawes, C. H. R. Palmer, R. H. Poyser, D. C. Thurlay, M. E. West, A. J. Bowdler, D. K. Luscombe.

THIRD M.B., B.S.—¹F. Afshar, ¹M. Aylward, ¹N. Buchanan, ¹P. J. Cole, ¹Jennifer M. Edwards, ¹R. D. Rubens, ¹P. D. Snashall, ¹W. St. C. Symmers, ¹M. G. Tweeddale, ¹M. Webley, D. J. Acres, Penelope J. Aeblerhard, E. B. D. Alimo, R. W. G. Allison, J. A. R. Anderson, M. K. Antio, C. C. Bailey, Rosemary A. Baker, M. J. M. Barker, Ann Barnicoat, G. A. Battersby, P. J. Baxter, R. H. J. Begent, M. J. Bendall, P. C. L. Beverley, D. R. Biddulph, R. J. Birts, M. C. Bishop, P. D. Black, K. C. Bouskill, Diana F. Bowie, M. M. Bowen, E. J. Bowen-Jones, J. E. Boys, E. M. Bradbury, P. J. Bradley-Watson, Ann L. Bridgewater, J. B. Broadfield, G. W. Brown, R. J. S. Browne, M. J. Brueton, J. M. Brummitt, G. D. Budhiall, H. Bush, J. R. K. Butcher, L. D. Byer, E. W. M. Carrette, Gillian Carrington, Frances E. Carter, Susan Caton, Elizabeth A. Charlesworth, A. K. S. Cheng, J. O. Clarke, J. Clubbala, A. M. G. Cochrane, R. G. Cockbain, Gillian M. Cockersole, A. J. Collyer, E. H. Compton, Delia M. Crawley, Catherine J. Crofton, R. D. Curr, J. P. J. Curran, B. Cvjetic, Linda J. Darby, Gillian R. Darch, J. R. T. Davidson, R. W. Davies, D. M. De Lacey, A. J. De Mello, R. A. J. Eady, P. G. Escourt, Ann de C. Evans, B. T. Evans, C. W. Evans, A. A. Fairclough, Judith K. Ferguson, Barbara J. M. Field, A. P. H. Fielding, S. A. Firth, D. C. Flemming, Priscilla M. Fogarty, D. P. Foster, R. M. Frankel, A. P. Freeland, R. S. Gale, Christine Garrett, J. R. Gibbs, C. J. Gorham, N. I. D. B. Gray, P. W. B. Green, A. Greenwood, Angela M. W. Greig, R. J. N. Gribble, A. W. Grieve, A. J. Hamilton, Janet M. I. Hamilton, M. H. J. Harari, R. A. Hares, T. B. Hargreave, N. E. M. Harker, P. Harker, P. C. Harland, Carolyn Haworth, A. R. Hayward, J. A. Hensel, Christine M. Holliday, J. J. Holmes, P. J. Holt, Elizabeth A. Horder, G. L. Horner, A. Hossencoccus, Jane R. Howard, A. J. Howgrave-Graham, Sally Hughes, C. P. Humphries, I. M. Hutton, Sylvia L. Inglis, N. Irish, Bridget A. Jack, P. Jaconello, J. P. H. Jago, I. D. James, S. N. Jarvis, I. M. Jaye, Katherine R. H. Johnson, R. W. Johnson, B. R. Jones, P. A. C. Julian, R. P. Juniper, Valerie H. Klein, R. A. Knight, A. Kuczyński, A. Kumar, Ruth M. Lacey, P. M. Lams, M. J. Lancaster, Diana E. Latham, Maureen E. Lawrence, B. Leatherdale, P. J. Leopard, P. J. Linnett, Nicola I. Lissau, M. J. Lockwood, R. N. Lucas, A. H. Lynn, G. P. C. McLaren, R. G. McLaren, E. W. McLarty, Jennifer M. McMillan, S. R. J. McNamara, Else J. Martin, P. J. Martin, J. H. Mather, Julia C. Mercer, D. P. B. Miles, R. Miller, C. J. Mitchell, Susan C. Mitchell, Susan E. Mithcley, R. J. C. Morris, P. P. Morton, Judy Moulds, G. H. Mumford, F. W. D. Narnor, Elizabeth J. Nevrlka, G. R. Newton-Smith, Janet L. Ockleshaw, J. P. J. O'Donovan, T. O. O. Ogunesli, A. W. O'Malley, W. G. Orr, D. J. Osborne, J. C. Pappin, H. R. Patel, J. Pemberton, Susan A. Pettit, Elizabeth R. Phipps, Madeline A. Pretty, R. W. Pulvertaft, D. H. K. Ratsey, J. A. Rees, P. Renton, A. D. Revel, P. A. Revell, B. F. Ribeiro, K. H. Riding, M. F. Robards, D. S. Robins, T. Roe, R. C. G. Rowe, S. G. Rubin, T. J. Rudman, D. J. Seager, J. A. Seaman, R. J. Sergeant, Z. K. S. Shariha, J. R. C. Sharp, Lynn Sherlaw, Valerie A. Shorter, Rosemary A. Sibert, J. S. Silverton, R. B. Simonis, A. G. Simpson, M. J. Sinclair, Diana L. Smith, I. R. M. Smith, Lydia C. Smythe, J. P. de H.-R. Spoor, Jennifer T. Spring, Monica H. Spring, B. Steer, J. D. Stephens, J. B. Stevens, Margaret A. M. Stewart, B. A. Stoner, D. Stratton, A. J. Sweatman, Heather Talbot, R. E. Taor, D. T. H. Tarbuck, E. W. Taylor, Patricia A. Taylor, M. D. G. Thomasse, D. Todd, I. H. Topham, M. J. Torrens, C. Townsend, C. Tranmer, P. J. C. Trenchard, Angela

M. Trueman, A. E. Twite, P. R. Vassall-Adams, J. D. Vaughan-Jackson, R. C. Volkers, J. G. V. Waite, N. J. Wald, J. S. Walker, N. M. Walker, P. T. Walling, R. Warner, R. J. Warrington, Hazel M. Watson, P. E. Watts, Judith A. W. Webb, M. Webber, Caroline R. Weinberg, W. H. Weston-Davies, J. Wezelman, P. D. Whiteman, Carol M. E. Williams, E. Williams, J. L. Williams, Melanie Williams, W. R. Williams, P. D. Wimberley, Rosemary J. W. Winteringham, P. M. Wood, Jean M. Worms, J. W. Wright.

¹With honours. ²Distinguished in pathology. ³Distinguished in medicine. ⁴Distinguished in applied pharmacology and therapeutics. ⁵Distinguished in surgery. ⁶Distinguished in obstetrics and gynaecology.

The following candidates at the Institute of Psychiatry have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part II:* J. R. W. Christie Brown, M. R. Eastwood, R. Gardner, G. T. Hollingworth, D. L. Julier, J. P. Leff, P. J. Noble, J. R. Pedder, J. Steiner, T. G. Tennent, J. P. Watson. *Part I:* M. J. Kelleher, A. Maiden, E. Tan.

MANCHESTER

Appointments.—Dr. M. R. Alderson, Dr. D. H. Vaughan (senior lecturers, social and preventive medicine); Dr. J. A. H. Nicholson (assistant lecturer, pathology); Dr. T. A. Cook (assistant lecturer, neuropathology).

WALES

WELSH NATIONAL SCHOOL OF MEDICINE

M.B., B.Ch.—K. Bartlett, J. M. Hussein, T. S. Loh, Esther I. K. Morgan, K. K. Ong, M. A. A. Oshodi, C. E. Rees, F. J. Shaw, N. G. Weinstock.

BIRMINGHAM

Appointment.—Dr. D. I. Rushton (lecturer, Department of Pathology).

LIVERPOOL

Appointment.—Mr. T. I. Baraket (research assistant in anatomy).

BRISTOL

Appointments.—Dr. K. D. Bhoola (senior lecturer in pharmacology); Dr. P. J. Curtis, Dr. R. A. Nicholson, Dr. O. B. Williams (demonstrators in anatomy); Dr. R. J. Harvey (lecturer in physiology); Dr. E. H. Mackay (demonstrator in pathology); Dr. E. S. Meek (lecturer in virology within the Department of Bacteriology); Mr. N. J. Moule (lecturer in radiodiagnosis); Dr. M. J. Purves (research fellow in physiology); Dr. J. A. O. Russell (lecturer in mental health (child psychiatry)); Dr. S. K. Mitra (research assistant in surgery).

ROYAL COLLEGE OF SURGEONS IN IRELAND

On 1 December the fellowship in surgery of the College was conferred on the following:

P. F. Bates, K. Haider, B. K. B. Hanna, A. T. E. Yip Hoi, A. A. Khan, S. H. O'Friel, K. A. Qasem, S. M. Rezaian, H. P. Sinha, J. M. Smith, R. E. Tattersall.

On 1 December the Licence in Surgery and Midwifery of the College was conferred on the following:

R. Bhageerutty, R. W. Charles, G. A. J. Fernandes, H. Govind, E. E. Hansrod, E. O. Isong, A. H. M. Jiwani, M. J. Khetani, Sau-Lan Lau, M. A. Molake, L. A. Mosuro, D. K. Naidoo, A. O. Ogunsola, B. M. Sandy.

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W. J. Irvine: Immunological Aspects of Endocrine Disorders and Atrophic Gastritis.

INSTITUTE OF NEUROLOGY.—6 p.m., neuro-otological clinical meeting.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Automation Experimental Unit of University College Hospital, 69-71 Chancery Mews, London W.C.2, 8.15 p.m., Automation in Medicine. Demonstration and discussion will follow.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—5 p.m., Douglas Guthrie history of medicine lecture by Lord Brock: Surgery Before 1850 as Illustrated by the Operating Theatre of Old St. Thomas's Hospital.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Cecil Joll lecture by Professor R. Y. Calne: The Present Position and Future Prospects of Organ Transplantation.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. W. P. Cleland: Management of Lung Cancer.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., symposium: Onchocerciasis, Entomological Aspects. Discussion will follow.

RUNWELL HOSPITAL.—At Wickford, Essex, 8 p.m., Dr. D. M. Shaw: Electrolytes in Psychiatry.

Friday, 15 December

BRITISH INSTITUTE OF RADIOLOGY.—2.30 p.m., Malignant Disease in Children.

BRITISH TUBERCULOSIS ASSOCIATION.—At Royal College of Physicians of London, 2 p.m., symposium: The Alveoli.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3 p.m., Mr. J. R. Cameron: Melanoma.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Sir Clifford Naunton Morgan: Inflammatory Diseases of the Colon. (2) 11.30 a.m., Mr. A. K. Monro: clinicopathological conference (rectal).

Saturday, 16 December

BRITISH INSTITUTE OF RADIOLOGY.—At Royal Society of Medicine, 10 a.m., meeting with Faculty of Radiologists, Royal College of Surgeons of England, and Radiological Section of R.S.M.

Appointments

BIRMINGHAM REGIONAL HOSPITAL BOARD.—R. M. B. Dowling, M.B., F.F.A.R.C.S. (whole-time consultant anaesthetist to the Hereford group); H. D. L. Campion, M.B., M.R.C.P. (whole-time or maximum part-time consultant physician (geriatrics) to the North Staffordshire group); C. Berry, M.B., D.P.M. (whole-time or maximum part-time consultant psychiatrist to the South Warwickshire group); B. G. P. Macnamara, M.B., M.R.C.P., D.C.H. (whole-time or maximum part-time consultant paediatrician to the Coventry group).

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—M. Strachan, M.R.C.S., D.P.M. (consultant psychiatrist, Ida Darwin Hospital, Fulbourn).

HOME OFFICE.—H. W. Eldridge, M.R.C.S., M.R.C.G.P. (senior medical officer, H.M. Prison, Wormwood Scrubs, London W.); M. W. Fowles, M.B., D.P.M. (medical officer, H.M. Prison, Lincoln); N. A. J. Mullen, M.B., D.P.M. (medical officer, H.M. Prison, Leicester).

MANCHESTER REGIONAL HOSPITAL BOARD.—K. S. R. Bedi, M.B., M.R.C.P.Ed., D.C.H., D.P.M. (whole-time or maximum part-time consultant psychiatrist, Parkside Hospital, Macclesfield); P. J. N. Howorth, M.Sc., M.B. (consultant pathologist with special interest in chemical pathology, Blackburn and District group of hospitals); D. K. Mukerji, M.B., F.F.A.R.C.S. (whole-time consultant anaesthetist, Bolton and District group of hospitals); E. A. G. Hamilton, M.B., D.M.R.D. (whole-time or maximum part-time consultant radiologist, North Lancashire and South Westmorland group of hospitals).

MINISTRY OF OVERSEAS DEVELOPMENT.—J. E. Blewett, M.D., F.F.R. (senior diagnostic radiologist, Government of Barbados).

NATIONAL HOSPITALS FOR NERVOUS DISEASES.—Patricia Painter, M.B., F.F.A.R.C.S. (consultant anaesthetist).

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—Shona Hodgson, M.B., D.Phys.Med. (consultant physician in physical medicine to Thames group of hospitals).

NORTHERN IRELAND HOSPITALS AUTHORITY.—P. J. Molloy, M.B., F.R.C.S. (consultant cardiac surgeon, Belfast Group); T. Freeman, M.D., M.R.C.P.Ed., D.P.M. (consultant psychiatrist, Holywell Group); P. B. Donnelly, M.B., F.F.A.R.C.S. (consultant anaesthetist, South Down Group); J. B. Walsh, M.B., M.R.C.P.I., D.P.M. (consultant psychiatrist, Tyrone and Fermanagh Hospital, Omagh).

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL.—T. Kumarasamy, M.B., F.R.C.S., M.R.C.P., M.R.C.O.G. (lecturer in the obstetric unit).

Deaths

Playfair.—On 21 November, at Dundee Royal Infirmary, Bessie Morrison Playfair (née Davidson), M.D., D.P.H., in her 71st year.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 16 DECEMBER 1967

Pointers

Carcinoma of Lung: Low incidence of tumour produced in mice exposed to cigarette smoke and air mixture (p. 637).

Spread of Staphylococci: General-practice survey in Edinburgh and North-east England showed that newborn babies acquired *Staph. aureus* more frequently in hospital than at home, but hospital strains were no more likely to spread within the family or to cause septic lesions than "domestic" strains (p. 642).

Liver Transplants: Prolonged survival obtained in pigs by Professor R. Y. Calne and his team, without the use of immunosuppressive agents, is thought to be a species effect (p. 645).

Diagnosis of Bacteriuria: Description of bacteriological culture method not requiring incubation at 37° C. and suitable as a screening method in general practice (p. 649).

Blood Loss in Haemodialysis: Reduced by wash-back technique using 1 litre of saline at end of dialysis (p. 651).

Traveller's Diarrhoea: Controlled prophylactic trial showed that this was reduced by Streptotriad (p. 653).

Urinary Leucocyte Excretion: Abnormality found before or after prednisolone provocation test in high proportion of pregnant women was not due to renal disease, and its cause is unknown (p. 655).

Cardiac Scleroderma: Dr. E. Fletcher and Dr. P. Morton show that its features may be masked by lung disease (p. 657).

Case Reports: Hypercalcaemia and carcinoma-tosis (p. 658); Budd-Chiari syndrome after oral contraceptives (p. 660); hepatomegaly and non-metastatic liver-cell dysfunction with hypernephroma (p. 660); relapsing polychondritis (p. 661).

Dysphagia: Dr. C. F. Hawkins's Current Practice article emphasizes the importance of careful history-taking and radiology (p. 663).

Nurse in General Practice: Use for making first visits to patients described by Dr. J. Weston Smith and Mrs. E. M. Mottram (p. 672).

Partnership in Medical Care: Summary of Maurice Bloch Lecture by Minister of Health (p. 675). Leader at p. 634.

Thamesmead: Plan for main and temporary mobile health centres (p. 676).

Operating-theatre Design: B.M.A. Symposium to commemorate Lister centenary (p. 678).

Salmonellae: Importance of animal reservoirs emphasized by Dr. R. C. Huckstep (p. 681).

G.M.C.: Report of Disciplinary Committee (Supplement, p. 77).

Review Body: Mr. Quintin Hogg, Q.C., to represent hospital staff (Supplement, p. 79).

Localization of Intracranial Tumours

Nearly a century ago Sir William Macewen (1848-1924), the father of brain surgery, described the brain as "the dark continent."¹ By this he meant there are seldom unequivocal signs or symptoms pointing accurately to the position of an intracranial mass. The brain surgeon cannot delve with his hand deeply into the brain, as the abdominal surgeon may into the abdomen, so that the dark continent remained dark after Macewen's time. But new methods of obtaining radiological contrast in the brain and of scanning it by means of radioactive isotopes have allowed much more precise information to be obtained. Nowadays it is usually possible to predict fairly accurately both the position of an intracranial mass and its pathological nature.

X rays were discovered in 1895, and as early as 1912 A. Schüller² wrote a book on the radiology of the skull, showing how valuable information could be obtained by accurate interpretation. W. E. Dandy³ introduced ventriculography and air encephalography in 1917, E. Moniz⁴ arteriography in 1927, and G. E. Moore⁵ isotope encephalography in 1948. Meanwhile H. Berger⁶ had introduced the electroencephalograph, and L. Leksell⁷ applied ultrasonics to the brain in 1955. But it is only in the last few years that all these methods have been clearly correlated. The diagnostic use of air in the brain and cerebral arteriography both carry a slight morbidity and even mortality. The modern trend, therefore, is to try to obtain the maximum information by other and harmless procedures. This course also has an economic advantage in saving the occupation of hospital beds. Concurrently with the discovery of these new techniques over the years clinical neurologists, psychiatrists, clinical psychologists, neuro-ophthalmologists, and neuro-otologists have made advances which enable them to point more firmly towards the diagnosis before ancillary aids have to be called in.

When an intracranial mass is suspected the skull is x-rayed. Four radiographs in appropriate projections are usually a sufficient survey, but if a lesion in the region of the optic or acoustic nerves is suspected it is necessary to take special projections in addition. In adults the chest is x-rayed as a routine. This is essential if the patient is middle-aged or over, because bronchial carcinoma, a frequent source of metastases in the brain, is now such a common disease. An E.E.G. and ultrasound examination can readily be performed at the same time. Having obtained the results of these examinations, the neurologist can then review the situation and decide what further investigations, if any, are necessary.

Before considering the more elaborate methods of radiological investigation it is important to be clear about the types of intracranial mass which might be found and their incidence. Firstly, it is not always possible to differentiate clinically between neoplasms, vascular lesions, and inflammatory masses. About one-half of all intracranial tumours belong to the glioma family; these infiltrate the brain in a haphazard fashion and usually have no discrete edge. About four out of five of them are

malignant. The majority of the remaining intracranial tumours are extracerebral—that is, with the important exception of metastases they press on rather than invade the brain. Meningiomas and pituitary tumours each account for about 15%, acoustic neuromas for about 8%. Intracerebral metastases were found to be relatively rare until recent times, accounting for rather less than 5% in most large series reported from neurosurgical clinics. However, nowadays the figure approaches 10% and may be more. Other types of tumour, though important, are relatively rare. Among the most likely non-neoplastic conditions are abscess, subdural haematoma, and intracerebral haematoma.

The pattern of investigation will vary much from patient to patient, depending partly on the provisional clinical diagnosis and partly on the patient's state of health. The latter can vary from almost normal health to intense coma associated with severe papilloedema. Before the invention of isotope scanning it was nearly always necessary to admit any case of suspected brain tumour to hospital for investigations. Nowadays this is not always essential, and the economic and social advantages of outpatient investigation are obvious. A good example is the case of a middle-aged or elderly person, usually male, who develops perhaps slight symptoms and signs of an intracerebral mass. Plain radiographs of the skull may be negative, and even if a mass is present in one hemisphere the pineal gland (if it is calcified) is not always deviated sufficiently to enable the radiologist to confirm it. However, the ultrasound examination will usually be positive in such cases and so may be the E.E.G. The chest will be x-rayed as a routine, for bronchial carcinoma is far and away the commonest primary site of a secondary in the brain. The next step is to scan the brain after injection of a radioactive isotope. This merely entails a small intravenous injection and is readily carried out on outpatients. If the chest x-ray is abnormal, and the scan shows more than one intracranial mass, the diagnosis is virtually certain. As many as six or seven metastases have been shown on brain scans, but the limiting factor is the size of the metastases, those less than 2 cm. in diameter not being demonstrable. Meningiomas nearly always give a positive scan, and a high percentage show characteristic changes on a plain radiograph. If these changes can be related to the size, shape, and position of the mass shown on the scan the diagnosis is sometimes sufficiently certain for a surgeon to explore. Scanning is usually positive with malignant gliomas and the larger acoustic tumours, and with subdural and intracerebral haematomas, but seldom with the pituitary group of tumours.

The large majority of patients suspected of having an intracranial tumour require admission to hospital. They are ill, and, besides needing expert nursing attention, many have to be examined by cerebral angiograms and air studies entailing the injection of air (pneumography) at lumbar puncture (lumbar encephalography) or by ventriculography. One or more of these investigations is frequently necessary even if the scan examination is positive, for the scan seldom provides all the necessary information on the site and nature of the tumour.

In the last few years most European and American neurosurgeons have tended to recommend carotid arteriography before pneumography. Arteriography has the advantage of not upsetting the intracranial hydrodynamics, which is inevitable when air is introduced by whatever route. Thus the patient is generally less upset after an angiogram. On the other hand, an angiogram is more limited in the information it gives. Thus one internal or common carotid

arteriogram may give useful information about one cerebral hemisphere but usually little or nothing about the opposite hemisphere or the mid-brain or posterior-fossa structures. Pneumography, on the other hand, outlines the whole ventricular system, and if the air is introduced by lumbar puncture the cisterns and sulci of the brain are also outlined. If there is a strong suspicion on clinical examination, ultrasonic testing, the E.E.G., plain radiography, and scanning that a lesion is restricted to one hemisphere then carotid angiography on that side is indicated as the first contrast investigation. This may show the position of the lesion by the deformity produced on the arteries and veins, and sometimes, in addition, characteristic pathological blood vessels may be outlined, as, for example, in meningioma and malignant glioma. Sometimes, however, arteriography does not give all the information required. Pneumography is then needed to provide further information. If the patient shows signs and symptoms of grossly raised intracranial pressure it is usually considered safer to undertake a ventriculogram, but if these signs are absent more information can be obtained by undertaking a lumbar encephalogram. The position of the tumour can be analysed by noting the deformity of the ventricular system or the subarachnoid pathways.

Sometimes it is impossible to determine clinically or by the preliminary radiological and other investigations whether the suspected mass is supratentorial or infratentorial, and so there is no pointer to which arterial tree should be outlined. In these cases an encephalogram should be undertaken before an arteriogram. Then again, if the lesion is thought to be lying in the mid-brain or posterior fossa, experience shows that pneumography is more reliable in delineating the lesion than either carotid or vertebral arteriography.

There is yet another useful radiological investigation which has a small place in the diagnosis of tumours, and that is positive contrast ventriculography. It is valuable in outlining masses in the mid-brain or posterior fossa. Patients with such lesions usually suffer from moderate or considerable hydrocephalus, and an air ventriculogram can severely upset the intracranial hydrodynamics. With positive contrast ventriculography only 2–3 ml. of contrast substance needs to be used; it is then manipulated into the appropriate part of the ventricular system under television control. By this means there is no serious upset of intracranial hydrodynamics. In addition, a positive contrast substance has the advantage in sometimes delineating the lesion far more sharply than a small air shadow might.

Since such remarkably refined methods of radiological investigation are now available, it might be thought that no tumour or mass will remain undetected. Unfortunately this is not the case. Very small tumours, such as meningiomas pressing on the optic nerve, can evoke serious signs and symptoms, yet by virtue of their small size may not be detectable by any radiological method. Again, large infiltrating gliomas may fail (sometimes for years) to distort the ventricular or arterial anatomy and may also fail to take up an isotope. Thus in the last resort the astute neurologist or neurosurgeon must make the final decision, sometimes defying the results of all the negative investigations.

¹ Macewen, W., *Brit. med. J.*, 1888, 2, 302.

² Schüller, A., *Röntgen-diagnostik der Erkrankungen der Köpfe*, 1912. Vienna.

³ Dandy, W. E., *Ann. Surg.*, 1918, 68, 5.

⁴ Moniz, E., *Rev. neurol.*, 1927, 34, 72.

⁵ Moore, G. E., *Science*, 1948, 107, 569.

⁶ Berger, H., *Arch. Psychiat. Nervenkr.*, 1929, 87, 527.

⁷ Leksell, L., *Acta chir. scand.*, 1956, 110, 301.

Acalculous Cholecystitis

The great majority of patients with disease of the gall bladder have stones in it, yet there is no doubt that acalculous cholecystitis, though unusual, does exist. In practice the conditions found at operation may range from a perfectly normal gall bladder removed because of suspected biliary disease, through gall bladders with mild histological changes in the wall, to undoubted examples of acute, indeed even gangrenous, cholecystitis in the absence of stones.

For some time the poor prognosis of patients submitted to cholecystectomy despite the absence of gross lesions in the gall bladder and with a cholecystogram that was only questionably abnormal cast doubt on whether a definite disease entity was being diagnosed. Thus W. A. Mackey, in a review of 243 such patients,¹ found over one-third had a poor functional result. He concluded that cholecystitis without stone "seems to belong to a region on the border line between functional and organic disease."

More recently F. Glenn and H. Mannix² studied a group of 135 patients who had neither stone nor acute inflammation; these patients were in a series of 3,110 undergoing cholecystectomy. The results were somewhat unhappy; 22 had severe postoperative complications (16.3%) and there were three deaths. Of 121 of the patients followed up, a quarter had no relief from their original symptoms. Careful microscopical examination of the excised specimens showed no difference between those cases with good results and those with no improvement, so that these authors state, "One may well question the actual role of cholecystectomy in the clinical improvement."

Yet undoubtedly acute cholecystitis, even progressing to frank gangrene and perforation, can occur in the absence of a stone. S. O. Hoerr and J. B. Hazard,³ in reviewing 14 such cases, define four possible causes. There may be non-calculous obstruction of the cystic duct from fibrosis, kinks, or twists, or from an anomalous cystic artery or tumour. There may be infarction of the wall of the gall bladder due to arteriosclerosis or embolism. There may be reflux of pancreatic juice, producing a chemical cholecystitis. Or there may be bacterial invasion of the gall bladder wall. Typhoid cholecystitis is a good example of the last group.

An interesting review of the whole subject of acalculous cholecystitis has recently come from A. M. Munster and J. R. Brown,⁴ of the Peter Bent Brigham Hospital, Boston. Out of 541 cholecystectomies 12 cases of acalculous cholecystitis were found (2.2%). There were four examples of acute cholecystitis, three more showed undoubted active chronic disease, and the remaining five had only minimal evidence of mild chronic cholecystitis. Not unexpectedly the patients with acute acalculous cholecystitis did well after surgical operation, whereas of the five with minimal disease two had persistent symptoms and one has been lost to follow-up.

The situation can be summed up as follows. If a patient has typical symptoms and signs of gall-bladder disease in the absence of radiological evidence of stone and with normal appearances on barium-meal examination of the upper gastrointestinal tract, the surgeon may still find himself forced to perform a laparotomy. He may detect some unsuspected lesion—for example, chronic pancreatic disease.

He may find tiny stones in the gall bladder which were undetected on x-ray examination, or there may be evidence of acalculous cholecystitis with gross thickening and inflammation of the wall of the gall bladder, adhesions to adjacent viscera, and other signs of disease. In these circumstances cholecystectomy will probably relieve the patient's symptoms. If the gall bladder appears normal, if the aspirated bile is clear, and if stones can still not be felt when the organ has been completely emptied, cholecystectomy is unlikely to be of value and will merely add to the possible risk of the exploratory operation.

Novelty at Nottingham

The creation of a complete new medical school at Nottingham presents the opportunity for putting into practice many of the imaginative ideas discussed at three world conferences on medical education and innumerable smaller gatherings since the war. It is therefore refreshing to see that a report¹ published this week offering recommendations for the administration of the teaching hospital contains an entirely novel proposal. This concerns the relationship between the teaching hospital, Nottingham University, and Sheffield Regional Hospital Board.

The central problem for a large undergraduate teaching hospital is to reconcile the need to provide comprehensive medical care to the population among whom it is set with the obligation to teach. In addition, it must offer facilities that will allow and even encourage research. For a variety of reasons England and Wales took a different path from Scotland when the National Health Service was introduced, and arrangements in Northern Ireland are again slightly different. Despite some criticisms over the years it cannot be said that there is any great dissatisfaction either with the separation of boards of governors of teaching groups from regional hospital boards in England and Wales or with the co-ordination of their functions under single boards beyond the Border. But when the local joint committee of Sheffield Regional Hospital Board and Nottingham University came to look at the problem it faced plans which, as its report says, are "without precedent or parallel in the United Kingdom." And these words too are a refreshing token of the Nottingham planners' disinclination, evident in the report, to follow precedent or trot along parallel lines.

If the new teaching hospital was placed under the existing regional hospital board it would have the disadvantage of being controlled by a body 40 miles away and separated by congested lines of communication. It is a body, too, which in England and Wales has no statutory responsibility to provide the university with facilities for teaching. Yet the setting up of new and elaborate hospital services for a large population can be done satisfactorily only in the closest co-operation with the existing regional board. This consideration, combined with the difficulties of communication that would hamper a separate board in Nottingham have weighed against the establishment of a new board of governors.

What the joint committee therefore recommends is a governing body—"University Hospital Board of Manage-

¹ Mackey, W. A., *Brit. J. Surg.*, 1934, 22, 274.

² Glenn, F., and Mannix, H., *Ann. Surg.*, 1956, 144, 670.

³ Hoerr, S. O., and Hazard, J. B., *Amer. J. Surg.*, 1966, 111, 47.

⁴ Munster, A. M., and Brown, J. R., *ibid.*, 1967, 113, 730.

¹ Sheffield Regional Hospital Board and the University of Nottingham, *Report on the Form of Government for the Teaching Hospital at Nottingham*, 1967. 2s. net. Obtainable from Secretary to Sheffield Regional Hospital Board, Fulwood House, Old Fulwood Road, Sheffield S10 3TH.

ment"—to be appointed by and responsible to Sheffield Regional Hospital Board but having wider powers than ordinary hospital management committees. The new board of management would have 15 members plus a chairman. Six would be nominated by Nottingham University and nine appointed by Sheffield Regional Hospital Board after consultation with local health authorities, executive councils, medical and dental staffs, and other organizations. The chairman would be appointed by the regional board after consultation with the university. On the all-important financial powers of the board of management the report goes on to recommend that it should be empowered to undertake capital works on the same conditions as is a board of governors, and that the Ministry of Health should earmark revenue allocations to the regional board for use by the board of management. Collaboration between the regional hospital board and the new board of management is to be further ensured by the creation of a special co-ordinating committee.

The joint committee's proposals, which have been approved by Nottingham University and Sheffield Regional Hospital Board, go to the Ministry of Health for consideration. They will also be more widely studied for their general interest. Though these are interim measures and are specifically intended for the novel situation at Nottingham, they must be thought relevant to the establishment of other new medical schools—for instance, the one at Southampton.

Monarticular Arthritis in Children

The child with chronic arthritis in a single joint can present a difficult problem in diagnosis. No doubt tuberculosis was once the commonest cause, but tuberculosis of joints is now seen much less frequently in Britain, and a number of other conditions have to be considered. These are rheumatoid arthritis (together with ankylosing spondylitis, psoriatic arthritis, and the arthritis of ulcerative colitis, which when presenting in a single peripheral joint are often indistinguishable from rheumatoid disease); the effects of injury, such as osteochondritis dissecans; and a very small group of rarer miscellaneous disorders, including brucellosis, histoplasmosis, blastomycosis, pigmented villonodular synovitis, synoviomia, haemangioma, and other tumours.

Juvenile rheumatoid arthritis, or Still's disease, usually affects multiple joints, but the onset is sometimes monarticular, and this form of the disease has been described in several recent studies.¹⁻⁹ The proportion of patients with Still's disease starting in a single joint varies in the different series from 10%⁴ to 39%³—no doubt owing to differences in case selection and in diagnostic criteria. Sex and age of onset do not appear to differ from Still's disease as a whole.

The knee is predominantly affected, with the ankle next most commonly; other joints include wrist, hip, elbow, midtarsal, and various joints in the fingers, toes, and cervical vertebrae. In some children the disease remains monarticular, but most eventually progress to a polyarthritis, usually within a year. Remission of disease activity is commoner in those with persistently monarticular disease than in those in whom it becomes polyarticular. Other useful signs of Still's disease, such as the typical fever and rash, are seen only occasionally in these patients. Though iritis is not always found among children with monarticular disease,⁵ it must be looked for carefully, because most reports indicate that it occurs with at least equal frequency to that in polyarticular disease, while in three series^{4, 7, 9} the incidence was higher in the monarticular group.

The main radiographic features consist of local growth abnormalities—longitudinal overgrowth of long bones, enlargement of epiphyseal ossification centres, accelerated epiphyseal maturation, and diminished size of small round bones such as the carpals. Erosion of bone is relatively late and inconspicuous. As with the polyarticular form of Still's disease, serological tests for rheumatoid factor are usually negative and the vascular complications of adult rheumatoid disease are rarely encountered.¹⁰ The appearances of biopsy specimens of synovium vary from a mild synovitis with some hyperplasia of synovial lining cells and minimal round cell infiltration to the classical appearance of rheumatoid synovial membrane with marked hyperplasia, lymphocyte aggregations, plasma cell infiltration, and deposition of fibrin. There is little correlation between the findings at biopsy and the subsequent course of the disease,⁴ but the procedure is of great value in excluding the presence of tuberculosis and other conditions.

There should therefore be no hesitation in carrying out synovial biopsy when—as is usually the case—some doubt exists about the diagnosis. General physical and ophthalmic examination, radiology of joints and chest, tuberculin testing, and microscopic and bacteriological examination of synovial fluid may all help in reaching the answer, but very often results are inconclusive. A needle biopsy nearly always yields adequate tissue for diagnostic purposes and causes none of the discomfort and inconvenience of an open surgical procedure, though the latter has the advantage of permitting direct inspection of the joint and selection of tissue for examination. Whatever the method, early biopsy avoids on the one hand any delay in the diagnosis of tuberculosis and on the other the equally unwarranted mismanagement of Still's disease with antituberculosis chemotherapy and harmful immobilization.

Partnership in Medical Care

Wherever the State and the medical profession come into working contact there seems to be excessive friction. Though in Britain there have been none of the "strikes" that periodically affect doctors in some other countries, relations between the Ministry of Health and the profession have at times been strained and have seldom been cordial. Mr. Kenneth Robinson took up the theme of the relationship between doctors and the State in his Maurice Bloch Lecture to Glasgow University last week, a summary of which is

¹ Sury, B., *Rheumatoid Arthritis in Children*, 1952. Copenhagen.

² Edström, G., *Arthr. and Rheum.*, 1958, 1, 497.

³ Grokoe, A. W., Snyder, A. I., and Schlaeger, R., *Juvenile Rheumatoid Arthritis*, 1962. Boston.

⁴ Bywaters, E. G. L., and Ansell, B. M., *Ann. rheum. Dis.*, 1965, 24, 116.

⁵ Laaksonen, A. L., *Acta paediat. (Uppsala)*, 1966, Suppl. 166.

⁶ Griffin, P. P., Tachdjian, M. O., and Green, W. T., *J. Amer. med. Ass.*, 1963, 184, 23.

⁷ Brattström, M., and Sundberg, J., *Acta rheum. scand.*, 1965, 11, 266.

⁸ Sundberg, J., and Brattström, M., *ibid.*, 1965, 11, 279.

⁹ Cassidy, J. T., Brody, G. L., and Martel, W., *J. Pediat.*, 1967, 70, 867.

¹⁰ Bywaters, E. G. L., and Scott, J. T., *J. chron. Dis.*, 1963, 16, 905.

printed at page 675. His subject was partnership in medical care provided under the National Health Service.

Mr. Robinson sees a relationship of mutual confidence between Government and profession as being essential if the N.H.S. is to achieve its full potential. He is puzzled that the efforts of successive Ministers of Health have failed to convince doctors that their suspicions of authority are groundless. He thinks that more doctors, particularly the younger ones, are happier in their environment than their leaders make out, and he notes in the public utterances of the profession's spokesmen a reluctance to give credit to the Government for what it has done and what it has said it intends to do for the Health Service.

There can be some sympathy for Mr. Robinson. He is sincere, and more than most of his predecessors in office he has tried to meet the doctors half way. They, on their part, have been quick to learn the practices of collective bargaining but perhaps slower to discover how to make their authoritative voice heard on matters more directly concerned with the well-being of a profession and of the public which it serves. And, however well intentioned, Mr. Robinson inevitably suffers from any layman's inability fully to understand the finer professional feelings of the doctors with whom he is dealing.

It is a welcome sign that Mr. Robinson has caught the new mood of objective inquiry into the working of the N.H.S. It is to be hoped that his review of its administrative structure will result, as he expects, in reforms that will put the management into proper shape to serve the needs of modern scientific medicine. He also sees the need for an administration that will lead to better co-operation in the functioning of the various branches of the medical services. But whatever changes come about—unless perchance they include a revolutionary decentralization of the responsibility for the provision of medical services—they are unlikely to do much to promote that partnership between the Government and the profession that Mr. Robinson is not alone in thinking to be desirable.

Partnership implies a division of work and a sharing of responsibility among equals. There is no difficulty in differentiating the work of the Minister of Health and his Ministry from that of the doctors. But when Mr. Robinson speaks of partnership does he mean one in which doctors would share equally with him the responsibility for making decisions? It is to be feared that he does not. Indeed, can he share responsibility that is placed on him by statute? The National Health Service multiplied the men in Whitehall and, for better or for worse, made them the masters of the men in the field. That has probably been the greatest single cause of the doctors' discontent, and it is at the root of their mistrust of Government.

Rather than pondering on the irrational behaviour of a seemingly unappreciative lot of doctors or surmising how many younger ones are happier than they are said to be, Mr. Robinson would do well to begin a dispassionate examination of the nature of the discontents that undoubtedly exist. Why do young doctors emigrate? What is there in their new environment which they think will give them the professional satisfaction that they failed to find in the N.H.S.? Why should discontent be if anything more rife among a generation that has never known anything but the N.H.S. than among their older colleagues? The answers to these and other questions might produce some facts which would lead to a better understanding by the Government of the profession's problems, and if not to a true partnership at least to an increase in mutual confidence.

Tetanus Prophylaxis

The treatment which should be given to prevent tetanus in injured patients is still not fully agreed. Each of the prophylactic methods available has drawbacks, and in addition to the difficulties of choosing between them on clinical grounds the doctor must also be concerned that medico-legal complications have an unfortunate association with tetanus and its prevention.

Under ideal circumstances, where the whole community has been actively immunized, there are few difficulties: patients then require only normal surgical toilet of the wounds, together with an injection of tetanus toxoid if more than two or three years have elapsed since a previous booster dose. Such ideal conditions exist in Britain only in the armed Forces and in some industries and institutions. Probably well under half of the general public have been actively immunized, and of these many are unaware of the fact and must often be regarded as non-immune when treated for an injury. Most casualties are thus either non-immune or doubtfully immune, and it is with these patients that the main difficulties of tetanus prophylaxis arise. Almost all of the difficulties would be solved if human tetanus antitoxin could be used; an injection of 250 units provides at least four weeks' protection and is virtually free from side-effects.¹ But only small amounts are available in Britain and at present prophylaxis must be provided by other means.

The first essential of tetanus prevention for all wounds (irrespective of the immune status) is a thorough surgical toilet. A decision must then be made whether further prophylaxis is needed. For fresh, clean wounds in which it is possible to remove completely all foreign matter and dead tissue further measures are not required.²⁻⁴ For wounds not seen until six hours or more after injury, however, 1,500 units of tetanus antitoxin (preceded in the usual way by a small trial dose) should be given, because there is a possibility that a lethal amount of toxin might already have accumulated.^{3, 5}

Patients with more severe wounds will usually require some form of prophylaxis in addition to the surgery, particularly if some doubt remains about the completeness of the toilet. If human antitoxin is not available the practical alternatives are horse serum antitoxin and an antibiotic, and the choice between the two is difficult and controversial. Both undoubtedly can fail; there are many reports of tetanus in patients who had received antitoxin,⁶ and in recent years the disease has been encountered in patients given antibiotic prophylaxis at the time of wounding.^{7, 8} It is not known which fails more often, but the failure rate of either in Britain is presumably very low, because tetanus is extremely rare in injured patients given either antitoxin or antibiotic in casualty departments.^{4, 7} As no properly controlled comparison has been made some grounds other than effectiveness must be used to choose between the two.

¹ *Brit. med. J.*, 1963, 1, 902.

² Parish, H. J., and Cannon, D. A., *Antisera, Toxoids, Vaccines, and Tuberculin in Prophylaxis and Treatment*, 1961, 5th ed. Livingstone, Edinburgh.

³ Laurence, D. R., Evans, D. G., and Smith, J. W. G., *Brit. med. J.*, 1966, 1, 33.

⁴ Sharrard, W. J. W., in *Proceedings of a Symposium on Tetanus in Great Britain*, Leeds, 1967, ed. M. Ellis, p. 137.

⁵ Smith, J. W. G., *Brit. med. J.*, 1964, 2, 1293.

⁶ Bianchi, R., *Helvet. med. Acta*, 1962, 29, 38.

⁷ Ellis, M., *Proc. roy. Soc. Med.*, 1965, 58, 224.

⁸ Lucas, A. O., and Willis, A. J. P., *Brit. med. J.*, 1965, 2, 1333.

In addition to sometimes failing to prevent tetanus both antitoxin and antibiotic may cause hypersensitivity reactions, and the available evidence suggests that horse serum is more dangerous in this respect. Mrs. C. A. Cox and her colleagues,⁹ for example, found that in Britain about 12% of patients developed a significant reaction to antitoxin. Of the antibiotics which may be used the penicillins are the group most likely to cause trouble, and, though there are no reliable figures of the incidence of reactions in Britain, in the U.S.A. it is perhaps 1%.¹⁰ On this evidence, therefore, antibiotics are to be preferred to antitoxin for routine use in Britain—though everyone does not agree with this view.⁷ Even when the antibiotic regimen is preferred there will nevertheless be some wounded patients for whom antitoxin is a wiser choice—when the wound is over six hours old, and also when the antibiotic possibly may not penetrate into the infected site, as when severe tissue damage is present or when the wound cannot be completely cleaned.^{3, 5}

A number of antibiotics are suitable for tetanus prophylaxis. If the patient can be trusted to take tablets cloxacillin is a good choice as it is not inactivated by penicillinase, which might be formed in a lesion by bacteria other than *Clostridium tetani*.⁵ If an injectable prophylactic is preferred a combination of long- and short-acting penicillins is suitable provided the wound is not otherwise infected. E. J. L. Lowbury¹¹ recently tested 50 strains of *Cl. tetani* and found that all were fully sensitive to the penicillins and to tetracycline and erythromycin, which also are suitable. Whichever of these antibiotics is used it should be given in full dosage for at least four days—or longer if healing of the wound is delayed, because there is evidence from experiments on animals that shorter periods of treatment can be unreliable.⁵ The local application of antibiotic powder to the wound is worth while,¹² as there is evidence, again from work on animals, that locally injected antibiotic can be particularly effective.¹³

If antitoxin is preferred for routine use, once again there are some patients for whom it is an unwise choice—those believed to be hypersensitive to horse serum as indicated by a history of previous reactions or a reaction to the trial dose.³ The injection of horse serum into a hypersensitive person is not only dangerous but can be valueless, because the serum is likely to be rapidly eliminated from the patient's body; reliance should instead be placed on surgery together with an antibiotic. If, however, as in the case of an extensive, badly soiled wound, antitoxin is considered essential, then every effort should be made to obtain human antitoxin, and small supplies have been made available by the Ministry of Health for this purpose.¹⁴

In addition to the immediate measures taken for preventing tetanus, all authorities advise that wounded patients should be started on a complete course of immunization with adsorbed toxoid.¹⁵ Though protection is unlikely to develop for at least four weeks, after this time the patient should need neither antitoxin nor antibiotic if he is again injured.

Commonwealth Links

At a time when the strong but ill-defined bonds between the countries comprising the British Commonwealth are under stresses of various kinds it is gratifying to note the excellent work being done by the Commonwealth Foundation. Its first report, issued after the initial 18 months of existence, has now appeared.

A registered charity with funds supplied by Commonwealth countries, the Foundation seeks to encourage interchange and co-operation throughout the Commonwealth, especially through the work of professional people in it, as may be seen from its terms of reference:

"(a) To encourage and support fuller representation at conferences of professional bodies within the Commonwealth.

"(b) To assist professional bodies within the Commonwealth to hold more conferences between themselves.

"(c) To facilitate the exchange of visits among professional people, especially the younger element.

"(d) To stimulate and increase the flow of professional information exchanged between the organizations concerned.

"(e) On request to assist with the setting up of national institutions or associations in countries where these do not at present exist.

"(f) To promote the growth of Commonwealth-wide associations or regional Commonwealth associations in order to reduce the present centralization in Britain.

"(g) To consider exceptional requests for help from associations and individuals whose activities lie outside the strictly professional field but fall within the general ambit of the Foundation's operations as outlined above."

To fulfil its aims the Foundation has been endowed with an annual income of £250,000, to which all the following Governments subscribe in varying proportions: Britain, Canada, Australia, New Zealand, India, Pakistan, Ceylon, Ghana, Malaysia, Nigeria, Sierra Leone, Tanzania, Cyprus, Uganda, Jamaica, Trinidad and Tobago, Malawi, Zambia, Malta, the Gambia, and Singapore. Guyana subsequently joined the Foundation in December 1966, Barbados in May 1967, and Kenya in July 1967. The chairman is Sir Macfarlane Burnet, O.M., F.R.S., who in 1960 jointly with Professor (now Sir) Peter Medawar, F.R.S., won the Nobel prize for medicine.

So far the Foundation's grants have been made chiefly to professional people, doctors prominently among them, "to attend worth-while conferences at which they can contribute as well as learn." Both the Commonwealth Medical Association and the British Medical Association have been beneficiaries, the latter by a grant to finance the attendance by members of Caribbean Branches at a regional council meeting in Antigua earlier this year. Many other medical organizations have likewise received grants to enable members to attend conferences on special branches of medicine and surgery. Outside medicine the beneficiaries have included engineers, lawyers, accountants, architects, and educationists. Another venture which promises to be helpful is the establishment in developing Commonwealth countries of "professional centres" with a small staff and a library. So far two have been set up—in Kampala, Uganda, and Port-of-Spain, Trinidad. The aim is that these premises shall be available for professional meetings and lectures.

In fostering professional relations within the Commonwealth the Foundation is helping to bring peace and prosperity to a world badly in need of both. And with a tradition that pays little heed to national frontiers doctors in particular will feel grateful to the Commonwealth Governments for setting up this worth-while organization.

⁹ Cox, C. A., Knowelden, J., and Sharrard, W. J. W., *Brit. med. J.*, 1963, 2, 1360.

¹⁰ Van Arsdell, P. P., *J. Amer. med. Ass.*, 1965, 191, 238.

¹¹ Lowbury, E. J. L., in *Proceedings of a Symposium on Tetanus in Great Britain*, Leeds, 1967, ed. M. Ellis, p. 100.

¹² Rubbo, S. D., *Lancet*, 1966, 2, 449.

¹³ McDonald, R. T., Chaikof, L., and Truant, J. P., *Surg. Gynec. Obstet.*, 1960, 110, 702.

¹⁴ Ministry of Health, *Prophylaxis of Rabies and Tetanus, and Treatment of Anthrax, Botulism, Organo-phosphorus Poisoning, Snake-bite, and Tetanus*, 1967, H.M. (67) 38. London.

¹⁵ *Principles on Tetanus*, Proceedings of the International Conference on Tetanus, Berne, 1966, ed. L. Eckmann, p. 576. Berne.

Papers and Originals

Production of Lung Carcinomas in C57BL Mice Exposed to a Cigarette Smoke and Air Mixture

R. J. C. HARRIS,* PH.D., M.C.PATH.; G. NEGRONI,* M.D.

[WITH SPECIAL PLATE BETWEEN PAGES 640 AND 641]

Brit. med. J., 1967, 4, 637-641

There is no doubt that the tar produced by condensing cigarette smoke is carcinogenic for mice (see Day, 1967). However, lung epithelium differs from the skin and the condensate differs from fresh cigarette smoke in, for example, the absence of the gaseous components. It appeared worth while to us, therefore, to attempt to produce lung carcinomas in mice by allowing them to breathe a mixture of cigarette smoke and air for a prolonged period.

Stewart and Herrold (1962), in a "critique of experiments on attempts to induce cancer with tobacco derivatives," review negative mouse inhalation studies by Lorenz *et al.* (1943) and by Dunn (1943) using Strong A mice (a strain with a 90% spontaneous incidence of lung adenomas at 18 months of age). Essenberg (1952), however, had exposed the same strain of mice to cigarette smoke for 12 to 14 months in a ventilated chamber and *increased the incidence* of papillary adenocarcinomas in these mice.

Mühlbock (1955) also claimed to have *increased the incidence* of lung tumours in a hybrid 020×DBA strain of mouse by puffing smoke from cigarettes into a sealed cage every two hours each day.

We believed, however, that we should use a strain such as C57BL, which apparently have a predominant gene for resistance to the induction of lung tumours (Bloom and Falconer, 1964), and in which Peacock and Peacock (1966) described only one deep-seated spontaneous papillary adenoma in an 817-days-old male.

We were thus aware of many negative results, but were not convinced that these experiments had been conducted under the optimum conditions. In most cases (except for Lorenz *et al.*) there was no evidence that the animals were actually taking the smoke droplets into their lungs.

Most observers agree that lung cancer in man is multifactorial, and that of these other factors chronic respiratory disease (bronchitis, bronchiolitis, and chronic pneumonitis) is probably the most important.

There are two ways in which lung disease might contribute to the occurrence of lung cancer. Firstly, the diseased lung might be less able to prevent retention of particulate carcinogens, such as smoke droplets; and, secondly, infectious agents such as respiratory viruses and mycoplasma might themselves produce areas of cellular proliferation which were susceptible to the effects of inhaled chemical (or viral) carcinogens.

As early as 1920 Winternitz *et al.* predicted that, since the changes produced by influenza viruses in the lung looked preneoplastic, the 1919 influenza pandemic should give rise

to lung cancers later. Straub (1937) observed similar lesions in the lungs of influenza-virus-infected mice, but single infections had no apparent effect in increasing the lung cancer incidence in A (lung adenoma-prone) or C57BL (lung adenoma-resistant) mice (Steiner and Loosli, 1950).

The studies of Kotin and Falk (1956) and Kotin *et al.* (1958), however, have now confirmed for mice the earlier hypothesis. They found, for example, that following infection with PR-8 and Lee strains of influenza the bronchial and bronchiolar epithelium of mice regenerated after about seven days, but that peribronchial hyperplastic foci remained for some time. Sendai (parainfluenza) virus produced extensive necrosis of the epithelium, followed by regeneration. Kotin *et al.* infected mice successively with these strains, hoping that the squamous metaplasias so produced would "progress" to squamous carcinoma.

The carcinogen employed by Kotin *et al.* was a "smog" of ozonized hydrocarbons. The animals given both influenza and smog showed areas of squamous metaplasia in their lungs, and where keratin was detected preneoplastic or neoplastic changes were also observed. The experiments ran for 31 months (Kotin, 1966), and whereas no squamous cell carcinomas (but only pulmonary adenomas) were found in control "smog"- or "flu"-treated groups the smog and influenza groups had 10% squamous cell carcinomas (33/328 mice). Kotin, however, gave no data concerning the transplantability of these tumours. Leuchtenberger and Leuchtenberger (1966) observed very similar histology for influenza-infected mouse lung. When mice were subjected to cigarette smoke in a large chamber "atypical proliferative lesions" were described by the same authors, and when these treatments were combined the dysplastic lesions of the bronchi and bronchioles were similar to those produced by influenza alone, but in addition there were histopathological features in the lung "resembling bronchogenic carcinoma."

We proposed, therefore, to study also the effect of previous infection with influenza viruses on the induction of lung tumours by cigarette smoke in the C57BL mice. There were, of course, a number of control groups of mice. Thus in summary:

Group 1: Exposure to infection by one or more serologically non-overlapping influenza virus aerosols.

Group 2: Exposure to an aerosol of 3:4-benzpyrene.

Group 3: Exposure for life to a cigarette smoke and air mixture.

Group 4: A combination of group 1 followed by group 2.

Group 5: A combination of group 1 followed by group 3.

Group 6: Exposure to aerosols of the aqueous suspending media for the virus or benzpyrene.

* Division of Experimental Biology and Virology, Imperial Cancer Research Fund, Mill Hill, London N.W.7.

An interim account of the experiments is given by Harris and Negroni (1966).

Materials and Methods

Mice.—Young adult C57BL mice of both sexes, random bred in these laboratories, were used. Their past history showed that they had a long life-span, a low incidence of spontaneous tumours of all kinds (but *not* of leukaemia, see below), and a nil incidence of lung carcinomas, though *thymectomized* mice of a hybrid CBA × C57BL strain do develop these (D. M. V. Parrott, personal communication).

Aerosol Production.—The aerosol generator of "closed-circuit" design described by Henderson (1952) gave reproducible results not only for the influenza viruses but also for the benzo(a)pyrene.

Influenza Viruses.—Whereas Kotin and Falk (1956) had used PR-8, Lee, and Sendai, we employed W.S., Swine, Lee, and Singapore strains. These were grown from seed virus in RIF-free embryonated Brown Leghorn eggs from our own closed stock. These strains are antigenically unrelated, and the immune response of the mouse to one strain does not interfere with subsequent infection with another. Where mice were infected with more than one strain there was one month's interval between infection, so that interferon, which is believed to play a part in oncogenesis by other viruses, might not interfere with subsequent exposure to carcinogens. Small doses of the influenza viruses produce pneumonia in the mice but do not kill them, and so this optimum dose had to be determined by direct titration of each virus in mice and in the embryonated eggs. Intranasal instillation or aerosols were used, but the latter gave a more reproducible result and a more uniform distribution of lung lesions in the infected mice. Ten animals were exposed at a time, and the aerosol technique only was used for the combination treatment of mice with viruses and cigarette smoke.

Benzo(a)pyrene.—The aerosol was generated from a solution of 3:4 benzo(a)pyrene (32 mg.) in aqueous (0.5%) gelatin (250 ml.) containing 1:10,000 thiomersalate.

Cigarette Smoke Generator

In preliminary investigations groups of mice were exposed to a smoke and air mixture in a 400-litre plastic chamber originally designed by Amsco as a sterile isolator for housing germ-free mice. A standard smoking-engine (ITC) used for the production of tobacco smoke condensate was adapted by H. G. East and Co. (Sandy Lane West, Littlemore, Oxford) to produce a dilute mixture of fresh cigarette smoke in air. We chose a ratio of 1:39 (25 ml. smoke to 975 ml. air), which approximates to that of one puff of a cigarette in the tidal volume of the human lung.

Under equilibrium conditions (72 cigarettes smoked) the nicotine concentration in such a chamber reached 0.1 mg./l. (Harris and Negroni, 1966), which the mice tolerated for more than three hours without apparent distress. Moreover, analysis of their lungs after such a period failed to reveal the presence of nicotine. We concluded that, under conditions of high humidity—condensation was readily apparent on the walls of the chamber—the hygroscopic smoke droplets (containing the nicotine) had increased in size until they were too large to penetrate to the lower respiratory tract of the mice.

We then developed a new type of manifold (Fig. 1) based on the machine developed by Henderson (1952) for the exposure of animals to aerosols of bacteria, etc.

In such a machine a fresh cigarette smoke and air mixture is continuously passed across the noses of the mice, and the noses alone are in contact with it. The concentration of nicotine in the mixture was again about 0.1 mg./l. (and the CO

concentration—0.064 volume %—much less than that in the large chamber—0.16 volume %). Under these conditions we found that the mice were initially unable to tolerate exposure for more than 12 minutes,* and that when they died under exposure the nicotine content of their lungs varied between 14 and 17 µg. (Harris and Negroni, 1966).

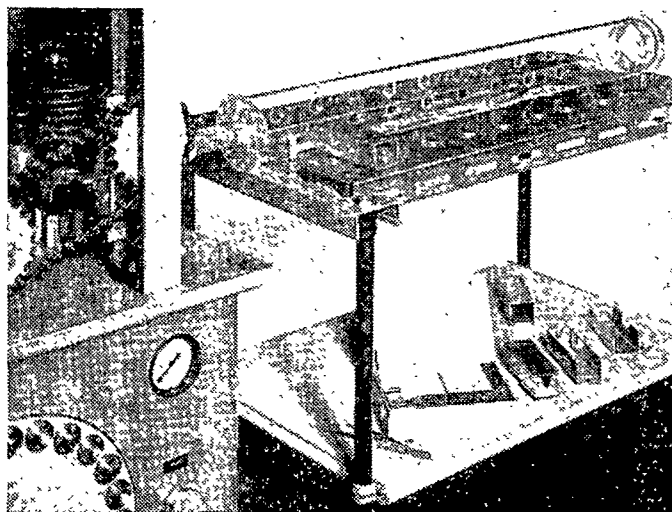


FIG. 1.—Plastic manifold for exposing mice to smoke and air mixture. The mice are held around the neck in metal boxes so that only their noses are in the smoke and air stream. The boxes are attached to the manifold magnetically. Reprinted by permission, from *Lung Tumours in Animals*, edited by L. Severi, University of Perugia, 1966.)

We then adopted the procedure of exposing 10 groups of 20 male and female C57BL mice to the smoke/air from 12 cigarettes (taking 12 minutes) every other day for the duration of their lives.

Controls

Control groups of equal numbers of each sex were housed under identical conditions and fed the same diet and water *ad libitum*. Each control group (50 males and 50 females) had been exposed to an aerosol of an aqueous suspending medium used to produce aerosols of influenza viruses (the results of these experiments will be separately reported) or of benzo(a)pyrene. Another control group consisted of 200 C57BL mice exposed on four occasions at monthly intervals (beginning when they were 5 months old) for a period of 10 minutes to an aerosol of 3:4-benzo(a)pyrene (32 mg.) in aqueous (0.5%) gelatin (250 ml.) containing 1:10,000 thiomersalate as a preservative in the Henderson machine. We calculated that in such an exposure the mice would receive in their lungs about as much 3:4-benzo(a)pyrene as they would receive from two years' exposure to the smoke and air mixture.

When each animal died a careful search was made to determine the cause of death. Sick animals were usually killed so that it might be possible to attempt transplantation (and thus to confirm malignancy) of any lung tumours produced.

Results

We had originally believed that strain C57BL had a low incidence of lymphosarcoma/leukaemia, but it became apparent, as the groups of mice aged, that the studies of others had probably not been continued in sufficiently elderly mice. Table I shows the cumulative incidence of lymphosarcoma/leukaemia in all groups for each sex.

Table II shows the cumulative incidence for all deaths, except for malignancies, for each sex in each group.

Mice also died from other tumours, and these are listed in Table III. Table IV (p. 640) shows the incidence of lung carcinomas in the six groups.

TABLE I.—Cumulative Percentage Mortality from Lymphosarcoma/Leukaemia

Group	Sex	Month													
		16	18	20	22	24	26	28	30	32	34	36	38		
Control	M	1	2	5	7	9	16	25	31	39	43	48	53		
	F	2	3	4	8	19	29	35	41	55	57	60	—		
Influenza	M	—	2	4	6	13	19	29	37	41	43	44	45		
	F	—	1	3	6	10	14	23	30	34	36	37	38		
Benzpyrene	M	—	—	1	4	6	16	23	27	34	40	41	42		
	F	1	1	3	5	10	20	31	43	52	60	64	66		
Smoking	M	4	8	8	15	25	31	37	46	57	65	69	70		
	F	2	3	4	8	11	22	28	32	35	39	41	44		
Influenza + benzpyrene	M	—	—	3	8	14	20	26	33	47	48	50	51		
	F	—	—	4	8	15	29	34	45	49	61	62	63		
Influenza + smoke	M	—	1	1	1	6	10	10	14	17	21	21	26		
	F	2	4	5	8	14	19	23	30	40	46	49	—		

TABLE II.—Cumulative Percentage Mortality from "Non-malignant" Diseases

Group	Sex	Month													
		16	18	20	22	24	26	28	30	32	34	36	38	40	
Control	M	6	7	10	17	20	21	23	27	29	32	33	35	37	
	F	10	15	16	19	21	21	26	26	28	28	32	35	—	
Influenza	M	8	10	11	14	21	24	28	32	34	36	39	39	—	
	F	16	19	22	25	28	30	34	37	38	39	40	40	—	
Benz-pyrene	M	22	23	26	28	33	37	41	44	50	57	58	59	—	
	F	11	13	14	20	23	26	29	32	34	36	38	39	—	
Smoking	M	5	8	13	15	16	21	21	23	25	26	—	—	—	
	F	8	8	11	11	16	21	36	42	48	48	49	50	51	
Influenza + benz-pyrene	M	2	5	5	7	8	15	20	23	26	31	35	37	—	
	F	5	9	9	10	13	15	16	23	25	27	30	31	—	
Influenza + smoke	M	6	6	7	11	15	18	24	29	35	40	43	45	47	
	F	5	6	6	7	10	16	18	19	28	30	31	31	—	

TABLE III.—Incidence of Tumours (Other than Lymphosarcoma/Leukaemia or Lung Carcinomas) in Experimental and Control Groups

Group	No.		Hepatomas		Carcinomas		Sarcomas	
	M	F	M	F	M	F	M	F
Influenza ..	342	340	23 (29)	10 (25)	1 (18)	3 (28)	1 (27)	6 (26)
Benzpyrene ..	100	100	14 (29)	5 (33)	—	—	—	1 (34)
Smoking ..	100	100	3 (25)	6 (25)	1 (30)	—	1 (30)	1 (16)
Influenza + benzpyrene	100	100	3 (29)	6 (26)	—	—	—	—
Influenza + smoke ..	72	83	5 (30)	3 (25)	—	1 (20)	—	1 (26)
Control ..	100	100	5 (31)	6 (28)	1 (20)	2 (18; 33)	1 (30)	1 (31)

Figures in parentheses are mean ages at detection in months.

Pathology

The following account of the pathological observations is reported in two sections: the first refers to the changes, other than lung lesions, observed in mice belonging to the various groups. The second is a detailed account of the macroscopic and microscopical changes in the lungs of mice which are summarized according to the treatment the animals received.

Lesions other than those Found in the Lungs

All the mice, no matter to which group they belonged, showed various lesions other than lung lesions. These, however, were common to all groups, and occurred quite independently of the treatment which the mice received. C57BL mice were chosen because, according to the current literature, they are supposedly free from tumours. This proved to be untrue, as lymphosarcoma/leukaemia occurred in a very high incidence in all groups of mice (Table I).

The incidence was the same in all groups, if one takes into account only animals which survived more than 20 months. A higher mortality rate before this age was observed in male mice treated with benzpyrene (Table II) and in females treated with influenza viruses (Table II). The incidence of leukaemia appeared to be lower in these groups than in the control group (Table II), but only because in these groups the mortality rate was higher up to 20 months of age.

Hepatitis of the type described by Tyzzer (1917), and more recently and carefully studied by Craigie (1966), in these laboratories was one of the major causes of death in one group. In other instances, enteritis, probably due to Tyzzer's micro-organism, was the cause of death. Salmonellosis does not occur in these laboratories.

Pneumonia, probably of viral origin, occurred sporadically. Urinary retention and cystic kidneys also occurred infrequently.

Tumours, other than leukaemia, were also observed—hepatomas, subcutaneous sarcomas, and carcinomas (Table III). Hepatomas in both male and female were the most frequent. Skin sarcomas and carcinomas, some of them originating from the skin glands, were also observed in very low incidence.

It is worth while stressing again that all these tumours occurred with equal frequency in mice which had received any of the treatments.

Lesions Found in the Lungs

This section refers to the lung pathology, and this is described separately according to the treatment each group of mice received.

Controls (Group 6)

The only lung lesions observed were those due to pneumonia, probably caused by viruses.

Mice Exposed to Cigarette Smoke (Group 3)

This group showed pneumonia occasionally, with an incidence not higher than that observed in the controls. Mice which had been exposed to cigarette smoke for a long time often showed emphysema. Marked peribronchial and perivascular infiltration with lymphocytes was seen, and this independently of the presence of tumours. Hyperplastic lesions similar to those described by Leuchtenberger and Leuchtenberger (1966) were not seen even in mice which survived smoking over a period of more than 30 months.

We did observe, however, a lesion which from its characteristics could be classified as hyperplastic. This had already been described by Kotin and Falk in mice which had breathed artificial smog (see Kotin, 1966). We have observed this in one mouse out of the 200 exposed to cigarette smoke. Macroscopically it was a small hard white nodule, 1 to 2 mm. in diameter, protruding from the surface of the lung. In this group it occurred alone, but may be found more frequently with the alveologenic carcinoma which is described below (for the influenza and smoke group). Microscopically they are little different from pearls of squamous cell carcinoma, having the pathological appearance of large cells and large empty nuclei, arranged in whorls with various layers of fibrous material which stains red in the H. and E. preparations. This fibrous material is also arranged in whorls. Despite the similarity of these lesions to highly malignant lung tumours in man we have been unable to transplant them serially from one mouse to another.

Adenocarcinomas occurred in eight mice exposed to cigarette smoke. Unlike the pearls described above some of these were

serially transplantable in mice, and to date three have survived respectively for 33, 51, and 67 transplant generations.

In the mice in which they originated they appeared as white round nodules, with a diameter of up to 10 mm., protruding from the lung tissue. Metastases were found in the chest wall or parietal pleura. Microscopically they are identical to those described by Andervont (1937) and classified as alveogenic carcinomas. The cells which compose these tumours are cuboid or columnar in shape and almost uniform in size and staining reaction. They contain round or oval nuclei with loose chromatin, and nucleoli are frequently seen. The cells are often present in mitosis. The tumour cells often form a continuous sheet, which distinguishes them from the adenomas which occur spontaneously, for example, in Strong A mice. In these adenomas the cells arrange themselves so as to give the appearance of a glandular structure. Infrequently we also observed these adenomas (Special Plate, Figs. 2 and 3).

Mice Infected with Influenza Viruses (Group 1)

These mice did not show the keratinizing lesions described above. Fifteen of them (Tables IV and V) have shown adenocarcinomas identical to those described in the group of mice exposed to cigarette smoke. Eight of these tumours were transplantable, and six of them have now undergone respectively 15, 18, 26, 71, 83, and 93 transplant generations (Special Plate, Figs. 4 and 5).

TABLE IV.—Incidence of Lung Carcinomas in C57BL Mice

Treatment	Number		Lung Carcinomas	
	M	F	M	F
Influenza	342	340	12 (26, 27, 28, 29, 30 (3), 31 (2), 32, 33 (2))	3 (29, 30, 34)
Benzpyrene	100	100	1 (25)	1 (34)
Smoking	100	100	4 (10, 27, 28, 29)	4 (11, 18, 21, 27)
Influenza + benzpyrene ..	100	100	3 (21, 28, 37)	—
Influenza + smoke ..	72	83	1* (18)	2* (23, 27)
Controls	100	100	0	0

Figures in parentheses are ages of mice at detection of tumour (months).
* One other male and three other female mice had keratinizing preneoplastic lesions in the lungs.

TABLE V.—Lung Carcinomas in Relation to the Strain(s) of Influenza Virus Used

Sex	Age of Mouse (months)	Influenza Strain(s) Used
Females		
1	29	W.S.
2	30	Singapore, Lee, Swine, W.S.
3	34	Singapore
Males		
1	26	Singapore, Lee, Swine, W.S.
2	27	Swine
3	28	Singapore, Lee, Swine, W.S.
4	29	Singapore, Lee, Swine, W.S.
5	30	Singapore, Lee, Swine, W.S.
6	30	Lee
7	30	Swine
8	31	Singapore
9	31	Lee
10	32	Swine
11	33	Lee
12	33	Lee, Swine, W.S., Singapore

There is one lesion which is characteristic of mice infected with influenza virus and surviving the acute disease. These lesions have already been described by Kotin and Falk (1956) and by us (Harris and Negroni, 1966). They occur in almost every mouse infected with influenza viruses, and are of a hyperplastic type. Macroscopically they differ from the keratinizing lesion (or the adenocarcinomas), as they do not protrude from the lung surface, which, however, acquires irregularities. They may appear as well-defined nodules, but usually they have a very irregular edge. Microscopically they consist of cells characteristic of epithelial cells, which replace the alveolar tissue. They probably originate from the extension of the bronchial epithelium in the alveolar wall, and the arrangement of the

cells, disposed in one or two layers, seems to fill the old alveolar structure which they have replaced. When these lesions become infected pneumonia follows, with heavy infiltration of polynuclear cells. The extent of these lesions is directly proportional to the number of infections and to the dose of virus used for each infection, as may be demonstrated when the animals die or are killed, largely after recovery from the acute pneumonia caused by the influenza. However, if the animals die or are killed long after the virus infection there is no direct relation between the number and extent of the lesions and the virus dose or number of infections which the animal has received (Special Plate, Fig. 6).

Thus it appears that these lesions are progressive, though we have no evidence that they are malignant, since all attempts at transplantation have failed.

Mice Exposed to Benzpyrene (Group 2)

Only two mice have shown an adenocarcinoma as described above. The tumour arising in the female mouse was transplantable, and is now in its fifty-fifth generation.

Mice Treated with Benzpyrene and Infected with Influenza Viruses (Group 4)

These again show the typical metaplastic lesions which have already been described for mice infected with influenza viruses. These lesions occur with the same incidence. Three male mice had malignant adenocarcinomas of the lungs, all of which have been transplanted serially for 5, 10, and 20 generations respectively.

Mice Infected with Influenza Viruses and Cigarette Smoke (Group 5)

The metaplastic nodules described for mice infected with influenza virus only were also observed in animals of this group, with equal incidence (Special Plate, Fig. 7). Six have shown the squamous pearls described for mice exposed to cigarette smoke only (Special Plate, Fig. 8), and these had adenocarcinomas similar to those described in mice infected with influenza virus alone or exposed to smoke alone. One of these is in its eighty-third transplant generation.

In one instance in which this lesion occurred together with an adenocarcinoma pearls were detected in the tumour of the first transplant generation, but these were no longer found in subsequent transplantations.

Features of the Transplanted Tumours

Many of the adenocarcinomas that have been described as occurring in mice treated in these various ways grow readily when transplanted. The great majority maintain the histological features of the original tumour. Some of them, however, and mainly those originating in mice treated with benzpyrene or cigarette smoke, undergo changes. When this occurs the epithelial cells no longer form a continuous sheet; instead, they separate into clusters divided by well-developed connective tissue, which has pathological features. The tumour then acquires the appearance of a scirrhous carcinoma.

Discussion

These data indicate the potential carcinogenicity of cigarette smoke and air mixture for the lungs of experimental mice. The animals are submitted to both the liquid and the gas

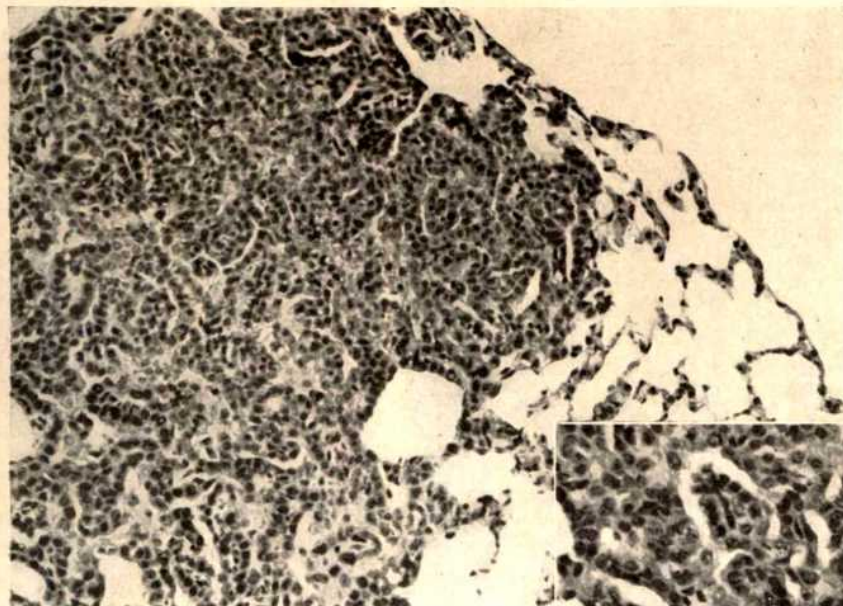


FIG. 2.—Lung adenoma in a 22-months-old mouse exposed to smoke and air mixture. These lesions are benign. (H. and E. $\times 170$.)

FIG. 3.—Detail of Fig. 2. (H. and E. $\times 280$.)

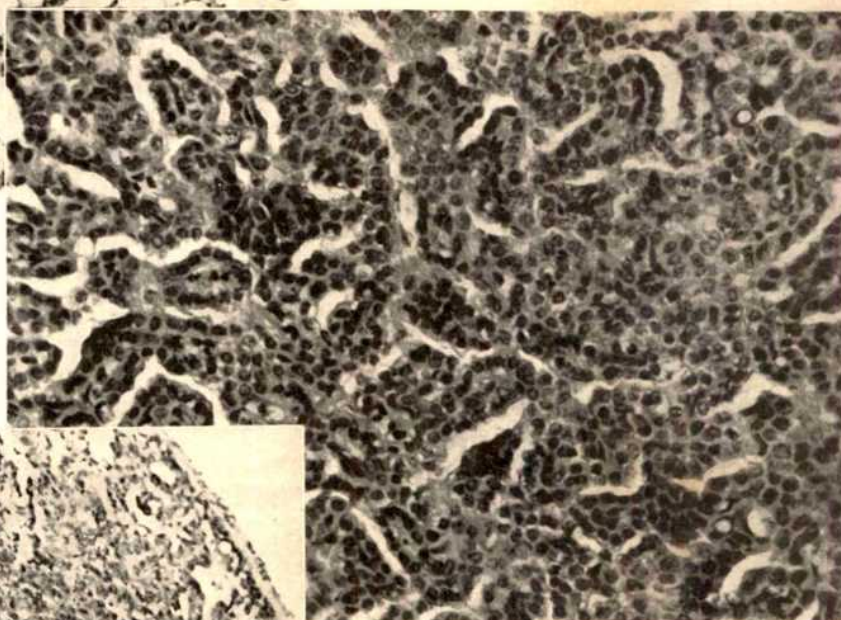


FIG. 4.—Lung adenocarcinoma in a 33-months-old mouse, following influenza infection. (H. and E. $\times 85$.)

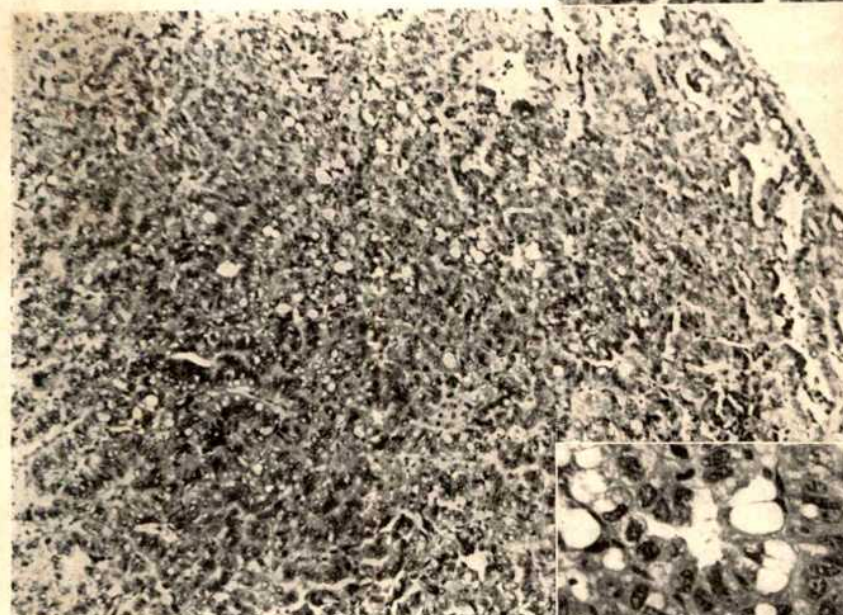
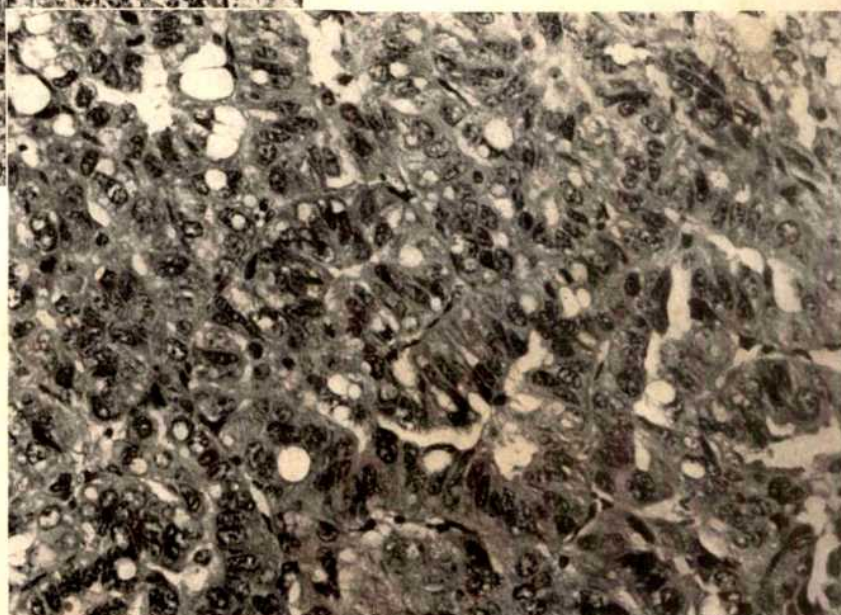


FIG. 5.—Detail of Fig. 4. (H. and E. $\times 280$.)



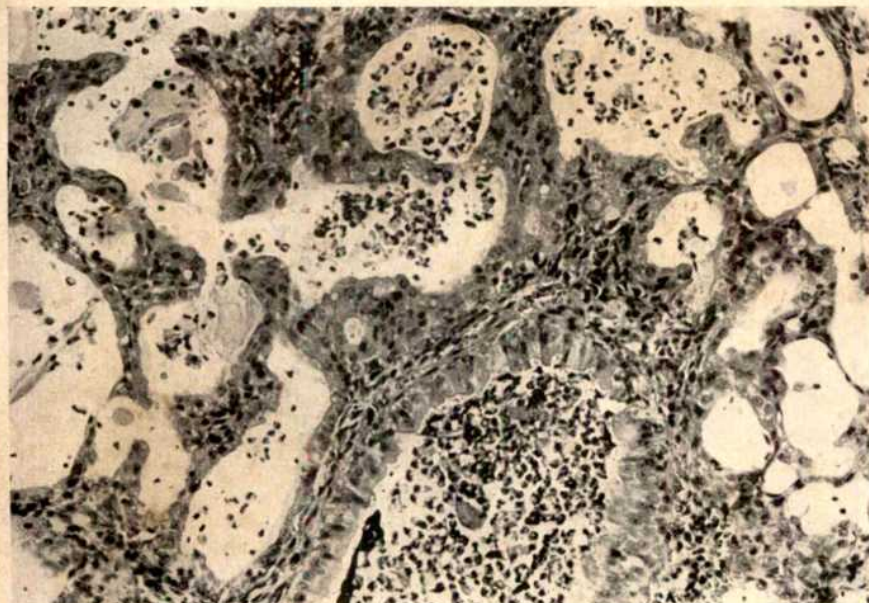


FIG. 6.—A metaplastic lung nodule originally induced by influenza in a 32-months-old mouse. Note the polynucleated white blood cells inside a bronchus and forming abscesses in the parenchyma. (H. and E. $\times 176$.)

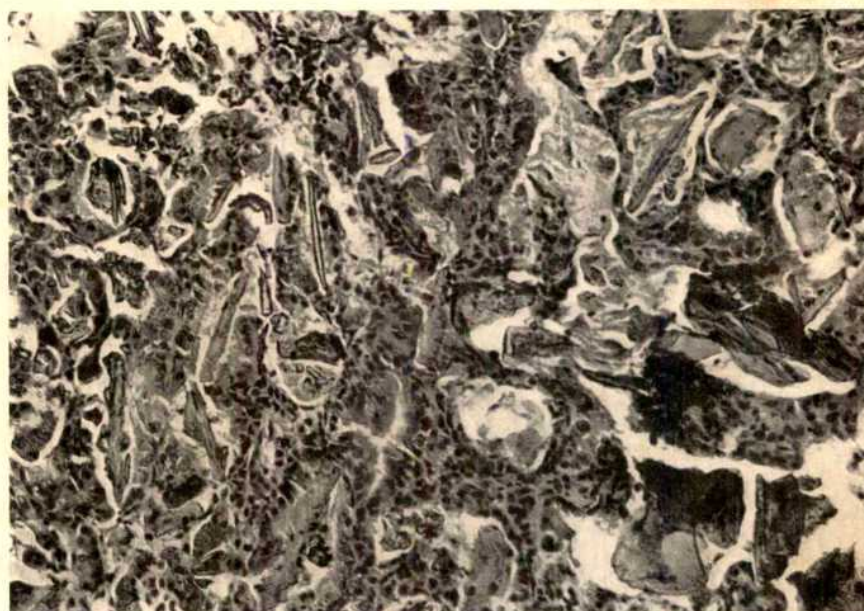


FIG. 7.—Metaplastic nodule in the lung of a 31-months-old mouse, previously infected with influenza and then exposed to smoke and air mixture. Note the crystalline protein structure in spaces between the metaplastic cells. (H. and E. $\times 165$.)

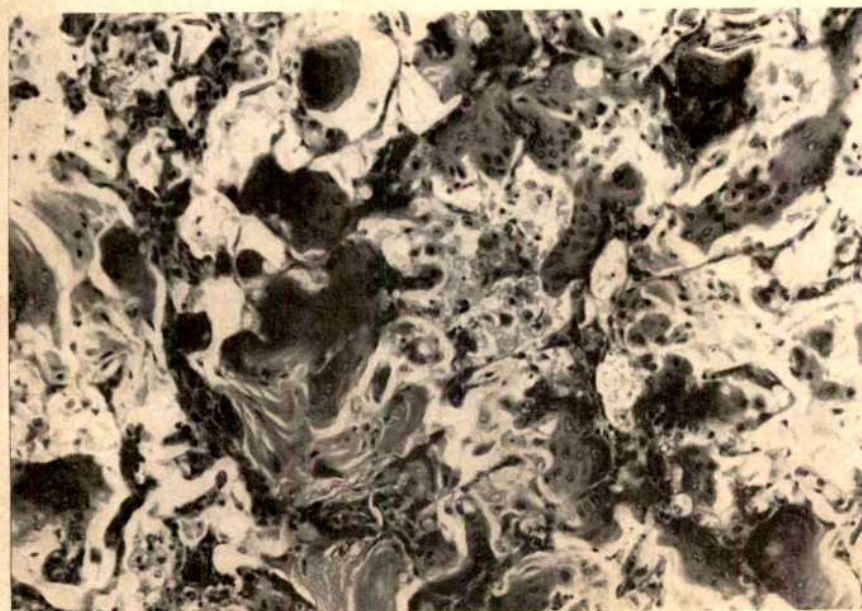


FIG. 8.—Keratinizing lesions in the lung of a 23-months-old mouse previously infected with influenza and then exposed to smoke and air mixture. Note the resemblance to the malignant keratinizing tumour of man. (H. and E. $\times 165$.)

phases of the smoke—an advantage over the technique of skin-painting with smoke condensate. The disadvantages from the point of view of an industry looking for a "safe" cigarette are manifold. It takes at least three years to make one test, and with the numbers of lung tumours so far produced it would be difficult to compare the carcinogenicity of different cigarette tobaccos. Moreover, as many other investigators have pointed out, the mouse lung cannot be equated histologically with the human lung, and so "degrees of carcinogenicity" derived in one system may have no validity for the other. Other tests may have to be used, though if the C57BL mice had been submitted more intensively to the smoke—for example, twice a day instead of once every two days—the lung tumour yield might well have been increased and the latent period decreased.

The smoke may not be the only cause of lung tumours, and endogenous factors such as latent viruses may be required.

It is difficult to explain the induction of lung tumours in C57BL mice by influenza viruses alone. It may be that these viruses are weakly oncogenic per se, or that there is a synergism between them and a natural but latent chemical or viral lung carcinogen in the mice, or that the influenza virus stocks were contaminated with a weakly oncogenic tumour virus for mouse lung. Polyoma would be excluded as a contaminant because the virus stocks were produced in RIF-free embryonated chicken eggs in which polyoma virus does not grow. If the third suggestion is correct, then all the virus stocks contain this virus, since lung tumours appeared in groups treated with some or all of the viruses (Table V). Moreover, since the incidence of other tumours in the influenza groups of mice was higher in the females than in the males (Table III), the hypothetical contaminant would be a specific weak lung carcinogen for males, but might produce other tumours in females. It is more probable that the second explanation is correct, and that the influenza infection "releases" a virus (such as polyoma) or a mycoplasma which is the immediate cause of the tumours.

We are currently investigating possible synergism between such chemical carcinogens as dimethylnitrosamine and cigarette smoke. If these lung tumours arose by some indirect mechanism—for example, the stimulation of a latent virus (such as polyoma)—then concomitantly one needs to postulate a general reduction in immunity which allows the "release" of virus-transformed tumour cells. It is necessary to have both steps because C57BL mice, even when newborn, are poorly responsive to large inocula of polyoma virus (Jahkola, 1965; Chang and Hildemann, 1964), though thymectomized animals (with reduced immunity) show a much higher yield of tumours. Moreover, the tumours induced in thymectomized mice by polyoma virus involve the salivary glands, kidney, bone, and hair follicles and *not* the lung.

Summary

C57BL mice subjected to breathing a cigarette smoke and air mixture for 12 minutes every other day for the greater part of their lives develop a low incidence (4%) of alveologenic carcinomas of the lung. Control animals subjected to non-specific lung damage did not develop tumours, but a group of 200 animals briefly exposed on four occasions to an aerosol of 3:4-benzopyrene developed two lung carcinomas. Attempts to influence lung tumour yield by infecting mice sequentially with influenza viruses, followed by exposure to benzopyrene or cigarette smoke and air mixture, showed that influenza viruses alone gave about 2% alveologenic carcinomas in C57BL mice—an incidence which was not exceeded in the other groups.

We acknowledge with gratitude the assistance of the Misses Ludgate, Coughlan, and Tomic and Mr. D. Stoddart in the conduct of these experiments. The apparatus was built by Mr. W. Caunt, and Mr. R. Baker has maintained it. The sections were prepared by Mrs. M. Phillips, and Mr. A. J. Pringle took the photographs.

We are grateful to the Tobacco Research Council and its director, Mr. G. F. Todd, for the provision of the cigarettes, and for advice on the smoking procedure.

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Spread of Hospital Staphylococci in Healthy Families—a Study from General Practice

Report* to the M.R.C. Committee for Research in General Practice

Brit. med. J., 1967, 4, 642-644

Babies born in hospital become carriers of *Staphylococcus aureus* very early in life (Hurst, 1957). The groin and umbilical stump are usually colonized first (Jellard, 1957; Gillespie *et al.*, 1958) but soon tend to lose the organism; in the nose staphylococci settle rather later but are more firmly established, and in some maternity units over 90% of the babies are nasal carriers of *Staph. aureus* on the day they go home (Hurst, 1957). Staphylococci that colonize these infants are derived much more often from hospital sources than from the infants' own mothers (Barber *et al.*, 1953) and are often antibiotic-resistant strains known to cause outbreaks of sepsis in hospitals. Their introduction into private homes might therefore lead to nasal colonization and sepsis in other members of the family. This has sometimes happened (Wentworth *et al.*, 1958; Hurst and Grossman, 1960), but these incidents occurred at the time when *Staph. aureus* of phage type 80/81 was spreading freely and causing many outbreaks of sepsis in maternity units. Later studies suggested that babies lost their hospital-acquired staphylococci quite soon after going home (Miller *et al.*, 1962; Hurst *et al.*, 1964) and that the incidence of sepsis in their families was much the same as in control families (Oliver *et al.*, 1964); Payne *et al.* (1965) found that staphylococci which were highly communicable in hospital spread less freely in the different environment of the private home.

The general practitioner is concerned to know which of these apparently opposing views is usually correct. He would like to know the answers to three questions about the behaviour of hospital staphylococci after their introduction into otherwise healthy families: do they spread to the noses of the family as they spread to other patients in hospital; do they have any special tendency to cause septic lesions; and what precautions, if any, should the family doctor take to protect families from the potentially dangerous strains that the babies, and to a lesser extent their mothers, bring from hospital?

This survey was an attempt to answer these questions. The plan was to determine the extent to which new strains of *Staph. aureus* were introduced into families by infants and mothers returning from maternity units and spread by them to other members of the family, and to record cases of sepsis caused by these organisms. The findings were compared with the spread of presumed non-hospital staphylococci introduced by other members of the same families. Comparative studies

were also made on organisms introduced into families where a baby was born at home.

Material and Methods

A group of general practitioners—24 in Edinburgh and 25 in North-east England—filled in a questionnaire for every pregnancy booked for delivery during a period of six months. The details of each family were then analysed and families were chosen by a statistician to give equal numbers of hospital and home deliveries. The statistician also managed to ensure that the number of families chosen from the two areas was about equal, that the social status of the families in the hospital and the home group was comparable, and that there were enough schoolchildren in the families for a study of the part they played as introducers of non-hospital staphylococci.

Of the 1,780 families considered 220 were chosen, but 97 were unable to participate because of miscarriage, removal from the district, illness, and other reasons. Thus 123 families were studied and swabbed—52 in Edinburgh and 71 in North-east England. These families contained 615 persons whose noses were swabbed regularly. The swabs from 34 lodgers or occasional visitors had to be discarded because so many had moved out of the area; but, apart from this, co-operation was extremely good and at least 18 swabs were obtained from every member of all the families except five. Even in these five families there were enough swabs for satisfactory analysis.

Once a family was regarded as suitable the practitioner was notified, and with the co-operation of the family, the local authority, the health visitors, and the local bacteriological laboratory nasal swabs were taken every fortnight from all occupants of the house. Swabbing started four to six weeks before the baby was due and continued every two weeks until the baby was a year old. Septic lesions in any members of the family were reported to the doctor and swabs taken from all those with accessible pus.

One dry cotton-wool swab was used for both anterior nares of each subject. The swabs were sent to one laboratory in Edinburgh and six in North-east England. All swabs reached a laboratory within 24 hours, and most of them very much sooner than this. Swabs were plated, without preliminary enrichment, on blood-agar or milk-nutrient-agar. The plates were examined after overnight incubation at 37° C., and, when necessary, again after 24 hours at room temperature to increase pigment production. Colonies of bacteria thought to be *Staph. aureus* were tested for coagulase production by the slide technique, and a tube test was also used in doubtful cases.

All colonies of *Staph. aureus*—that is, coagulase-positive colonies—were tested for antibiotic sensitivity and were phage-typed. Some of the laboratories to which specimens were sent were not equipped to do phage-typing, and sent cultures to the typing centres that they normally used. Phage-typing methods and the criteria for identifying different strains were those specified by Blair and Williams (1961). In a few difficult cases antibiotic-sensitivity patterns were used to clarify the evidence of phage-typing.

* *Co-operating Bacteriologists.*—Dr. R. Blowers (Middlesbrough); Dr. P. B. Crone (Sunderland), Dr. J. C. Gould (Edinburgh), Dr. Mitchell (North Shields), Dr. A. E. Wright (Newcastle). Statistician: Mr. Stanley Sklaroff.

Co-operating General Practitioners.—*North-east England:* Drs. W. Abels, H. G. Barnes, M. Bell, G. Birch, J. Blackledge, W. A. Brown, F. E. Butterfield, J. Carmichael, A. Colling, S. Croft, P. Edmundson, G. R. Freedman, I. C. Fuller, A. Graham, N. Gofton, G. H. Hardie, G. L. Hindson, J. Hobbs, K. Hodgkin, A. A. Johnstone, J. D. Little, W. Moonie, A. M. Porteous, F. Roythorne, A. Smith, D. Smith, D. S. Strachan, G. Stout, J. Whewell, R. H. Wattsford. *Edinburgh:* Drs. E. S. Blackadder, D. Carter, D. Cruickshank, R. M. Dean, S. M. Dean, V. W. Delorey, H. P. Dinwoodie, W. A. Elliot, S. L. Forrest, E. V. Kuenssberg, A. Large, A. Leadbitter, S. Lipetz, D. McVie, D. McLean, I. McRobbie, M. Moss, A. P. Motley, J. E. M. Munro, J. Simpson, I. H. Stokoe, R. Scott, W. P. Thomson, J. Walker.

Report prepared by Dr. R. Blowers, Dr. K. Hodgkin, and Mr. Stanley Sklaroff (statistician).

Results

The fortnightly swabs from the noses (and lesions) of 615 persons in 123 different families were analysed. Into these families 125 babies were introduced—63 from hospital and 62 from home deliveries.

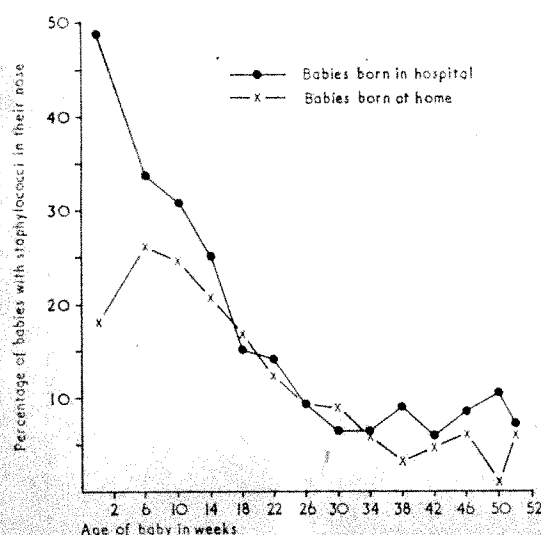
General Pattern of *Staph. aureus* Carriage

The widespread existence of *Staph. aureus* in normal families was confirmed. *Staph. aureus* was present at some time in 119 (97%) of the families and in 475 (77%) of persons. Table I shows the carriage rates for different family members. We have distinguished between "temporary" and "frequent" carriers—defined arbitrarily as those from whom *Staph. aureus* was recovered on less than and more than 20% of swabs respectively. Twenty-three per cent. of persons never carried *Staph. aureus* in their noses, 40% were temporary carriers, and 37% were frequent carriers (Table I). Gould and McKillop (1954) obtained almost identical results from a study of 520 persons.

TABLE I.—Nasal Carriage of *Staph. aureus* in Different Members of the Family

Group	No. Examined	Non-carriers		Temporary Carriers (<20% swabs positive)		Frequent Carriers (>20% swabs positive)	
		No.	%	No.	%	No.	%
Fathers ..	123	31	25	45	37	47	38
Mothers ..	123	26	21	45	37	52	42
Schoolchildren ..	132	24	18	47	36	61	46
Pre-schoolchildren ..	112	28	25	44	39	40	36
Newborn infants ..	125	31	25	63	50	31	25
All except newborn infants ..	490	109	22	181	37	200	41
All persons ..	615	140	23	244	40	231	37

There was no significant difference between the carriage rates of the various family members other than the newborn babies. In this group temporary carriage was more common than in any other family member, while frequent carriage was less common. The reason for this difference is shown in the Chart. The babies' carriage rates were high during the first few weeks after birth but declined to very low levels by the end of the year. From the eighteenth week onwards the mean carriage rate for all babies was only 7.6%. The Chart also shows great differences between the initial carriage rates of babies born in hospital and those born at home.



Staphylococcal carriage rates for the first year of life in babies born in hospital and in those born at home.

Staph. aureus Acquisition by Babies in Hospital

During the first few weeks of life *Staph. aureus* carriage was more common in babies born in hospital than in those born at home, but after 18 weeks there was no significant difference between the two groups (see Chart).

Staph. aureus was isolated from 31 (49%) of the 63 babies arriving home from hospital. Phage-typing and antibiotic sensitivity patterns suggested that in every case the strain was one that had not previously been present in the household, so we presumed, as other workers have found—for example, Barber *et al.* (1953) and Cook *et al.* (1958)—that the babies acquired the staphylococci from hospital sources. Thus there were 31 families in which hospital strains of *Staph. aureus* were introduced by a baby and had the opportunity to spread to other members of the family.

Effect of Introducing a Newborn Baby into a Family

After the three initial fortnightly swabbings had indicated the family pattern of *Staph. aureus* carriage, a new strain was reckoned to have been introduced if it had not been previously isolated from any member. The person responsible for the introduction was assumed to be the member who first yielded the new strain. Sometimes a new strain was first isolated from two members of the same family in the same fortnight; both were then counted as "introducers." Of the babies who came home after birth in hospital, 31 (49%) introduced new strains of staphylococci into their families; this was more than twice the rate of introduction by other members of the family (Table II).

TABLE II.—Introduction and Spread of New Strains of *Staph. aureus* in 123 Families

	Place of Confinement	Newborn Infants		Mothers		Members of Family other than Infants		All Persons	
		No.	%	No.	%	No.	%	No.	%
No. of individuals examined	Hospital	63		62		233		296	
	Home	62		61		257		319	
No. of individuals introducing new strain	Hospital	31	49	21	34	55	24	86	29
	Home	14*	23	15	25	61	24	75	24
No. of these individuals transmitting new strain to another member of family	Hospital	11	36	12	57	26	47	37	43
	Home	2	14	8	53	30	49	32	43

* See note in text.

Of the babies born at home 14 (23%) appear to have introduced staphylococci into the family. In two instances this was a "shared" introduction and the baby may not have been responsible. In one instance the home-born baby was admitted to hospital, and this was the probable source of the new strain. The remainder of new strains that were introduced by home-born babies probably resulted from fondling by neighbours and friends.

Of the new strains introduced by non-infant members of the family (presumably from non-hospital sources), just under half (49% and 47% in the home and the hospital groups respectively) spread to other members of the family (Table II). The 31 hospital strains introduced by infants showed no tendency to spread more freely than this; indeed, in only 11 (36%) was there any evidence from phage-typing that it had spread to other family members. These hospital strains were transmitted mainly to the mothers of the infants and to a less extent to the fathers and school-age siblings.

In 82 families one or more individuals were carrying staphylococci before the baby arrived. In 45 (56%) of these the baby picked up the family strain; Table III shows when this occurred. The percentage acquiring the original family strain

of staphylococcus was the same for babies born in hospital as for babies delivered at home.

TABLE III.—45 Babies (Hospital and Home-born) Who Picked up a Family Strain of *Staph. aureus*; Showing the Age (in Weeks) When the Pre-existing Family Strain Was First Isolated from the Baby's Nose

Age (weeks)	2	4	6	8	10	12	14	16-22	24	26-34	36
No.	14	10	8	4	3	3	1		1		1

These 45 babies include those born in hospital and those born at home.

Thus our evidence suggests that staphylococci brought home by hospital-born babies were soon replaced by family strains and that they showed, if anything, less capacity to spread within the family than staphylococci introduced from other sources.

Incidence of *Staph. aureus* Sepsis

Possible staphylococcal lesions occurred in 50 (41%) of the 123 families. Twenty-eight (23%) of the 123 families and 43 (7%) of the 615 individuals in the survey had lesions that yielded *Staph. aureus* (11 boils; 7 septic spots; 4 impetigo; 4 infected eczema; 3 septic wounds, 2 each of whitlow, conjunctivitis, and sty; 1 each of paronychia, ophthalmia neonatorum, and nappy rash; and 5 unspecified).

Phage-typing failed to show any special tendency for staphylococci from hospital to cause lesions. *In only one instance was a lesion shown to be of a similar strain to that introduced into the family by a hospital-born baby.*

Relation between Nasal Carriage and Septic Lesions

Of the 43 persons with *Staph. aureus* lesions there were 34 in whom clear-cut phage types enabled a comparison to be made with nasal strains carried by other family members. In 24 (70%) of these the strain found in the lesion was the same as that in the patient's nose; in 5 (15%) it was the same as that in the nose of another member of the family; and in 5 (15%) it was not associated with any nasal strain or with any other manifestation in the family. In families with staphylococcal lesions nasal carriage was somewhat more common than in families without lesions (45% as compared with 36%).

Nasal carriage rates in families with lesions were the same before the appearance of the lesion as after it, suggesting that lesions followed rather than caused the higher nasal carriage rates.

Discussion

This work confirms the many earlier studies on the frequency of *Staph. aureus* nasal carriage. Of the 615 persons studied in the survey 40% were classed as "temporary" carriers and another 37% as "frequent" carriers. During their first few weeks of life newborn babies had the highest carriage rates, but these quickly declined to a mean rate of 7.6% from the eighteenth week after birth onwards. The reason for this very low rate for babies once they have become established members of the family is not clear; perhaps it is due to unknown immunological mechanisms or perhaps to their having more thorough washing and fewer outside contacts than the rest of the family. Schoolchildren, who had the highest carriage rates, usually wash the least thoroughly and have many close outside contacts.

We have also confirmed the earlier reports that newborn babies acquire *Staph. aureus* much more often in hospital than at home. At the time of the first swabbings the carriage rates were 49% for babies born in hospital and 18% for babies born at home, but by the eighteenth week there was no difference between the two groups (see Chart). The rate for hospital-born babies is relatively low when compared with the rates obtained

by other workers. This could be a result of the slight delay between the time of discharge and the babies' first swabbing. It might also reflect the general trend towards lower nasal carriage rates in hospital-born babies that has been noted since 1960.

There are two possible explanations for the difference between carriage rates in the hospital and those in home-born babies: one is that staphylococci inhabiting hospitals are strains of greater inherent "communicability"; the other is that infants in hospital are exposed to a greater concentration of staphylococci and more opportunities for acquiring them. Our observations do not support the first of these possibilities; indeed, strains brought into the family by hospital-born babies spread within the family rather less often than strains introduced by other members from (presumably) non-hospital sources.

Staphylococcal lesions occurred with what seems to be the usual frequency. We detected them in 7% of our subjects; Kay (1962) reported a sepsis rate of 9% from a general practice in Manchester. But of the 34 lesions in our series from which typable strains of *Staph. aureus* were recovered, in only one had the organism been brought into the family by a hospital-born baby.

Families with staphylococcal lesions had higher nasal carriage rates than families without, and it has already been noted that the lesions appeared to be the result and not the cause of the high carriage rate.

It therefore seems that the questions we set out to study may be answered thus: (1) hospital staphylococci have no special tendency to spread in ordinary homes; (2) they have no special tendency to cause septic lesions outside hospitals; and therefore (3) the family doctor need make no special arrangements to protect families from staphylococci brought home from hospital by mothers and infants.

Summary

Noses and septic lesions of 615 persons in 123 families were swabbed every fortnight for four to six weeks before and for 52 weeks after the birth of a baby. Sixty-two babies were born at home and 63 at hospital. During the first 18 weeks of life babies born in hospital had higher *Staphylococcus aureus* carriage rates than babies born at home.

Hospital staphylococci brought home by babies were no more apt than were "domestic" strains to spread within the family or to cause septic lesions.

Staphylococcal lesions appeared to be the result rather than the cause of high nasal carriage rates within a family.

Thanks are due to the medical officers and health visitors of the following areas: Edinburgh, Newcastle, Northumberland, North Shields, Sunderland, Durham, Stockton, Middlesbrough, and Redcar.

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Prolonged Survival of Liver Transplants in the Pig*

R. Y. CALNE,* M.S., F.R.C.S.; H. J. O. WHITE, M.CHIR., F.R.C.S.; D. E. YOFFA, F.R.A.C.S.
R. M. BINNS, VET.M.B., M.R.C.V.S.; R. R. MAGINN, M.D., F.A.C.S.; R. M. HERBERTSON, M.A., M.D., M.C.PATH.
P. R. MILLARD, M.B., B.S., M.R.C.S.; V. P. MOLINA, M.D.; D. R. DAVIS

Brit. med. J., 1967, 4, 645-648

Our preliminary experience with orthotopic liver transplantation in the pig has been reported (Calne *et al.*, 1967). Out of 19 animals operated on 13 survived the procedure and six lived for a week or more. Focal necrosis of liver cells and round-cell infiltration in the portal triads of these six transplants was thought to represent evidence of a weak rejection process. One pig died after seven months from intestinal obstruction with minimal evidence of liver damage. Three pigs developed severe gastrointestinal haemorrhage due to mucosa erosions of the stomach and duodenum. We were impressed with the relatively mild rejection occurring in liver transplants in the pig, and it is the purpose of this paper to present our further

10%. This technique will be published in detail elsewhere. In brief, halothane anaesthesia is used for donor and recipient without any premedication. The donor liver is cooled by an infusion of cold physiological saline through the portal vein. When the liver has been removed from the recipient animal the blood from the inferior vena cava and portal vein is shunted to the superior vena cava via two separate shunts to the right and left jugular veins respectively (Fig. 1). The animal is systemically heparinized during this procedure. Anastomoses are performed in the following order: suprahepatic inferior

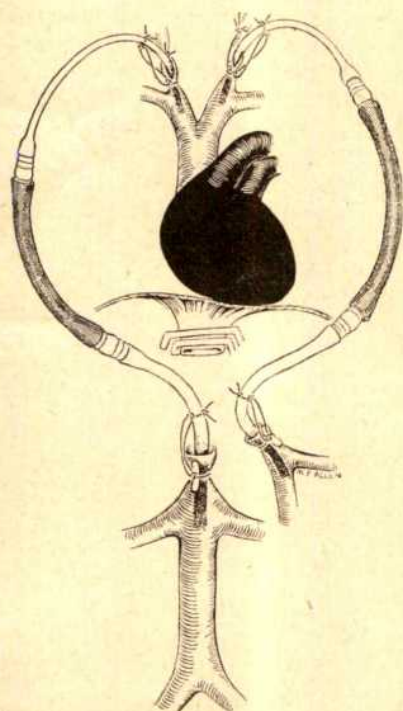


FIG. 1.—Diagram of the shunting procedure for the inferior vena cava and the portal vein in the recipient animal after removal of the liver.

experience in this field. We have added vagotomy and gastroenterostomy in an attempt to prevent the gastrointestinal haemorrhage and have related the rejection of liver transplants in the pig to transplants of kidneys and skin in this animal.

Materials and Methods

Orthotopic Liver Transplantation, Vagotomy, and Gastroduodenostomy (36 Experiments)

In the course of our experiments details of technique have been modified and the present technique, which has been used in the last 20 transplants, has had an operative mortality of

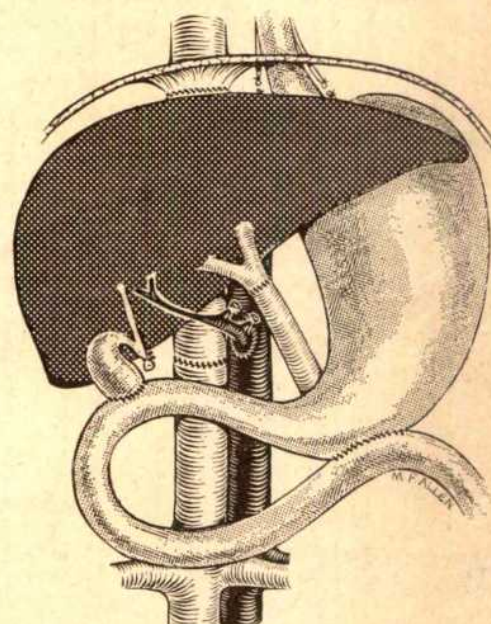


FIG. 2.—Diagram of the completed operation and anastomotic procedures; shows vagotomy, gastroduodenostomy, suprahepatic and infrahepatic vena caval anastomoses, cholecystoduodenostomy, end-to-end porto-portal anastomosis, and Carrel patch with the orifice of the coeliac artery anastomosed to the aorta.

vena cava, portal vein, coeliac artery with a Carrel patch of aorta to recipient aorta, infrahepatic inferior vena cava, cholecystoduodenostomy,† and gastroduodenostomy (Fig. 2). The vagi are divided just above the gastro-oesophageal junction. In some experiments the animal's spleen was removed; details of animals surviving four or more days are shown in Table I. The pigs were between 20 and 30 kg., and of either sex. All recipient animals were Large White pigs. Donor animals were either Large Whites or completely unrelated Landrace pigs. Details of donor and recipient are also shown in Table I. After removal of the liver from the donor animal the pig was exsanguinated, the blood collected in ACD bags and used for transfusion to the recipient. Though total blood loss was often less than 100 ml., all animals received between 1 and 2 litres of donor blood, 150 ml. of 5% sodium bicarbonate solution,

* Departments of Surgery and Pathology, University of Cambridge.

† In one animal (No. 16, Table I) choledochoduodenostomy and cholecystectomy were performed.

and 500 ml. of dextrose saline solution containing 1 g. of chloramphenicol. At the end of the operation the animals were given an infusion of 500 ml. of 5% dextrose with an additional 25 g. of glucose. Anaesthesia was maintained as light as possible, the animals breathing spontaneously. Total operative time was between two and three hours; the total ischaemic time was usually between 30 and 40 minutes, except in two experiments in which the donor animals died during the induction of anaesthesia, and the ischaemic time was in excess of an hour. After operation the animals were fasted for 24 hours and then given an ad lib. commercial pig food diet.

Kidney Transplantation (23 Experiments)

Anaesthesia was the same as for liver transplantation. Pigs were the same weight and breed. The left kidney was transplanted orthotopically, the renal vein being anastomosed to the renal vein, and the renal artery, with a Carrel patch of aorta, being anastomosed to the aorta. Usually reciprocal transplants were performed, the animals were systemically heparinized during the transplantation, and the ureters were implanted into the bladder. The period of ischaemia was usually between 15 and 30 minutes. The opposite kidney was removed.

TABLE I.—Orthotopic Liver Transplantation (Animals Surviving Four or More Days)

Exp. No.	Donor	Sex of Pigs	Splenectomy	Survival (Days)	Cause of Death	Transplant Histology
1	Half sib*	M→M	No	36	Intraperitoneal haemorrhage	Suppurative cholangitis
2	" "	M→F	"	14	Portal venous obstruction	Hepatic abscesses
3	Littermate	M→M	"	7	Stenosis of cholecystoduodenostomy	Centrilobular hepatic necrosis.
4	"	F→M	"	8	Undetermined	Mild cholangitis
5	Unrelated	M→M	Yes	81	Intestinal obstruction from incisional hernia	Slight increase in fibrous tissue of portal tracts
6	Half sib*	M→M	No	Alive 112		
7	" "	F→F	Yes	11	Peritonitis	Suppurative pyelophlebitis
8	Littermate	M→M	"	81	Hepatic infection	Suppurative cholangitis
9†	Unrelated	F→F	"	46	Bronchopneumonia	Mild cholangitis
10	Littermate	M→F	"	Alive 62		
11	Half sib*	F→F	"	Alive 55		
12	Different breed	F→M	"	Alive 48		
13	Unrelated	M→F	"	Alive 47		
14	Half sib*	F→F	"	Alive 34		
15	Different breed	F→F	No	Alive 33		
16‡	Unrelated	F→F	"	Alive 27		
17§	Different	F→F	"	Alive 20		
18§	Unrelated	F→F	"	7	Intestinal obstruction—adhesions	Mild cholangitis
19§	"	F→F	"	Alive 12		
20§	Different breed	M→F	"	Alive 5		

* Common sire, different dam. † Cadaver donor. ‡ Choledochocholestomy and cholecystectomy. § Skin graft at time of liver transplant.

Skin Grafting

Split skin grafts were applied to a subcutaneous fat bed on the dorsum of the chest of the animal and pressure was used. The first inspection was on the fourth day; subsequently, daily inspections were made (Binns, 1967). Four animals were skin-grafted immediately after liver transplantation at the same operative session. An autograft was always performed at the same time as the homograft.

Pathological Studies

All animals dying were subjected to a post-mortem examination. Microscopical sections were taken from the transplanted liver, lymphoid tissue, gastrointestinal tract, kidneys, and lungs. Red blood cell grouping and cross-matching of the donor and recipient were not done. Biochemical and haematological studies were performed on 10 animals (Table II).

Results

Liver Transplantation (36 Experiments).—Four animals died during the operation and a further 12 pigs died during the first three days. The causes of these 16 early deaths varied. In some cases there was an obvious surgical error, in others no cause was determined. There was, however, no evidence of immunological rejection of the liver. Nine animals died between 7 and 81 days. Eleven animals are alive and well; four of these had skin grafts performed from the donor at the same time as the liver transplantation, and at the time of writing all four grafts were surviving between 5 and 20 days.

Renal Transplantation (23 Experiments).—Ten animals died within the first four days from a variety of causes but not from rejection of the transplants. Thirteen animals survived between 4 and 33 days (Table III).

Histological Findings

In the nine allograft livers examined microscopically more than four days after transplantation (Table I) none has shown

TABLE III.—Renal Transplantation (Animals Surviving Four or More Days)

Exp. No.	Donor	Sex of Pigs	Splenectomy	Survival (Days)	Cause of Deaths	Histological Evidence of Rejection
1	Littermate	M→F	No	10	Intestinal obstruction	Present
2	"	F→F	"	11	Uraemia and gastrointestinal bleeding	
3	"	F→F	"	4	Obstruction of ureteric anastomosis	
4	"	F→F	Yes	5	" " "	"
5	"	F→F	No	9	Uraemia	"
6	"	F→F	Yes	33	"	Nil
7	"	F→F	No	12	Obstruction of ureteric anastomosis	
8	"	M→M	"	15	Peritonitis and uraemia	Present
9	"	F→F	Yes	20	Obstruction of ureteric anastomosis	"
10	Different breed	M→M	"	6	Dehiscence of ureteric anastomosis	"
11	"	M→M	No	11	Uraemia	"
12	"	F→M	"	4	Leakage of urine from ureteric anastomosis	"
13	"	M→F	Yes	8	Uraemia	"

TABLE II.—Haematology and Liver-function Tests

Fig. No.	Days after Orthotopic Liver Transplant	Hb (g./100 ml.)	P.C.V. (%)	Total W.B.C./cu. mm.	Differential (%)					Serum Bilirubin (mg./100 ml.)	S.G.O.T. (Normal Range 5–32 Units)	Serum Alk. phos. (Normal Range 3–13 K.A. Units)	Comments on Serum Electrophoresis
					N	E	B	L	M				
6	99	10.7	32	20,000	23	5	—	72	—	<0.5	27	21	Albumin slightly reduced
8	76	10.6	30	18,000	35	5	—	60	—	<0.5	80	14	Slight rise in gammaglobulin
9	49										90	29	Albumin reduced
10	49	10.5	36	23,000	34	5	2	58	—	2.2	14	16	Albumin slightly reduced
11	42	10.3	39	23,000	57	1	—	36	6	3.2	20	12	Raised gammaglobulin. Reduced albumin
12	34	12.9	34	22,000	49	2	—	37	12	<0.5	66	35	Albumin reduced
13	34	9.8	32	15,500	28	17	—	52	3	<0.5	40	16	" "
14	20	10.3	35	18,800	45	2	5	39	8	5.8	73	18	" "
15	20	12.6	34	25,000	60	5	3	20	12	<0.5	53	23	" "
16	13	12.1	37	28,000	50	4	2	17	27	2.0	80	19	Albumin slightly reduced

evidence of rejection changes similar to those described in canine liver allografts by McBride *et al.* (1962). Only slight lymphocyte, plasma cell, and other mononuclear cell infiltration was present in portal tracts and interlobular septa. Similar cells were not present in the sinusoids or around central veins (Fig. 3). Some long-term survivors showed an increase of fibrous connective tissue in the portal tracts and interlobular septa (Fig. 4). In animal No. 5 (Table I) and also in the long-term survivor of the previously reported series (Calne *et al.*, 1967) there was slight fibroelastic intimal thickening of some hepatic arteries. A variable degree of cholangitis, sometimes with abscess formation, was present in seven of the nine animals. This may have resulted from the cholecystoduodenostomy.

In contrast 12 out of 13 kidneys examined from four days onwards showed histological evidence of rejection. Lymphocytes and other mononuclear cells were present in the interstitial tissue between tubules, around glomeruli, and especially in the walls of veins and surrounding tissue. Thrombosis of arcuate and interlobular veins was conspicuous in short-term survivors (Fig. 5). In animal No. 6 there were thrombi in some glomerular capillaries. One transplant from a littermate (No. 7, Table III) showed no significant abnormalities at 12 days. The reciprocal transplant was in the longest-surviving pig (No. 6, Table III).

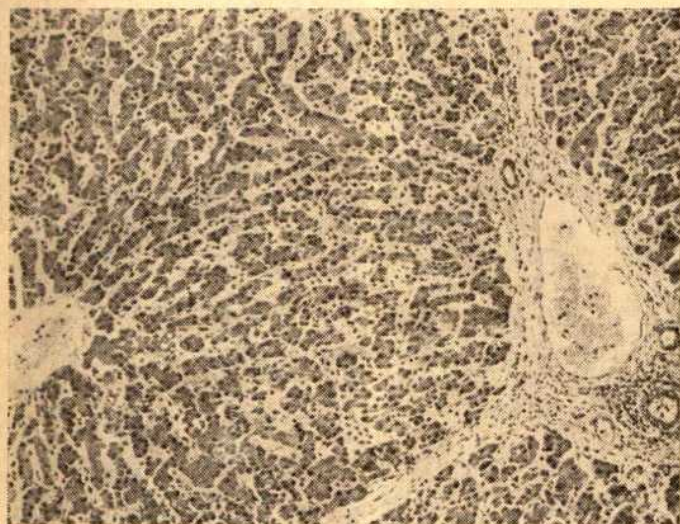


FIG. 3.—Section of liver transplant at eight days (animal No. 4, donor littermate, Table I); shows slight oedema and mononuclear cell infiltration of portal tract and interlobular septa. Liver cells appear normal. (H. and E. $\times 87$.)

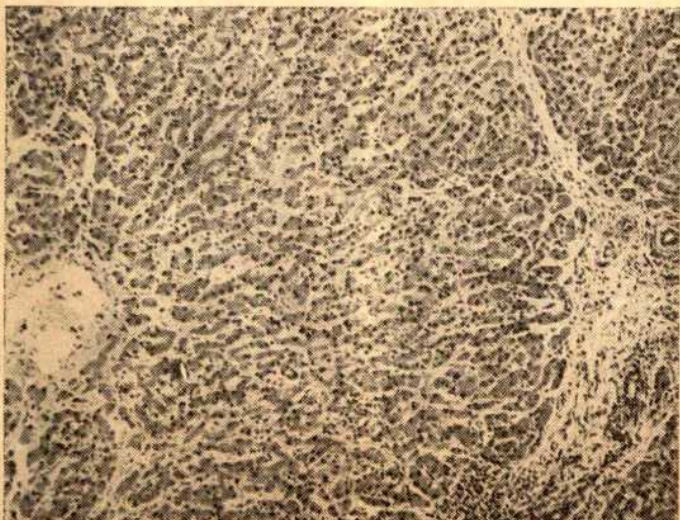


FIG. 4.—Section of liver transplant at 81 days (animal No. 5, donor unrelated, Table I); shows slight increase of fibrous connective tissue in portal tract and around central vein. Liver cells appear normal.

Haematology and Biochemistry

The results of haematological and biochemical investigations in 10 pigs between 13 and 99 days after transplantation are shown in Table II. All animals were slightly anaemic with high total white blood cell counts. The serum bilirubin was normal in five animals and raised in the remaining four from 2 to 5.8 mg./100 ml. The S.G.O.T. was normal in three animals (normal range 5–32) and raised in the others, the highest value being 90. Alkaline phosphatase was normal in one and raised

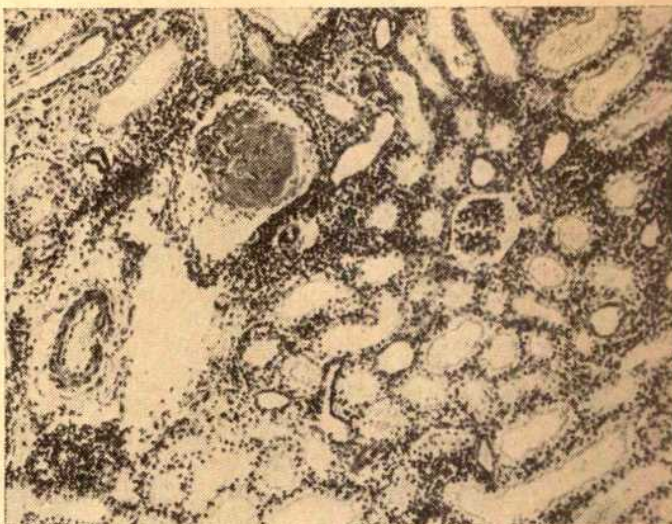


FIG. 5.—Section of transplant kidney at five days (animal No. 4, donor littermate, Table III). Abundant mononuclear cell infiltration with thrombus in an interlobular vein. (H. and E. $\times 87$.)

in the remaining animals, the highest being 35 K.A. units. Serum electrophoresis showed reduction in the albumin in most animals and an elevated gammaglobulin in two. These investigations reveal moderate impairment of liver function in most animals, but the function was consistent with clinically healthy animals.

Discussion

The results reported here confirmed our preliminary impressions and the experiments of Terblanche *et al.* (1967), which suggested that, in the pig, rejection of the liver is a slow and sometimes remarkably mild process. There has been no instance of gastrointestinal bleeding in this series of transplants, which would suggest that vagotomy and gastroduodenostomy has been an effective prophylaxis against gastrointestinal mucosal erosions. Stuart *et al.* (1967) found a high incidence of gastrointestinal ulcers in dogs with orthotopic liver transplants and were unable to prevent ulceration by vagotomy and pyloroplasty; total gastrectomy, however, was effective. Terblanche (personal communication) also observed a high incidence of gastric haemorrhage in pigs with orthotopic liver transplants. A common complication in our experiments has been the development of cholangitis in the transplanted liver. This might be preventable by substituting a choledochoduodenostomy for the cholecystoduodenostomy. The behaviour of the transplanted liver in the pig contrasts remarkably with that of renal and skin homografts, both of which are rejected aggressively over a period similar to that observed in the dog. This reaction is fairly rapid even when donor and recipient are littermates.

The pattern of skin-graft rejection in the pig has been described by Binns (1967); an example of the histological changes is shown in Fig. 6. In untreated dogs, liver transplants may survive a little longer than kidney; nevertheless fairly typical rejection, with mononuclear cell infiltration around the portal triads and hepatic veins and hepatic cell necrosis, has been described consistently by Moore *et al.* (1960), Starzl *et al.*

(1961, 1965), McBride *et al.* (1962), and Stuart *et al.* (1967). Most dogs died from rejection of the liver within a week of transplantation. There are peculiar difficulties of liver transplantation in the dog that are not encountered in the pig and presumably would not be encountered in man. These are hepatic outflow obstruction that develops readily in the dog and the occurrence of pathogenic organisms in the portal blood of normal dogs. There are not enough data to reach any conclusions on the behaviour of livers transplanted in man without immunosuppression. In patients treated with azathioprine, corticosteroids, and antilymphocyte globulin, cellular infiltration

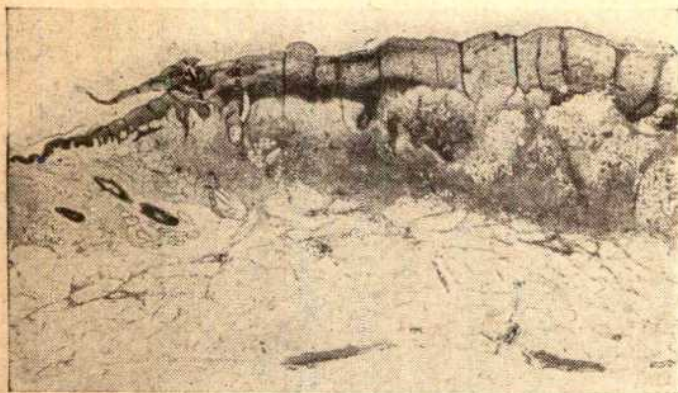


FIG. 6.—Section of skin homograft from unrelated donor at nine days. Shows advanced rejection of homograft epithelium (right) and underlying mononuclear cell infiltration. Normal skin on left. (H. and E. $\times 4$.)

tion in the presence of good hepatic function has been observed in four recent liver transplants (T. E. Starzl and K. A. Porter, personal communication).

The results reported here cannot be explained in terms of close relationship of donor and recipient, splenectomy, or standard immunosuppression. It will be seen from Table I that long survival occurred even when donor and recipient were of different breeds and whether or not the recipient was splenectomized. No immunosuppressive agents were given. It might be argued that the transfusion of donor blood at the time of operation could have produced immunological unresponsiveness, but Terblanche *et al.* (1967) have used indifferent non-donor blood and also obtained long-term survivors. Donor blood did not influence the survival of kidney or liver transplants in dogs (Calne *et al.*, 1966; Stuart *et al.*, 1967). The main lymphatic sac is opened in dissecting the aorta for both hepatic and renal transplants, and any possible immunosuppressive effect would presumably have been shown in the renal transplants as well as the hepatic transplants. The number of lymphocytes in the main lymphatic trunks in the pig is less than in other animals (Binns and Hall, 1966), but here again any effect of this would be expected to relate to kidney as well as liver. We are therefore compelled at present to attribute the long survival of liver transplants in the pig to some quality peculiar to the liver in this species. The mechanism of long acceptance of the liver is of theoretical interest. There are obvious possibilities that can be considered:

(1) The liver is producing a state of tolerance or immune paralysis specific for donor tissue. The preliminary observations of skin grafts placed at the same time as liver transplantation would

be consistent with such a hypothesis, but further experiments are planned to investigate this more fully.

(2) The liver is producing immunological enhancement and is being protected from immunological damage by a coating of specific blocking antibodies. So far no attempt has been made to identify enhancing antibodies in pigs with liver transplants.

(3) The liver is surviving owing to some property specifically related to the nature of liver tissue or hepatic metabolism. Certainly the liver is fully antigenic in the dog, as demonstrated by the rejection of canine livers after transplantation. In our experiments vascular endothelium, hilar lymph nodes, and whole blood are transplanted together with the liver. These tissues would be expected to be antigenic. The transplanted liver presumably continues to produce donor-type proteins and other metabolites, but there are no data available on metabolic processes of the liver that can be related to transplantation immunology.

Orthotopic liver transplants in the pig can survive and function for prolonged periods without any obvious deleterious effect on the recipient. The transplanted liver can be accepted even when the donor and recipient are from widely disparate genetic sources—that is, different porcine breeds. The surviving pigs are in good condition, though their gain in weight is not as rapid as in control animals. These observations in immunologically mature animals constitute what might be regarded as an ideal type of graft acceptance. It is certainly a stimulus for further investigation, since if the mechanism of acceptance were discovered clinical application might resolve many of the present difficulties of organ transplantation. Liver transplantation in the pig may prove to be a useful model for analysis of immunological mechanisms in transplantation biology.

Summary

Further experience of orthotopic liver transplantation in the pig showed that vagotomy plus gastroduodenostomy seemed to prevent the previous high incidence of gastrointestinal haemorrhage. Liver transplants without immunosuppression consistently survived for long periods of time in immunologically mature animals even when the donor and recipient were from widely disparate genetic sources. The behaviour of the liver is in marked contrast to kidney and skin transplants, which are rapidly rejected in similar pigs.

This work would not have been possible without the help of many of our colleagues. We are particularly indebted to Drs. M. Zakiewicz and J. Samuel. We are grateful to Mrs. M. Allen and the Department of Medical Illustration, Addenbrooke's Hospital, for the drawings, and to Dr. R. D. Keynes and the staff of the A.R.C. Institute of Animal Physiology, Babraham, for the use of their facilities and for their help.

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Method for Detection of Bacteriuria Suitable for Use in General Practice

J. M. BRADLEY,* M.B., B.S.; N. CROWLEY,† M.R.C.S., L.R.C.P., F.C.PATH.

J. H. DARRELL,‡ M.B., D.C.H., M.C.PATH.

Brit. med. J., 1967, 4, 649-651

A completely satisfactory screening method for bacteriuria requiring the minimum of apparatus and bench expertise and suitable for use in general practice has still to be described. Even where laboratory facilities are readily available to general practitioners transport of the specimen without the delay which would upset the quantitative aspects of the investigation is often impossible. In addition, hospital laboratories would be unable to cope with the demands that ought to be made on them if all diagnosed urinary tract infections were adequately followed. The investigation of patients whose symptoms are less conclusive but who nevertheless may have urinary tract infections (Mond *et al.*, 1965) would add considerably to the volume of work.

A method employing disposable commercial swabs to inoculate MacConkey plates that has been developed and used for the screening of antenatal patients for significant bacteriuria at the Royal Free Hospital overcomes these disadvantages. The method has been employed without difficulty in the clinic by nursing staff, in general practice, and by medical students.

Methods

The Swab.—Pre-sterilized disposable commercially available swabs having a tightly wound cotton-wool tip 1 cm. in length were used to inoculate the medium. A machine-made swab was selected to minimize variation in size.

The Test.—Fresh preferably clean voided specimens were obtained in sterile wide-mouthed jars. In all cases specimens were plated by immersing the entire cotton-wool tip in the urine and briefly draining it against the inside of the jar before

using it to inoculate a single dried MacConkey plate. An inoculum of four parallel blocks, each comprising four strokes of the swab, was made without rotating the swab (Fig. 1).

Variation in Uptake of Urine by the Swabs.—Twenty swabs were weighed before and after charging with urine to discover the variation in absorbency.

Correlation between Swab Plating, Standard Loop Inocula, and Viable Counts.

—With the use of a technique modified from that of Miles and Misra (Cruickshank, 1965) viable counts were done on 20 specimens which were also plated by the swab method. In addition approximately 500 specimens were plated by the swab and standard loop (Guttmann and Stokes, 1963) methods. The standard loop method had been extensively compared with viable counts when it was first adopted in this laboratory for the routine culture of urine specimens six years ago (unpublished observations). Twenty-six further specimens were examined by both the standard loop and Miles and Misra methods.

Incubation.—Cultures were routinely incubated at 37° C. One hundred specimens were inoculated in duplicate by the swab method, and the duplicate plates were held at room temperature (17-22° C.). Another 26 specimens were held at 4° C. for up to 120 hours before incubation at 37° C.

Results

The Test.—By not rotating the swab during plating a slight progressive dilution was obtained. The final block inoculated

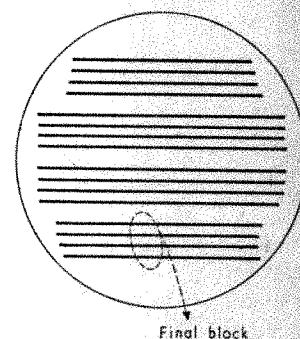


FIG. 1.—Pattern of swab inoculum

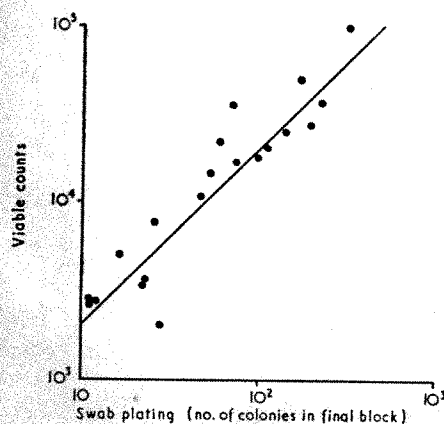


FIG. 2

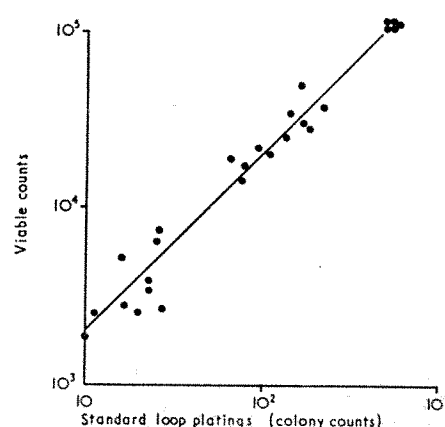


FIG. 3

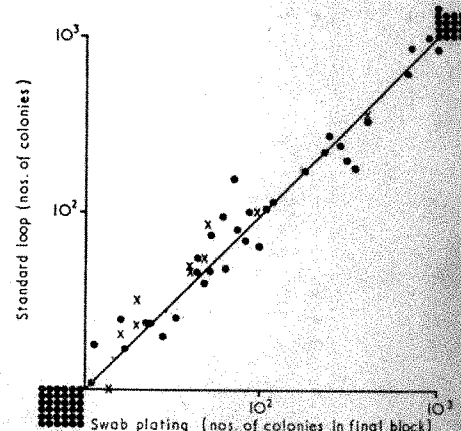


FIG. 4

FIG. 2.—Comparison between numbers of organisms per ml. of urine calculated by the Miles and Misra method and colony counts of the final blocks of swab platings. FIG. 3.—Comparison between numbers of organisms per ml. of urine calculated by the Miles and Misra method and colony counts of standard loop platings. FIG. 4.—Comparison between colony counts of standard loop platings and the final block of swab platings. Crosses represent infections with Gram-positive cocci, and dots infection with Gram-negative rods. The unrealistic number of specimens in the 50-500 colonies per inoculum range is due to selection of suitable specimens for comparison.

was used to read the test, and, following our usual practice, colonies were counted up to about 300 colonies per inoculum and estimated above this.

Variation in Uptake of Urine.—The weights of urine absorbed by the 20 swabs ranged between 0.1106 and 0.1441 g., with a mean of 0.1262 g. and a standard deviation of 0.0115 g. Three weighings differed from the mean by more than one standard deviation.

Correlations.—Fig. 2 shows the correlation between the swab-plating method and the viable counts done on 20 specimens. Fig. 3 shows the correlation between the standard loop plating method and the viable counts done on 26 specimens. Fig. 4 shows the correlation between the numbers of colonies in the last block of each swab plating and the standard loop method for 102 specimens collected and plated in general practice and further investigated in the hospital laboratory. Similar results were obtained with about 400 more specimens treated this way in hospital. Figs. 5 and 6 show standard loop and the corresponding swab platings. It has also been the experience of one of us (N.C.), when using similar swabs to make subcultures from liquid media, that it is practically impossible to overload the swabs, or to vary the amount of fluid absorbed, by alterations in the contact time between swab and fluid medium. The swabs are exceptionally absorbent and are fully loaded instantly.

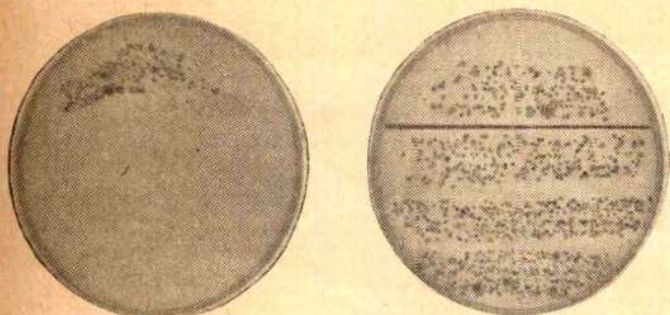


FIG. 5.—Standard loop and corresponding swab inoculum of an insignificant mixed growth of two types of lactose-fermenting organisms.

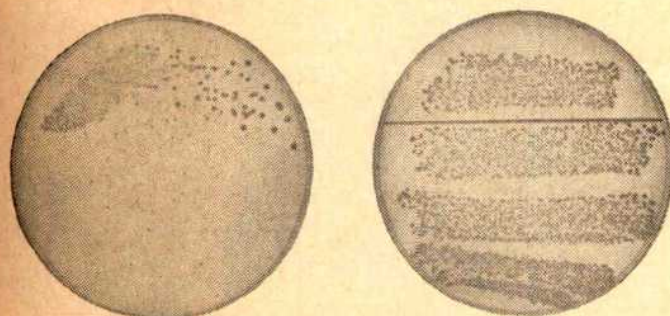


FIG. 6.—Standard loop and corresponding swab inoculum of a significant growth.

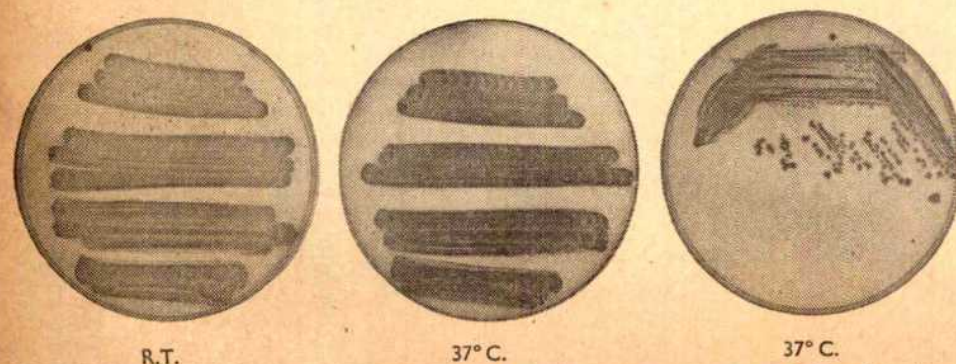


FIG. 7.—Comparison between urine culture inoculated by swab and standard loop methods and incubated at 37° C. overnight, and inoculated by swab method and retained at room temperature (approximately 21° C.) for 48 hours. The organism was *Escherichia coli*.

Incubation.—Though in routine practice plates were incubated at 37° C. overnight, plates held at room temperature overnight were often readable, and, apart from one *Proteus* species which did not grow at room temperature, all members of the Enterobacteriaceae were easily visible at 48 hours (Fig. 7). At the cooler temperatures Gram-positive cocci required up to 72 hours to be readily visible to the untrained eye. Periods of refrigeration at 4° C. for up to 120 hours before incubation at 37° C. had no effect on the final outcome.

Interpretation.—Negative plates and those with a light or mixed growth can be confidently discarded. A heavy pure growth (greater than about 300 colonies per final block) is provisionally designated as positive. Identification and antibiotic sensitivity testing can be performed from the growth, and, when indicated clinically, treatment can be started without further investigation. An equivocal result, or a positive result without clinical indication of infection, is reinvestigated either by a second screening test or, preferably, by routine laboratory methods before instituting treatment.

Discussion

The necessity for a simple screening method for the diagnosis and follow-up of urinary tract infections in hospital and in general practice is well recognized (*Brit. med. J.*, 1965). For routine laboratory practice most authors regard semiquantitative methods, such as the standard loop methods (Hoeprich, 1960; O'Sullivan *et al.*, 1960; Guttman and Stokes, 1963), as satisfactory substitutes for potentially more accurate but time-consuming dilution methods. Non-quantitative and uninterpreted methods are no longer acceptable (Bradley and Little, 1963).

Chemical methods for detecting significant bacteriuria such as the triphenyl tetrazolium chloride test (Simmons and Williams, 1962) or the Griess nitrite test (Smith *et al.*, 1961) have been used with variable success. In the hands of its authors the former showed 95% of infections (Simmons and Williams, 1962), but in another series only 44% of infections in the 10⁵–10⁹ organisms per ml. of urine range were detected (Hinton and van der Hoeven, 1965). The latter test is apparently even less satisfactory (Kincaid-Smith *et al.*, 1964).

Whatever their accuracy chemical reactions reveal only that significant numbers of organisms are present. It is possible to obtain a positive result from a contaminated specimen, and while proper midstream specimens are desirable they are not always obtained. It is therefore important to be able to differentiate between contamination and infection. If a positive chemical test is obtained another specimen must be examined by conventional methods to identify the responsible organism (essential for proper follow-up studies) and to determine its antibiotic sensitivity pattern.

Cultural screening methods overcome these disadvantages of chemical tests. Methods such as the Leigh and Williams (1964) blotting-paper strip method, the dip-inoculum transport medium of Mackey and Sandys (1965), or the dip-slide method of Guttman and Naylor (1967) require special equipment, admittedly minor in the blotting-paper method, and expert interpretation.

As the swab-plating method is satisfactory over a relatively wide temperature range it can be used where bacteriological incubators are not available, so long as the room is reasonably temperate. Keeping the plates at room temperature is preferable to incubating them in an airing or similar warm cupboard, as the heat tolerance of members of the Enterobacteriaceae above 37° C. is far less

than at a temperature below this. Thus, from general practice, the inoculated plate can be sent to the laboratory for incubation and interpretation. If this is impossible the plates can be kept by the practitioner and only "positives" submitted for identification and sensitivity testing. Unfortunately organisms causing infections in other situations are much more fastidious in their growth requirements, and it is not possible, therefore, to use modifications of this method for other bacteriological investigations.

MacConkey plates were used because they support the growth of virtually all organisms responsible for acute urinary tract infections, and they inhibit the swarming of *Proteus* species. They can be obtained pre-poured from commercial sources and do not deteriorate during 7 to 10 days at room temperature, especially if kept in plastic bags.

Other commercial cotton-wool swabs could doubtless be used equally well, but would require initial calibration with more accurate methods. Serum-coated swabs, being water-repellent, are unsuitable.

Though 10^5 organisms per ml. of urine has come to be regarded by many as the figure below which urinary infection is not present this is not always so. As was pointed out in Kass's (1955) original paper one of the circumstances in which, with an active urinary infection, fewer organisms are found is when there is frequency of micturition. There is then insufficient incubation time in the bladder for organisms to reach 10^5 /ml. of urine. In general practice there is often "built-in" frequency, as many patients micturate immediately before leaving home. Specimens of urine obtained in these circumstances may therefore have fewer than 10^5 organisms per ml. in the presence of infection. Diuresis also significantly reduces the number of organisms (Roberts *et al.*, 1967). Other less well recognized factors, such as the excretion of inhibitory substances from the diet, may also account for fewer than 10^5 organisms per ml. in the presence of infection. These factors must be considered in reading screening tests, just as they are in the interpretation of routine cultures. It is not necessarily of any disadvantage, therefore, that accurate counts between 250 and 500 colonies per inoculum are not possible. Indeed, it is questionable whether the rigid application of accurate

methods is justifiable on such variable material. This can sometimes be undoubtedly misleading.

Summary

A cultural method for the investigation of urinary tract infections using commercially available cotton-wool swabs to inoculate MacConkey plates with freshly voided urine is described. This is simple to use, and does not necessarily require incubation at 37°C . Cultural methods have advantages over chemical screening tests, but some described previously require special equipment and thus are an added burden on laboratory preparation facilities.

We wish to acknowledge the co-operation of Dr. Betty Bass in the part of the investigation carried out in general practice and of Sister E. F. Williams, of the Gynaecological Outpatient Department at the Royal Free Hospital, and the technical assistance of Mrs. J. Wood, B.Sc.

Disposable swabs were obtained from Grahams Medical Products Ltd., St. Jude Works, Westmoor Street, London S.W.7. Pre-poured MacConkey plates can be obtained from Oxoid Ltd., London S.E.1

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Blood Loss Using the Modified Two-layer Kiil Dialyser

D. B. EVANS,* M.B., M.R.C.P.; E. M. CLARKSON,† B.Sc.; J. R. CURTIS,‡ M.B., M.R.C.P.

Brit. med. J., 1967, 4, 651–653

One of the factors contributing to the anaemia of patients undergoing intermittent haemodialysis is blood loss due to blood remaining in the dialyser and extracorporeal circuit at the end of dialysis.

The present study was undertaken to determine the volume of blood remaining in the dialyser and arterial and venous blood lines at the end of dialysis, and to compare the efficiency of various techniques used to rinse back the blood in the dialyser and blood lines into the patient via the venous cannula at the end of dialysis.

Methods

Methods of Determining Volume of Blood Remaining in Dialyser and Blood Lines at End of Dialysis

A sample of the patient's blood was taken into a Sequestrene tube at the end of dialysis. Suitably diluted, this served as a standard with which to compare the haemoglobin concentration

in the wash solution obtained from the dialyser and blood lines.

When dialysis had been discontinued the blood lines and dialyser were washed through with tap-water until the washings were colourless. The dialyser was then dismantled and any blood remaining on the cuprophane membranes was washed off with tap-water. All washings were collected and the total volume was measured. After careful mixing, an aliquot from the washings was taken and stored at -15°C . or $+4^\circ\text{C}$. with the post-dialysis blood sample from the patient until the haemoglobin concentrations were estimated. Then 0.2 ml. of well-mixed whole blood from each patient was diluted to 50 ml. with 0.05% ammonia. Any intact red cells remaining in the wash solution were lysed by the addition of a small amount of

* Senior Medical Registrar, Renal Unit, Addenbrooke's Hospital, Cambridge.

† Biochemist, Charing Cross Hospital Medical School, Fulham Hospital, London.

‡ Lecturer in Medicine, Charing Cross Hospital Medical School, Fulham Hospital, London.

saponin. The wash solution was centrifuged and then diluted in 0.05% ammonia solution to give approximately the same haemoglobin concentration as the whole blood standard.

The haemoglobin concentration in each diluted wash solution was compared with its own whole blood standard either as oxyhaemoglobin by reading direct in a colorimeter at 540 m μ or as cyanmethaemoglobin. Conversion of the haemoglobin to cyanmethaemoglobin was found to be necessary only when bloods and wash solutions had been stored at 4° C. for more than 24 hours. The mean difference in 20 estimations carried out by the two methods in parallel was 0.7% (S.D. 2.6).

The haemoglobin remaining in the dialyser and blood lines at the end of dialysis was expressed as millilitres of the patient's blood.

Dialysis Techniques

Permanent Teflon-Silastic arteriovenous shunts are used. A single pass system is employed with modified two-layer Kiil dialysers and cuprophane membrane (PT 150). Initially the dialysis fluid was not heated, and this necessitated long venous blood lines so that the patient's blood could be rewarmed before being returned from the dialyser to the venous cannula. The dialysis fluid is now heated to 37° C. so that blood rewarming is no longer necessary and shorter venous lines can be used.

Wash-back Techniques at End of Dialysis

(1) During the period when blood rewarming was employed and long venous blood lines were used a comparison was made between two methods of washing back the blood at the end of dialysis. In one technique, at the end of dialysis the arterial blood line was clamped and cut near the patient's arterial cannula and then 500 ml. of 0.9% saline was infused into the arterial line. The dialyser in this technique was kept in the horizontal position throughout. The dialysis flow was continued at 500 ml./minute throughout. The other technique was similar except that the dialyser was tilted at an angle of 45°, with the arterial end raised during the last half-hour of dialysis. Each technique was carried out on 10 occasions in the same dialyser and on nine occasions in another dialyser. The volume of blood remaining in the dialyser and extracorporeal circuit was determined on each occasion.

(2) After the first study the technique of dialysis was changed and warm dialysis fluid was used so that rewarming of the blood was unnecessary. As a result of this it was possible to use shorter venous lines. After the introduction of these modifications two other wash-back techniques were compared. In one the dialyser was tilted at 45°, with the arterial end raised for the last half-hour of dialysis, and then at the end of dialysis 1,000 ml. of 0.9% saline was infused into the arterial line. In the other method the dialyser was tipped vertically with the arterial end uppermost during the last half-hour of dialysis and then at the end of dialysis 1,000 ml. of 0.9% saline was infused into the arterial line. With both of these techniques the dialysis flow was continued at 500 ml./minute throughout. Each technique was employed on nine occasions with the same dialyser, the volume of blood remaining in the dialyser and extracorporeal circuit being measured on each occasion.

Use of Most Efficient Wash-back Technique in Different Kiil Dialysers

The most efficient wash-back technique proved to be the one which included vertical tipping of the dialyser during the last half-hour of dialysis together with a rinse of 1,000 ml. of 0.9% saline at the end of dialysis. In the final part of the study this technique was used in nine different Kiil dialysers and the residual blood volumes were compared.

Results

(a) *Use of Long Blood Lines (Blood Rewarmed) + 500 ml. 0.9% Saline and Dialyser Horizontal or Tilted 45°.*—Table I shows volumes of blood remaining in the dialysers and blood lines with the two techniques. Twenty experiments were carried out with dialyser S II and 18 with dialyser S III. The volume of blood remaining when the dialysers were tilted during the last half-hour of dialysis tended to be smaller than when they were kept horizontal, but the difference between the means was not significant.

TABLE I

S II Dialyser Volume of Blood (ml.)		S III Dialyser Volume of Blood (ml.)	
45°	Horizontal	45°	Horizontal
75	60	71	54.5
74	117.5	84	112.5
43	140	78	97
99	122	68	107
83.5	278	90	118
106	99	102	142
118	94	130	120
105	108	106	146
67	149	89	119
120	263		
Mean 89	143	91	113
S.D. 23	68	18	25
Range 43-120	60-278	68-130	54.5-146

(b) *Using Short Blood Lines (Warm Dialysis Fluid) + 1,000 ml. 0.9% Saline and Dialyser Tilted to 45° or Vertically.*—Table II shows results of 18 experiments in one dialyser. The mean volume with the dialyser at 45° was 52.9 ml., while with the dialyser vertical it was 16.9 ml. The difference between the means was highly significant ($t=8.3$; $P<0.001$).

TABLE II.—H III Dialyser. Volume of Blood (ml.)

45°	Vertical	28.6	68.6	68.4	35.5	51.2	51.2	64.2	53.4	55.4*
Vertical	..	18.3	13.0	10.0	30.9	32.7	14.8	15.8	10.3	6.7†

* Mean = 52.9. S.D. = 13. Range = 28.6-68.6.
† Mean = 16.9. S.D. = 8.6. Range = 6.7-32.7.

(c) *Use of Most Efficient Wash-back Technique in Different Kiil Dialysers.*—Vertical tipping of the dialyser during the last half-hour of dialysis together with a rinse of 1,000 ml. of 0.9% saline at the end of dialysis proved to be the most efficient of the wash-back techniques used in this study. The results of residual blood volumes found in nine different Kiil dialysers after using this technique are shown in Table III.

TABLE III

Dialyser	A2	A3	A5	B2	B6	C1	C2	C5	C8
Volume of blood (ml.)	31.3	16.9	29.2	21	4	4	0.9	6.4	0.4

Mean = 12.6. S.D. = 11.5. Range 0.4-31.3.

Discussion

Priming with blood is unnecessary with the Kiil dialyser, but relatively large volumes of blood may be left in the dialyser and extracorporeal circuit at the end of dialysis. This loss of blood with each dialysis contributes to the anaemia of patients on intermittent haemodialysis.

Various techniques have been described to wash the blood remaining in the dialyser back into the patient via the venous cannula at the end of dialysis.

Cole *et al.* (1962), using Kiil dialysers, stated that if the dialyser was kept in the horizontal position at the end of dialysis and an attempt made to rinse the blood back with saline most of the red cells remained behind while mainly plasma was washed back into the patient. It was estimated that probably more than 100 ml. of packed cells was left behind in the dialyser at the end of each dialysis. If, however, the

dialyser was tipped vertically, with the blood flowing downwards during the last 10 minutes of dialysis, and was then rinsed with saline, Cole *et al.* (1962) estimated that the loss of red cells was reduced by a half to one-quarter. This change in the wash-back technique resulted in a reduction in average transfusion requirements from 5 units/month to 2.5 units/month.

Cole *et al.* (1963), again using Kiil dialysers, made some measurements of the volume of blood remaining in the dialyser and extracorporeal circuit by means of two wash-back techniques. In the first the dialyser was kept in the horizontal position throughout and 400 ml. of saline was used to rinse back the blood. With this technique the mean volume of blood remaining was 140 ml. (32 determinations). The second wash-back technique used was rather complicated and involved elevation of the arterial end of the dialyser by 15 in. (38 cm.) during the last half-hour of dialysis. In addition the dialysate flow was changed from countercurrent to concurrent by switching the dialysate tubes to opposite ends of the dialyser and increasing the dialysate flow from 500 ml./minute to 3–4 litres/minute. The dialyser was then rinsed with saline, 100-ml. aliquots being run in via the arterial blood line with the dialysate flow temporarily stopped. The dialysate flow was then increased again to 3–4 litres/minute until blood flow ceased. This process was repeated until a total of 400 ml. of saline had been used to rinse the dialyser. With this technique the mean volume of blood remaining in the dialyser was very significantly reduced to 35 ml. (92 determinations).

Johnson *et al.* (1966), also using Kiil dialysers, rinsed the dialyser at the end of dialysis with 150–250 ml. of saline and found an average of 20 ml. of blood left behind. These workers do not state whether the dialyser was tilted in any way towards the end of dialysis.

In the present study we have confirmed that large volumes of blood may remain in the Kiil dialyser at the end of dialysis. Various wash-back techniques are compared, the most satisfactory of which involves tipping the dialyser vertically, with the blood flowing downwards, during the last half-hour of dialysis and rinsing with 1 litre of saline at the end of dialysis.

The mean volume of blood remaining when this technique was employed in nine experiments with the same dialyser was 16.9 ml. This method was then used in nine different dialysers, the mean volume of blood in the nine dialysers being 12.6 ml. Another factor contributing to these results is the improvement in the quality of the dialysers now produced by various manufacturers. It is notable that in five dialysers, four of which were produced in the last year, blood losses with the above wash-back technique were extremely small, with a mean of 3.1 ml. (range 0.4–6.4 ml.). It is also essential to be able to tip the Kiil dialyser vertically towards the end of dialysis, and trolleys designed to hold these dialysers must incorporate this facility.

Summary

Large volumes of blood may remain in the Kiil dialyser and extracorporeal circuit at the end of dialysis if inefficient wash-back techniques are employed and will contribute to the anaemia of patients on intermittent haemodialysis.

Several wash-back techniques were tried, and in three of these the mean volume of blood remaining in the Kiil dialyser and extracorporeal circuit varied from 52.9 to 143 ml.

The most efficient method used involves tipping the dialyser vertically so that the blood flows from the top downwards during the last half-hour of dialysis and rinsing with 1 litre of 0.9% saline at the end of dialysis.

This method was used with nine different Kiil dialysers. The mean volume of blood remaining in the dialyser and extracorporeal circuit was 12.6 ml.

We are indebted to Sister J. M. Storey and the staff of the Haemodialysis Unit, Fulham Hospital, for assistance in carrying out this study.

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Traveller's Diarrhoea: a Survey of Symptoms, Occurrence, and Possible Prophylaxis

ANTHONY C. TURNER,* M.R.C.S., L.R.C.P., D.OBST.R.C.O.G.

Brit. med. J., 1967, 4, 653–654

Traveller's diarrhoea, described by Gordon (1965) as a notorious world-wide illness lasting one to three days, presents a precipitous onset of loose stools and variable symptoms, including nausea, vomiting, abdominal cramps, etc. It often occurs sporadically as isolated cases, though epidemics occur within families or groups of travellers of all ages. The incidence varies according to geographical locations (Kean and Waters, 1958).

Previous studies (bacteriological and prophylactic) have been undertaken (Lie Kian Joe, 1956; Kean and Waters, 1959; Varela *et al.*, 1959; Kean *et al.*, 1962; Nelson *et al.*, 1962) without producing definite conclusions regarding the value of prophylactics or the causal relation between diarrhoea and considered pathogens.

Dr. D. J. Cussen attended the U.K. Olympic teams in Rome 1960 and gave one tablet of Streptotriad twice daily; other

teams had an appreciable amount of diarrhoea, but no cases occurred in the U.K. teams. As neomycin is widely used in gut infections, it was decided to undertake an extensive controlled prophylactic trial comparing Streptotriad, a neomycin-sulphonamides compound, and a placebo in B.O.A.C. personnel and their families going abroad.

Method

Tablets A, B, and C were randomly allocated to 1,383 subjects (see Table), except that complete families were given the same tablet to avoid interchange of medication. Anyone with known drug allergy was excluded. Participants were told to maintain their usual standards of food hygiene and received instructions regarding dosage and duration of medication as follows: one tablet twice daily for the first two weeks while away, one tablet daily for the third week, then stop. Children under 12 years were given half this dosage. Two sealed letters indicating the

* Senior Overseas Staff Medical Officer, Air Corporations Joint Medical Service, London Airport, Hounslow, Middlesex.

identity of the tablets were given to each participant—one addressed to the B.O.A.C. appointed doctor at the visited territory and one to the subject's local doctor. One of these was to be given to the appropriate doctor if diarrhoea developed during the overseas visit or on return home. A questionnaire was completed by each patient, and the data were coded and analysed by means of a punch-card system.

There were three males for every two females; 10% were 19 years or less, 20% 50 years and over, and the remainder 20 to 49.

Treatment Groups	
Group A. Inert control	385
Group B. Neomycin-sulphonamides (each tablet containing neomycin sulphate 200 mg., sulphadimidine 100 mg., sulphadiazine 100 mg., and sulphathiazole 100 mg.) ...	355
Group C. Streptotriad (each tablet containing streptomycin sulphate 65 mg., sulphadimidine 100 mg., sulphadiazine 100 mg., and sulphathiazole 100 mg.) ...	364
Excluded from analysis	279*
	1,383

* 258 failed to comply, 21 stopped tablets within five days because of reaction or side-effects (details see below).

Results

Just over 1,100 completed the survey with practically equal numbers in each treatment group. Streptotriad was found to be beneficial in reducing the diarrhoea and associated symptoms, while neomycin-sulphonamides, though reducing the associated symptoms, did not affect the diarrhoea.

The incidence of diarrhoea was significantly less in the Streptotriad group, and was confirmed by statistical analysis ($\chi^2=11.86$, $\eta=4$, $P<0.02$). Though the incidence of diarrhoea was slightly higher with neomycin-sulphonamides than with placebo there was no statistical difference between them.

Among those in whom the length of attack was known, it lasted one day in 33.8% and no more than three days in 75.2%. This duration confirms Gordon's (1965) description of traveller's diarrhoea. The participants who had three or more stools on the third day were significantly fewer in the Streptotriad group.

The results confirm the description of Gordon in that out of 186 patients having diarrhoea, 64 had abdominal pain, 39 felt tired, 27 lost appetite, 27 had nausea, and 26 vomited. Few patients thought they were febrile. The total incidence of associated symptoms was significantly and statistically less with both active tablets than with the placebo.

Other common symptoms of travellers overseas were also noted: constipation, colds, sore throats, and mouth ulcers. Approximately 10% had constipation; this was mostly ascribed to taking the tablets, but the incidence was slightly higher among those receiving the placebo. The constipation was almost certainly due to the upset of the circadian physiological rhythms associated with long-distance flights.

The incidence of diarrhoea related to territory emerges as follows: Africa 25.9%; Middle East 23.5%; South Europe 16.9%; North and Central Europe 15.6%; Asia (including India and Pakistan) 15.4%; South America and Caribbean 12.6%; Australasia 11.3%; North America 7.7%. The one surprising result is the low incidence in India and Pakistan.

Adverse Reactions.—Twenty-five persons stopped taking the tablets because of suspected reactions, 21 within five days and four within 10 days. Fourteen were thought to be unconnected with medication (seven were placebo reactors). Of the 11 prob-

ably connected, most occurred in the neomycin-sulphonamides group; five developed rashes, and six developed diarrhoea which cleared after stopping the tablets. There were two reactions reported with Streptotriad,* but these were thought to be unconnected.

Discussion

Though traveller's diarrhoea is not a serious illness it can be incapacitating, especially to the business man carrying out extensive air travel within a tight schedule. A three-day stay in an overseas capital to collect the year's export orders could be completely lost. The plan, therefore, was to try to find a prophylactic agent which would be effective in reducing the incidence of this complaint and at the same time to obtain further information regarding incidence, associated symptoms, and geographical distribution.

Since the termination of the survey, frequent requests have been received for further supplies of tablet C (Streptotriad).

In view of the finding by Kean and Waters (1958) that 63% of cases of diarrhoea occur during the first week, it might be advisable to double the suggested dosage in the first week only.

Summary

This report describes a comparison of Streptotriad with neomycin-trisulphonamides and a placebo in the prophylaxis of traveller's diarrhoea involving about 1,100 B.O.A.C. personnel and families taking trips abroad. Medication was randomly allocated and given for three weeks, one tablet twice daily for the first two weeks while away and one daily for the third week. Children under 12 were given half dosage. The commonest places of occurrence were Africa (25.9%) and the Middle East (23.5%).

Streptotriad was statistically beneficial in reducing both diarrhoea and associated symptoms. Neomycin-trisulphonamides was statistically beneficial in reducing symptoms, but not diarrhoea; abdominal pain was the commonest associated symptom: 75% had a duration of three days or less. Adverse reactions were practically nil with Streptotriad, which was by far the most popular medication as noted by the number of subsequent requests.

In view of Kean's work it might be worth considering whether the dosage of Streptotriad should not be doubled during the first week.

Thanks are due to May & Baker Ltd., who provided the tablets and printed material; to Professor A. W. Woodruff for his frequent advice; and to Dr. J. Graham Taylor, Director Medical Services, Air Corporations Joint Medical Service, for permission to publish.

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Urinary Leucocyte Excretion in Hypertension in Pregnancy

M. A. CHADD,*§ M.B., B.CH., D.C.H.; D. MICHAEL HUMPHREYS,* M.B., CH.B.
H. M. LEATHER,† M.D., M.R.C.P.; S. A. WILLS,‡ A.I.M.L.T.

Brit. med. J., 1967, 4, 655-656

Little (1966) showed that urinary white cell excretion rates were normal—that is, less than 200,000 per hour—in 95% of pregnant women free from bacteriuria and in only 28% with bacteriuria. Kincaid-Smith and Bullen (1965) found persistently raised urinary white cell excretion rates, despite successful treatment of bacteriuria, in pregnant women who were subsequently found to have established renal disease. Cross and Leather (1965) reported abnormal white cell excretion rates in hypertension in pregnancy irrespective of the clinical cause of the hypertension. The present study has been made to determine how long after delivery this abnormal leucocyte excretion persists, what relation it bears to continued hypertension in the post-partum period, and in particular whether it is associated with pyelonephritis.

The series includes 61 patients with hypertension in pregnancy and a further control group of 54 normotensive pregnant subjects. The effect on the leucocyte excretion of a course of ampicillin in 26 of the hypertensive patients and of lowering the blood pressure with hypotensive drugs in a further 15 patients was determined.

Material and Methods

Control subjects were healthy normotensive pregnant women from 16 to 38 weeks of gestation, with no history of urinary tract infection and in whom the urine was sterile. The hypertensive patients' period of gestation ranged from 16 to 36 weeks. For the purpose of this study hypertension was defined as a diastolic blood pressure of 90 mm. Hg or more, and at least two such readings were required before admission to the series. Urinary leucocyte excretion before and after prednisolone provocation was determined by the method of Houghton and Pears (1957) with the modification that three urine specimens were collected at 90-minute intervals after prednisolone. To avoid contamination of the urine, specimens were collected by the method of Leather and Hutchings (1960). Resting leucocyte excretion levels below 200,000 cells/hour were regarded as normal (Little, 1966). A prednisolone provocation test was regarded as positive when in one of the post-prednisolone urine specimens the leucocyte excretion rate was double that of the control period and also exceeded 300,000 cells/hour (Leather, Wills, and Gault, 1963). Urine was cultured on blood agar and MacConkey's media. In all cases a colony count was performed with the serial dilution technique. Urine studies were repeated throughout pregnancy and at intervals up to one year after delivery. Excretion urography was carried out in the hypertensive patients two months or more after delivery.

Results

Control Subjects.—The 54 normotensive patients were aged 16-43 years, and 26 were primiparae. In 16 resting leucocyte excretion was abnormal, and a further 15 became abnormal

after prednisolone. The urine was infected (>100,000 org./ml.) in six, of whom five showed abnormal leucocyte excretion before or after prednisolone. Excretion rates were more often abnormal in late than in early pregnancy: thus 15 out of 22 pregnancies of more than 30 weeks' gestation were abnormal, compared with 16 out of 32 pregnancies of less than 30 weeks. Neither age nor parity seemed to influence the abnormal rates.

Hypertensive Subjects.—The 61 hypertensive patients were aged 19-43 years; 21 were primiparae. In 28 the resting leucocyte excretion was abnormal and in a further 20 it became abnormal after prednisolone. Thus only 13 out of the 61 were entirely normal. In all cases leucocyte excretion was estimated at least twice during the pregnancy. In nearly all cases these repeated results were in the same range as the initial count. The urine was infected in eight, of whom four showed abnormal leucocyte excretion. In contrast to the control subjects, leucocyte excretion was not raised more often late in pregnancy; thus all 13 before 30 weeks were abnormal, compared with 35 out of 48 after 30 weeks.

Effect of Blood Pressure Control on Leucocyte Excretion.—Of the hypertensive patients 35 were currently in a study to determine the effect of control of hypertension in pregnancy; 20 of these received no hypotensive agents and in 15 the blood pressure levels were controlled with hypotensive drugs. Leucocyte excretion was studied before and after a period of observation (average 67 days). Of the 20 controls, 17 were abnormal at the first count and 18 subsequently; of the 15 treated cases, 13 were abnormal at first and 11 subsequently. There was therefore no evidence that control of hypertension influenced the leucocyte excretion rate (Table I).

TABLE I.—*Urinary Leucocyte Excretion During and After Pregnancy in Hypertensive Patients*

Group	Abnormal White Cell Excretion			
	During Pregnancy		Post-partum	
	No. Studied	No. Abnormal	No. Studied	No. Abnormal
Untreated hypertensives ..	20	18	15	4
Treated hypertensives ..	15	11	14	10
Ampicillin-treated ..	26	19	19	10

Effect of Antibiotics on Leucocyte Excretion.—Twenty-six were given a course of ampicillin (average duration 17 days), 19 of these having abnormal counts initially. After ampicillin therapy all 19 patients remained abnormal. There was no evidence that antibiotic therapy affected the abnormal excretion rate (Table I).

Urinary Leucocyte Excretion After Delivery.—In 48 out of 61 hypertensive patients urinary leucocyte excretion was abnormal during pregnancy. Of the 48 who were restudied up to 12 months post-partum, 24 were abnormal and 24 were in the normal range; the remaining 13 failed to attend (Table I).

Urographic Findings.—Excretion urography was performed on 44 of the hypertensive patients: 27 were normal or showed non-pathological variations; 5 showed post-pregnancy changes with dilatation of the renal pelvis and dilatation and tortuosity of the ureters, and 12 were definitely abnormal and included

*Research Registrar.

†Consultant Physician.

‡Technician.

§ Present address: Department of Clinical Research, Plymouth General Hospital.

§ Present address: Department of Child Health, United Cardiff Hospitals.

pyelonephritis (5 cases), renal ischaemia (2 cases), unilateral renal atrophy (2 cases), reflux hydroureter (2 cases), and polycystic disease (1 case).

Relation Between Urographic Findings and Abnormal Leucocyte Excretion.—White cell excretion before and after delivery was known in all patients who were radiographed. Abnormal excretion persisted after delivery in roughly the same proportion in those with normal x-ray picture, post-pregnancy change, or pathological change (Table II).

TABLE II.—*Relation Between Radiological Findings and Abnormal Leucocyte Excretion*

	No.	Abnormal Excretion	
		Ante-partum	Post-partum
Normal x-ray picture ..	27	20	12
Post-pregnancy change ..	5	5	2
Pathological change ..	12	11	6

Relation Between Urographic Findings, Persistent Hypertension, and Post-partum Urinary Leucocyte Excretion.—In all 44 patients in whom excretion urography was performed leucocyte excretion was measured after delivery. In 23 it returned to normal and in 21 it remained abnormal. The incidence of normal or abnormal urographic findings and of persistent hypertension was similar in both groups (Table III).

TABLE III.—*Relation Between Urographic Findings, Persistent Hypertension, and Post-partum Urinary Leucocyte Excretion*

Urinary Leucocyte Excretion	No.	Urography		Hypertensive Post-partum
		Negative	Positive	
Returned to normal ..	23	15	8	11
Remained abnormal ..	21	12	9	10

Discussion

Both normotensive and hypertensive non-infected non-pregnant women give urinary leucocyte excretion rates within the accepted range of normal (Pears and Houghton, 1959; Hutt *et al.*, 1961), and Little (1966) reported normal excretion rates in a very high proportion of pregnant women without bacteriuria. Cross and Leather (1965) reported raised urinary leucocyte excretion before or after prednisolone provocation in 29 out of 31 pregnancies complicated by hypertension but without bacteriuria.

In the present series of 115 pregnant women, urinary white cell excretion was abnormal in more than 50% of apparently normal subjects and in 80% of hypertensive patients. There was no evidence from association with symptoms of

urinary tract infection, positive urine cultures, or response to antibiotics that it was necessarily a manifestation of infection in the urinary tract. In the hypertensive group it was not modified by the use of hypotensive drugs and had no clear association with the persistence or otherwise of hypertension after pregnancy. Finally, there was no evidence from the subsequent urographic findings that it bore any relation to established renal disease as assessed by radiology.

The reason for the increased urinary leucocyte excretion in pregnancy remains therefore unexplained. It is possible that it represents some form of vascular response to the pregnancy itself, since there was evidence in some of the groups studied that the number of abnormal tests increased with advancing gestation and that in some of the cases it returned to normal after pregnancy. However, its value as evidence of infection or of anatomical abnormality of the urinary tract appears to be negligible.

Summary

Urinary leucocyte excretion was abnormal before or after prednisolone provocation in 31 out of 54 normotensive pregnant subjects and 48 out of 61 hypertensive pregnant subjects. In the hypertensive group treatment with antibiotics or hypotensive agents failed to alter the abnormal leucocyte excretion, which in nearly half the cases returned spontaneously to normal after delivery. There was no evidence that abnormal leucocyte excretion was a manifestation of pyelonephritis or that it bore any relation to the persistence or otherwise of hypertension after delivery.

We wish to thank the obstetricians of the Plymouth General Hospital—Messrs. J. G. Dumoulin, G. M. Davidson, and I. Cunningham—for ready access to patients under their care and for encouragement and help during this study. We are grateful to Dr. H. T. ApSimon for reviewing the radiographs. Three of us (M. A. C., D. M. H., and S. A. W.) were in receipt of research grants from the Research Committee of the South-western Regional Hospital Board.

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Scleroderma Heart Disease

E. FLETCHER,* M.D., F.R.C.P.; P. MORTON,† M.D., M.R.C.P.ED.

Brit. med. J., 1967, 4, 657-658

Generalized progressive scleroderma is characterized by visceral involvement concerning which there are many important reviews in the literature (Beigelman *et al.*, 1953; Leinwand *et al.*, 1954; Oram and Stokes, 1961). Weiss *et al.* (1943) firmly established scleroderma heart disease as a clinical entity. Oram and Stokes (1961) summarized the cardiac manifestations, which include myocardial failure, pericarditis, chronic cor pulmonale, various arrhythmias, and incidental findings such as cardiomegaly, cardiac murmurs, and electrocardiographic anomalies.

The clinical, electrocardiographic, and necropsy findings in two cases with cardiac involvement are reported here. One of us (E.F.) has already published two additional cases with pathological findings in the heart (Roesler and Fletcher, 1963, Figs. 46 and 47).

Case 1

A woman aged 50 had had joint pains and stiffness for about 10 years. At the time the E.C.G. shown in Fig. 1 was recorded she had extensive scleroderma involving the limbs and trunk. She complained of shortness of breath. The heart sounds were normal and there was a basal systolic murmur. Blood pressure was 102/70 mm. Hg, serum calcium 10 mg./100 ml., and serum potassium 4.6 mEq/l. Radiological examination showed extensive soft-tissue calcinosis. X-ray examination of the chest showed a normal heart shadow and extensive fibrosis of the lower lobes of the lungs. Three months after the electrocardiogram was recorded she developed bronchopneumonia and died. No digitalis had been given at any time.

At necropsy the heart weighed 400 g. Both ventricles were hypertrophied. Microscopical sections of the ventricular myocardium showed areas of small haemorrhages and fibrosis with perivascular

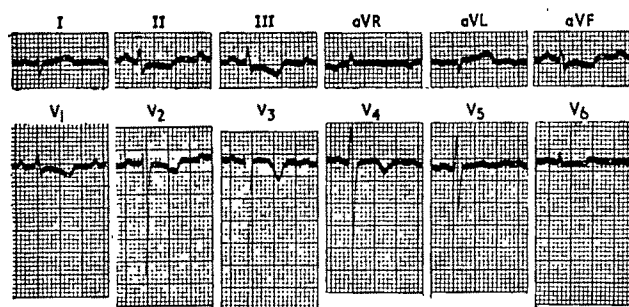


FIG. 1.—Case 1. Scleroderma heart disease. Abnormal S-T segment and T-wave changes.

infiltration by plasma cells and eosinophils. The coronary arteries showed minimal atheroma with no evidence of occlusion of any coronary vessel of significant size. The valves were all normal. Both lungs showed extensive fibrosis.

In Fig. 1 the limb leads show abnormal low voltage, no deflection exceeding 5 mm. in amplitude. There is sinus rhythm, rate 88 a minute. The mean QRS axis is deviated towards the right, with a deep S deflection in lead I and a late R deflection in lead aVR. The P-R interval measures 0.15 sec. and the QRS interval 0.09 sec. The Q-T interval measures 0.37 sec., which is the upper limit of normal for the heart rate. The S-T segments are abnormally depressed in leads II, III, and aVF, with reciprocal slight

elevation in leads I, aVR, and aVL. The chest leads show low QRS voltage in lead V1 adjacent to the right ventricle, and also in lead V6 adjacent to the left ventricle. The S-T segments are displaced downwards in leads V1, V2, and V6, and the T waves are negative in leads V3 and V4. The T wave in lead V5 is abnormal in shape.

Comment.—The abnormal S-T segment and T-wave changes indicate myocardial impairment due to the extensive infiltration of the myocardium found at necropsy. The biventricular hypertrophy resulted likely from compensation for the loss of myocardial fibres from progressive fibrosis. The abnormal low QRS voltage recorded in spite of the hypertrophy may reflect changes in the conduction properties of the lungs associated with pulmonary fibrosis. The R deflection in lead V1 is relatively high in amplitude compared with the S deflection, which may be due to right ventricular hypertrophy noted at necropsy. In leads V2, V3, and V4 the QRS voltage is normal or increased, as these leads are adjacent to the "bare area" of the heart with little intervening abnormal lung tissue. The right axis deviation appears to reflect right heart strain associated with extensive pulmonary disease.

Case 2

This patient began to develop multiple joint pains at about the age of 30. They were insidious and progressive, and two years after their onset she had a medical examination in hospital. The only abnormality discovered was a raised blood sedimentation rate. An electrocardiogram was reported as normal. She was next seen in hospital at the age of 40, when she was found to have extensive scleroderma. In the intervening years she had had intensified joint pains and stiffness. She complained of shortness of breath and dysphagia. The facial structures were shrunken and she had a "small mouth." There were flexion deformities of the limbs due to scleroderma. The heart sounds were normal and there was a basal systolic murmur. Blood pressure was 110/70 mm. Hg, serum calcium 10 mg./100 ml., and blood urea 40 mg./100 ml. She died five months after the electrocardiogram (Fig. 2) was recorded. No digitalis had been given.

At necropsy there was a pericardial effusion of blood-stained fluid. The coronary arteries and valves were normal. The heart weighed 370 g. The right ventricle measured 0.7 cm. in thickness and the left ventricle 1.2 cm. Microscopical sections of the myocardium showed diffuse interstitial fibrosis. Both lungs also showed fibrotic changes. The kidneys were normal.

The E.C.G. in Fig. 2 shows sinus rhythm, rate 86 per minute, P-R interval 0.16 sec., QRS interval 0.08 sec. The QRS voltage is normal and the mean QRS axis is normally directed. The S-T segments are abnormally depressed in leads I, II, aVL, and V4 to V7. The high-amplitude R deflection in lead Ve measuring 6 mm. is

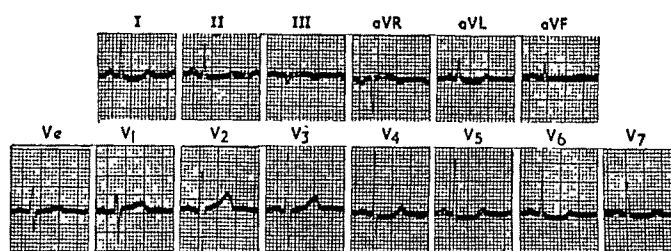


FIG. 2.—Case 2. Scleroderma heart disease. Abnormal S-T segment changes.

* Physician in Charge, Cardiovascular Unit, Belfast City Hospital, Belfast 9.

† Physician, Cardiovascular Unit, Belfast City Hospital, Belfast 9.

greater than the S deflection, and this may reflect right ventricular hypertrophy, as this lead is located at the xiphisternum.

Comment.—The electrocardiogram was recorded five months before death, so that close correlation with the necropsy findings has less meaning. Nevertheless, it is reasonable to assume that the abnormal S-T segment changes reflect myocardial impairment due to the diffuse myocardial fibrosis found at necropsy.

Discussion

These two patients had primary myocardial infiltration and fibrosis associated with advanced scleroderma. They complained of breathlessness, but assessment of this symptom is difficult in view of the pulmonary fibrosis and restriction of respiratory effort in extensive scleroderma. Radiological and auscultatory findings were not particularly helpful. The electrocardiogram alone afforded objective evidence of primary myocardial involvement, as noted in the above comments. The abnormal findings were confined chiefly to S-T segment and T-wave changes, indicating abnormal repolarization of the ventricular myocardium on the basis of extensive myocardial impairment supported by necropsy findings. Windesheim and Parkin (1958) reviewed the electrocardiographic findings in 27 similar cases, of which three showed low QRS voltage and T-wave changes similar to those described above. Pulmonary involvement or metabolic abnormalities in scleroderma may also

produce secondary electrocardiographic anomalies, as noted in the interpretations. Neither patient had hypertension to complicate the electrocardiographic findings. The cause of death was probably not related directly to the cardiac abnormality in either case.

Summary

Two cases of generalized progressive scleroderma are described with electrocardiographic and necropsy findings. Cardiac symptoms may be masked by pulmonary involvement. The electrocardiogram gave the most useful objective evidence of the primary myocardial infiltration, confirmed at necropsy, when correlated with the clinical findings. The S-T segment and T-wave changes, however, are non-specific in character, and this requires to be taken into account in generalized scleroderma, which may also be associated with renal hypertension and metabolic imbalance.

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Medical Memoranda

Fatal Hypercalcaemia Complicating Carcinoma of Breast, Resistant to Cortisone and Phosphate Administration

Brit. med. J., 1967, 4, 658-659

One in three patients suffering from carcinoma of the breast metastases five years after the menopause may be expected to achieve temporary suppression of these metastases by the use of oestrogens (Taylor, 1956). This therapy is often chosen first in the post-menopausal woman, as it causes less endocrine upset than either androgens or cortisone. The effects of oestrogen therapy are always carefully observed in each patient, as some metastases in the elderly are oestrogen-dependent and flare up on treatment. One of the methods used to detect this dependence has been the increased urinary calcium excretion which occurs (Emerson and Jessiman, 1956), and on occasion hypercalcaemia (Kennedy, Nathanson, Tibbetts, and Aub, 1955). Several authors mention that this complication of therapy may be fatal (Herrmann, Kirsten, and Krakauer, 1949), and eight cases have been recorded (Kleinfeld, 1962). We had the opportunity of observing and treating a similar patient while she was on a fixed dietary intake of calcium in preparation for other metabolic measurements.

CASE HISTORY

A 66-year-old widow was admitted to hospital for investigation of a three-month history of tiredness, nose bleeds, and nodules in the skin. On questioning she admitted to a mass in the breast which had been present for at least eight years to her recollection.

On examination she was pale, there were multiple skin secondaries stemming from a hard fixed mass in the right breast which had not ulcerated, and bruises on the back and over both knees. The liver was enlarged 3 cm. below the right costal margin. There was no

bone tenderness. Blood pressure was 155/90 mm. Hg. Further systemic examination was normal.

Investigations.—Haemoglobin 6.8 g./100 ml.; W.B.C. 4,600/cu. mm., with 5% myelocytes and 25 nucleated red cells/100 W.B.C.s; platelet count 13,000/cu. mm. Radiographs of chest and spine showed diffuse osteolytic metastatic infiltration involving the ribs, dorsal and lumbar spine, sacrum, and pelvic region. Lung fields were clear. Serum proteins 6.3 g./100 ml., electrophoretic pattern normal. Serum alkaline phosphatase 6.6 K.A. units/100 ml. (normal 3-14) (King and Armstrong, 1934). Serum alanine aminotransferase 15 units/ml. (normal 0-25 units) (Reitman and Frankel, 1957). Plasma calcium 9.7 mg./100 ml. by flame photometry (MacIntyre, 1961). Plasma inorganic phosphorus 3.3 mg./100 ml. (Fiske and Subbarow, 1925). Na 143, K 4.3, HCO₃ 20 mEq/litre. Blood urea 42 mg./100 ml. The 24-hour urinary excretion of calcium on admission was 36.5 mg. on a ward diet. Electrocardiogram was normal. Biopsy of skin nodules showed a spheroidal-cell carcinoma infiltrating the dermis and fat.

She was transfused with 4 pints (2.3 litres) of blood, one of the skin nodules was biopsied, and she was started on a calcium balance. Stilboestrol 60 mg./day was given from 11 May 1966, and the progressive changes in the plasma calcium were noted from 15 May. Stilboestrol was discontinued two days later and 150 mg. of hydrocortisone a day was given intramuscularly. On the third day on this regimen with no immediate response, 500 ml. of 1% buffered sodium phosphate was given, and later that day (19 May) the patient died. Details of the calcium balance, electrolytes, and cardiogram are given in Figs. 1 and 2.

Post-mortem Findings.—The subject was a wasted female with a large carcinoma which involved most of the right breast and invaded the interstitial tissues and pleura. Metastases were present in the skin of the chest and abdomen, and in the ribs, vertebrae, and pelvis. The lymph nodes were not involved. Both lower limbs showed extensive subcutaneous haemorrhages. Only minor abnormalities were noted in the gross appearances of the other organs, including brown pigmentation of the myocardium, oedema and congestion of the lungs, fatty changes in the liver, and nodularity of the thyroid. Four parathyroids were dissected out and noted to be normal in size. Histology showed a poorly differentiated cellular carcinoma of the breast. Sections stained with von Kossa's stain

for calcium showed calcification of the cardiac muscle fibres, one lobe of the thyroid, renal tubules, parenchymal cells of the liver, and small arteries and arterioles. The renal involvement was unequal.

COMMENT

Previous to any therapy the patient was in approximate balance with a normal urinary calcium (230 mg./day), electrolytes, blood urea, and electrocardiogram. Within three days of her receiving oestrogens the plasma calcium had begun to rise, and three days later it had reached 14.7 mg./100 ml., with a urinary calcium of 650 mg./day. The mechanism of the hyper-

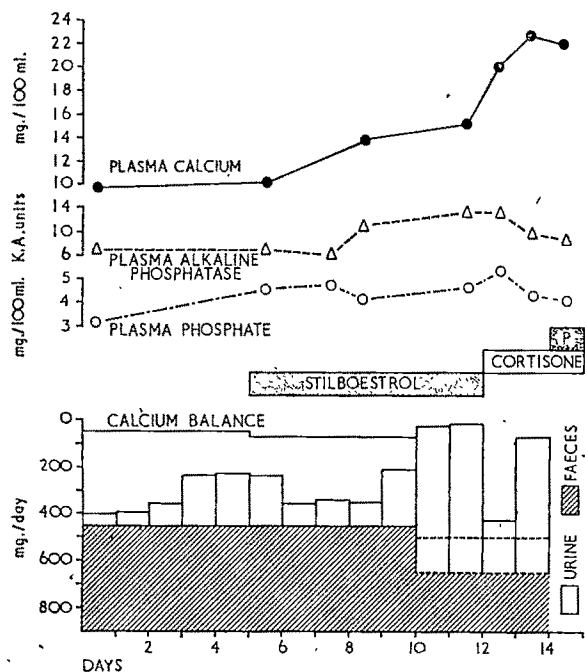


FIG. 1.—Serial estimations of the plasma concentrations of calcium, alkaline phosphatase, and phosphate. Calcium balance (incomplete terminally) is calculated by constructing the daily food intake downwards and adding the faecal and urinary excretion for each period upwards; negative balance is seen when the faecal and urinary excretion exceed the food intake and project above the zero line in the upper part of the diagram. P=Phosphate infusion.

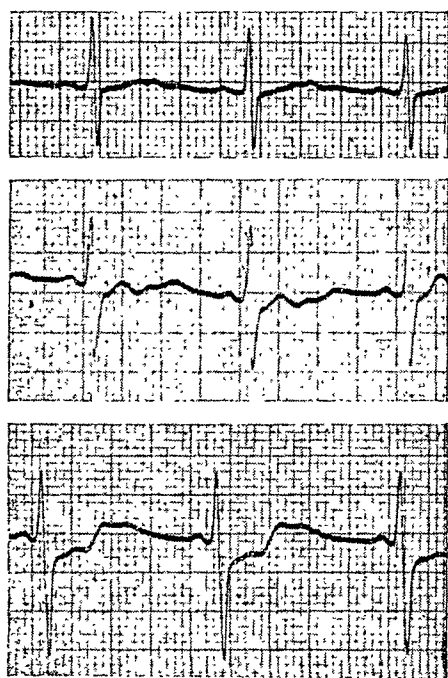


FIG. 2.—Electrocardiographic record. Above, 28 April. Centre, 18 May. Below, 19 May.

calcaemia of malignant disease has often been reviewed (Watson, 1963); it can be due to simple osteolysis, the production of parathyroid-hormone-like peptides, or a nonspecific hypertrophy of the parathyroid glands (Kohout, 1966), and on occasion to the production of osteolytic steroids. In view of the extensive lytic deposits and the rising phosphate concentrations, the first cause seems most likely. Despite cessation of stilboestrol and the substitution of cortisone the plasma calcium continued to rise with the onset of uraemia and cardiographic changes (Fig. 1).

The usual recorded cardiographic features of hypercalcaemia are shortening of the Q-T interval, more rarely prolongation of P-R interval and inversion of the T wave, and on occasion bradycardia, A-V block, and bouts of fibrillation (Bradlow and Segal, 1956; Beck and Marriott, 1959; Bronsky, Dubin, Waldstein, and Kushner, 1961; Voss and Drake, 1967). In the three recordings the P-R interval remained short between the range 0.12 to 0.10 over the 12-mg. range from 10 to 22 mg./100 ml., the Q-T interval, corrected according to the formula $QT_c = QT \sqrt{R-R}$, ranged from 0.33 to 0.22, and the final cardiogram showed either considerable lengthening of this interval or that the T wave was buried in the S-T segment depression the next wave being a prominent U wave which was clearly apparent the day before. On the day of her death, with the infusion of phosphate, abrupt changes in the cardiogram took place with widespread S-T depression over the anterolateral segments (Fig. 2). In these circumstances, with the plasma calcium over 20 mg./100 ml. unresponsive to cortisone, it appears safer to rely on a profuse diuresis, possible dialysis, or chelating agents (Lischer, 1965) rather than on the administration of intravenous phosphate as recommended by Goldsmith and Ingbar (1966). This may lead to a $Ca \times PO_4$ ion product in excess of 2.4×10^{-6} moles/litre, which produces precipitation calculated from regression equations confirmed from the reduction of calcium both in normal and in hypercalcaemic subjects infused with phosphate (Hebert, Lemann, Petersen, and Lennon, 1966).

Injected calcium phosphate is preferentially taken up by cells lining small vessels (Gersh, 1937), and this may partly explain the calcification of the intima and media of the small arteries and arterioles of the myocardium.

We would like to thank Professor J. Anderson for his help and advice, and Mrs. P. Giles for technical assistance. Miss E. Knight was supported by the B.E.C.C.

V. PARSONS, D.M., M.R.C.P.,
Senior Lecturer in Medicine.
G. STIRLING, M.D., M.C.PATH.,
Senior Lecturer in Pathology.
E. KNIGHT, M.PHIL., B.SC.,
B.E.C.C. Research Biochemist.

King's College Hospital, London S.E.5.

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Budd-Chiari Syndrome after Taking Oral Contraceptives

Brit. med. J., 1967, 4, 660

Budd (1846) reported a case of hepatic vein thrombosis caused by an abscess of the liver. Subsequently Chiari (1899) described three and reviewed 10 cases. Parker (1959) was able to find 149 cases described in the literature and contributed a further 18 cases. The syndrome seems to be more common in men than in women, and the average age at necropsy is 34 years. The possibility of an increased risk of thromboembolic disorders in patients taking oral contraceptives has been discussed lately. A number of case reports of thrombophlebitis and pulmonary embolism have been published, and the Medical Research Council (1967) has examined the question. Only one case of hepatic vein thrombosis in a young woman on oral contraceptive has been reported (Ecker *et al.*, 1966). The patient had been on norethisterone and mestranol (Norinyl) for 14 days when her symptoms started.

We have seen the Budd-Chiari syndrome in a previously healthy woman taking an oral contraceptive. Because of the possible causal relationship we consider the case worth reporting.

A 28-years-old housewife was admitted to hospital on 20 December 1966. Previous health had been excellent. For contraception she had periodically taken lynoestrenol plus mestranol (Lyndiol) during 12 to 18 months. The treatment was withdrawn on 12 December 1966 because of nausea. She had been taking no other drugs. During the last month before admission to hospital she had gradually increasing abdominal distension, epigastric pains, loss of appetite, and nausea. No jaundice or discoloration of faeces or urine were noted.

On admission her general condition was fairly good; no signs of anaemia or jaundice; no spider naevi or palmar erythema; abdomen grossly distended, with dilated abdominal veins; the liver was felt 8–10 cm. below the right rib margin, smooth, not tender; the spleen was enlarged; ascites present; on the side of the neck were several small lymph nodes.

Laboratory investigations showed: Haemoglobin, 14.7 g./100 ml. Erythrocyte sedimentation rate 7 mm. Leucocytes, 6,520/cu. mm., normal distribution. Alkaline phosphatase, 12.1 King-Armstrong units. S.G.O.T., 1.1. Thymol turbidity test, 0.07.

Epilepsy and Liver Dysfunction in Association with Hypernephroma

Brit. med. J., 1967, 4, 660–661

Mohamed (1965b) reported the case of a patient with a hypernephroma who died after a protracted illness associated with fever, anaemia, loss of weight, progressive hepatosplenomegaly, and, preterminally, episodes of grand mal epilepsy. At necropsy there was no evidence of metastatic spread, and Mohamed suggested that the epileptiform seizures and the liver-cell dysfunction would have resolved if the renal tumour had been resected during life. The present report would seem to support this prediction.

CASE REPORT

A 69-year-old man was admitted to hospital at the end of August 1965 because of drop attacks. He gave no history of loss of consciousness, vertigo, injury, or incontinence in association with these episodes. For three months before admission he had been unwell, anorexic, and losing weight. He also complained of a feeling of weakness in his legs, a tremor of his hands, frontal headaches, and nocturia.

Prothrombin, 71%. Bromsulphalein retention, 2%. Creatinine, 1.0 mg./100 ml. Benzidine reaction on faeces negative. Urine: no albumin, no sugar. Electrophoresis: albumin, 3.1%; gamma-globulin, 0.78%. Sigmoidoscopy, normal, no piles. Gynaecological examination normal.

X-ray examinations showed only raised diaphragm.

Needle liver biopsy (9 January 1967): liver tissue with acute congestion and fibrosis, presumably cirrhosis. Splenoportography (20 January) partly unsuccessful; rather large accumulation of contrast medium at the site of the spleen; faint filling of the normally formed vena lienalis. Microscopical evaluation of spleen puncture: relative lymphocytosis, otherwise no pathological changes.

The general condition of the patient deteriorated. Oedema of the legs developed and the ascites increased. Despite treatment she died on 14 March after repeated haemorrhages.

Necropsy.—Liver: 30 by 18 by 8.5 cm.; weight 3,330 g. Surface nodular consistency compact. Colour of surface varied from dark red to light bronze. In the right lobe were several 1- to 2-cm. yellow, soft necroses. Large confluent areas of the parenchyma showed haemorrhagic infarcts. Histological examination showed endophlebitis obliterans. A small hepatic vein showed thrombosis besides infarcts and some cirrhotic changes. Vena cava inferior: no thrombosis; all venae hepaticae were occluded at the junction with vena cava; in the liver a small thrombus in a larger hepatic vein.

Oesophagus: large contorted veins; 10 cm. from cardia a thrombosed vein in the wall.

Spleen: 16 by 10 by 6 cm.; weight 440 g.; congested.

Prospective studies running over a sufficiently long period are urgently needed to evaluate the risk of oral contraceptives.

We owe thanks to Dr. Ole Werdelin, University Clinic, Department of Pathology, for the necropsy report.

KIRSTEN STERUP, M.D.

JOHANNES MOSBECH, M.D.

St. Elisabeth's Hospital,
Department of Medicine,
Copenhagen, Denmark.

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On examination he was cachectic, pale, and apathetic. There was generalized muscle-wasting with fasciculation, and muscle power was diminished. Reflexes were present and equal, and the plantar responses were flexor. Some impairment of sensation in both feet and incoordination of movement of the left leg were found. Pulse rate was 48 and regular. Blood pressure was 140/80. There were no signs of cardiac failure. The liver edge extended three fingerbreadths below the costal margin and was firm and regular. Splenomegaly was not detected. Initially the patient was afebrile, but later he developed an intermittent pyrexia, his temperature being as high as 101° F. (38.3° C.) on several occasions.

Investigations.—Erythrocyte sedimentation rate was 134 mm. in first hour (Westergren). Haemoglobin was 7.7 g./100 ml., the red cells being hypochromic and microcytic. The reticulocytes were 1.4/100 red cells. The white cell count was 6,000/cu. mm. Examination of the sternal marrow showed evidence of active normoblastic erythropoiesis with occasional macronormoblasts. There was no excess of megakaryocytes or plasma cells. Iron storage appeared to be abundant. Plasma urea, electrolytes, bilirubin, aspartate aminotransferase, and alanine aminotransferase were all normal. The plasma alkaline phosphatase was raised to 33 K.A. units/100 ml., and the bromsulphalein test was abnormal, there being 35% retention at 25 minutes and 28% at 45 minutes. The prothrombin time was 17 seconds (control 15 seconds). The plasma albumin/globulin ratio was reversed. Electrophoresis showed an increase in all globulin fractions, especially alpha-2. Urine analysis was negative.

Two weeks after admission the patient had a grand mal convulsion. This attack appeared to be different from the episodes he had had before admission. C.S.F. examination was negative. E.E.G. showed considerable generalized abnormality, the background activity being dominant from between 6 and 7 cycles per second.

By about the third week of admission the liver appeared to have diminished in size, and it was then possible to detect a separate ballotable mass in the left hypochondrium. A few pus cells and red cells were noted in the urine, and these findings led on to intravenous pyelography. This revealed some displacement and deformity of the calices of the left kidney, and possibly a mass arising from the midportion of that kidney.

A left nephrectomy was performed on 30 September 1965 (Mr. W. Campbell). The kidney was seen to be completely replaced by tumour tissue, and there was extension into the renal vein. Histology confirmed that the tumour was a hypernephroma. There was no evidence of hepatic secondaries, either grossly or on microscopy of a biopsy specimen.

The patient made a good recovery after the operation. He gained weight rapidly, the hepatomegaly disappeared, and the liver-function

tests reverted to normal (see Chart). Two months after the operation an E.E.G. was normal. Ten months after the nephrectomy the patient was still very well. Four months later he died quite suddenly. Necropsy was limited to determining the cause of death. This was due to coronary thrombosis. There was no macroscopic evidence of metastasis in the liver or other organs, but the brain was not examined.

COMMENT

Hepatomegaly and non-metastatic liver-cell dysfunction, with return to normal on removing the renal lesion, is now well documented (Stauffer, 1961; Greenberg *et al.*, 1964; Mohamed 1965a), our case being the fifteenth to be reported. It is important that this syndrome is recognized, for there is a tendency to refuse operation to patients with hepatomegaly and a raised alkaline phosphatase on the assumption that the patient already has liver metastasis and the condition is then irremediable (Sherlock, 1963). Patients with hypernephroma may have extreme cachexia and impairment of cell function without metastasis (Creevy, 1935; Mohamed, 1965b).

The reversal of the signs and symptoms after nephrectomy in the above case could also have been related to spontaneous regression of carcinoma at other sites, and this possibility cannot be definitely excluded, particularly in relation to the brain.

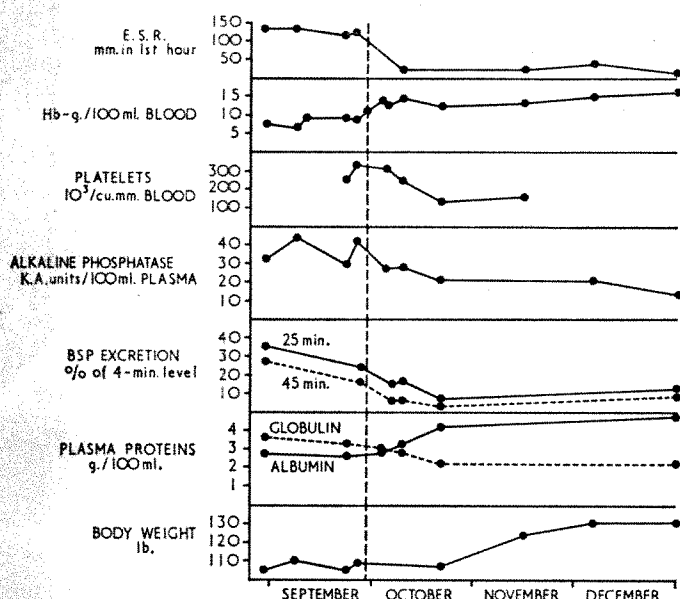
It is a pleasure to acknowledge the assistance given by Dr. John Laidlaw, Chalfont Colony, Bucks, with the interpretation of the E.E.G.s. We are grateful to Mr. W. Campbell, who performed the nephrectomy and liver biopsy, and to Dr. D. G. Rushton, who carried out the necropsy.

A. G. STEWART, M.B., M.R.C.P., M.R.C.P.ED.,
Lecturer in Therapeutics, University of Dundee.

J. G. SPRUNT, M.B., B.S.C., M.R.C.P.ED.,
Senior Lecturer in Therapeutics, University of Dundee.

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Changes in E.S.R., haemoglobin, platelets, plasma alkaline phosphatase, B.S.P. excretion, plasma proteins, and body weight before and after nephrectomy have been plotted. The vertical dotted line indicates the day of operation. The improvement in haemoglobin level before operation was due to blood transfusion.

Relapsing Polychondritis

Brit. med. J., 1967, 4, 661-662

Relapsing polychondritis is a disease of which the main features are episodic inflammation, followed by dissolution, of cartilage throughout the body. In addition, there is often inflammation of the iris and sclera. It should be noted that the disease has been described under various titles. These include "chondromalacia," "chronic atrophic perichondritis," "diffuse perichondritis," "polychondropathia," and "relapsing polychondritis." The latter designation has been favoured by most recent authors.

The first case was probably described by Jaksch-Wartenhorst (1923). Since then nearly 50 cases have been reported, but only two of them are in British literature (Rhys Davies and Kelsall, 1961; Thould, Stansfeld, and Wykeham Balme, 1965).

CASE REPORT

A housewife had been in previously good health apart from a cough which she said she had had all her life. Her family history was non-contributory. In 1956, when aged 41, her cough became worse, and some wheezing and mucopurulent sputum developed. The symptoms were all worse in the winter.

In 1961 painful swelling of the ankles and knees developed. The erythrocyte sedimentation rate (E.S.R.) at this time was 60 mm. in one hour (Westergren). The Rose-Waaler test was said to be positive but the titre was not known. She was given a short course of corticosteroids and her joint symptoms subsided.

In January 1962 she became short of breath and developed stridor. Her voice became hoarse. She developed swelling of both pinnae and her ears became "like cauliflowers." At the same time she had an episode of right-sided iritis. Effusions into both knee joints were noted. At this point some falling in of her nose was noticed. Laryngoscopy showed "swelling and spasm of the whole laryngeal inlet." A biopsy of the tracheal wall showed extensive chronic granulation tissue deep in the wall with dense hyaline fibrosis

of the lamina propria. The Rose-Waaler and Kveim tests were negative. Renal function tests were normal. Tracheostomy was performed because of the respiratory obstruction. A small dose of radiotherapy was given to the larynx.

She had a persistent cough with much sputum, which required to be aspirated many times daily. Her ears gradually returned to their normal size. Apart from several further episodes of iritis her condition remained otherwise virtually unchanged until February 1965, when she experienced some difficulty with inserting the tracheostomy tube. Bronchoscopy showed narrowing of both the trachea and the origins of the main bronchi (see Table) and the mucosa was granular and irregular. Biopsy of the tracheal mucosa showed squamous metaplasia with marked fibrosis. At this point prednisolone 20 mg. daily was given.

Corrected Measurements of Tracheal and Bronchial Diameters

	Normal Control	Patient
Trachea 2 cm. above carina	2 cm.	0.74 cm.
Right main bronchus 1 cm. below carina	1.2 "	0.67 "
Left " " 1 " " " "	1.0 "	0.67 "

She was admitted to the Churchill Hospital in April 1965, under the care of Dr. J. M. K. Spalding, because of difficulty with her tracheostomy. The depression of the middle of her nose was pronounced (Fig. 1) and the nasal cartilages were very soft. The right ear was somewhat soft and flabby. Her hearing was normal to ordinary ward testing. There was no objective evidence of past iritis. The tracheostomy tube was in situ and appeared to be satisfactory. There was some tenderness over the sternomanubrial joint. The other joints were objectively normal.

Investigations showed a mild hypochromic anaemia. The E.S.R. was 11 mm. in one hour (Westergren). The Wassermann reaction and Rose-Waaler test were negative. L.E. cells were not seen. No antinuclear factor was demonstrable. The total serum proteins



FIG. 1.—Photograph showing depression of middle of nose.

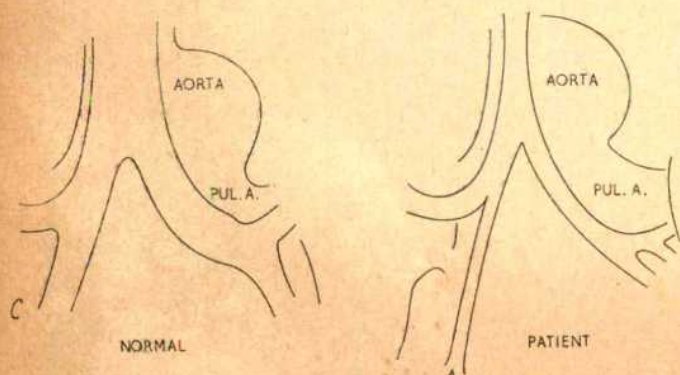


FIG. 2.—Tracing of inclined frontal plane tomograph taken through the plane of trachea and main bronchi.

were 6.6 g./100 ml. Serum electrophoresis showed a slight increase in the alpha-2-globulin and gammaglobulin. A midstream specimen of urine was normal. There was no excess of mucopolysaccharides in the urine. The blood urea was 26 mg./100 ml. The maximum urinary specific gravity was 1020. The creatinine clearance test was 82 ml./min.

Plain x-ray films of the chest were normal, but tomograms revealed gross narrowing of the trachea and main bronchi (Fig. 2). Lung-function tests were performed by Dr. R. Marshall, who reported as follows: "In this patient there is considerable increase in airway resistance. At normal flow rates (up to 0.5 l./min.) the resistance during inspiration is approximately the same as during expiration. At higher flow rates the resistance increases on expiration and the maximum possible expiratory flow is about 0.7 l./sec." There was sclerosis of the sternomanubrial junction. X-ray examination of the cervical and lumbar spines showed only non-specific degenerative changes. X-ray films of the hands and knees were within normal limits.

Since April the patient had remained reasonably well and was taking prednisolone 5 mg. t.d.s. In October 1965 she had a mild relapse involving painful swelling of both ears. This subsided without a further increase in her steroid therapy.

DISCUSSION

This patient shows the classical features of relapsing poly-chondritis. Most authors have reported single cases. Kaye and Sones (1964) reviewed 14 personal cases, together with 27 cases collected from the literature.

The disease is characterized by episodes of activity in which cartilage in various sites becomes inflamed. The episodes are often accompanied by low-grade fever and malaise. Recurrent episodes of activity ultimately produce softening of the affected cartilage. The pinnae become soft and flabby and the nose assumes a "saddle-nose" deformity. Involvement of the middle and inner ear may lead to deafness.

The cartilages of the respiratory tract are often involved, and ultimately narrowing of the trachea and bronchi may occur. This involvement of the respiratory tract is the usual cause of death. Cartilaginous joints such as the symphysis pubis and the manubrium sterni are sometimes affected. Synovial joints are affected in some cases, and occasionally a polyarthritis resembling rheumatoid arthritis may occur (Thould *et al.*, 1965). Three of the cases reported by Kaye and Sones (1964) fulfilled the criteria for definite rheumatoid arthritis laid down by the American Rheumatism Association (1959). The eye is involved in about one-third of reported cases. Scleritis, conjunctivitis, and iritis may all occur.

The E.S.R. is often raised during an exacerbation. Tests for rheumatoid factor are usually negative. During an exacerbation there may be an increase in urinary mucopolysaccharide excretion. The cause of the disease is unknown.

Steroids appear to suppress the inflammatory reaction, and if the respiratory tract is involved, long-term steroid therapy is probably indicated. Treatment is otherwise symptomatic.

My thanks are due to Dr. J. M. K. Spalding for permission to publish this case; and to Dr. D. Davies, Physician-Superintendent, Ransom Hospital, Rainworth, near Mansfield, Notts, for referring the patient and for the early investigations. I also wish to thank Dr. R. Marshall for undertaking the lung-function studies.

RICHARD L. HEWER, M.B., B.S., M.R.C.P.,
Senior Registrar in Neurology to the United Oxford
Hospitals.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Dysphagia

CLIFFORD F. HAWKINS,* M.D., F.R.C.P.

Dysphagia is a precise symptom that must never be ignored. The diagnostic net must be cast widely, but three likely causes are carcinoma, achalasia, and hiatus hernia—the most important to exclude being carcinoma. The oesophagus is of interest to the cardiologist, as pain arising from it can mimic myocardial ischaemia, and some patients with oesophageal obstruction may first be seen by the chest physician because of aspiration pneumonia.

Accurate diagnosis is possible in most cases if the taking of a careful history is combined with thorough radiographic examination. This may include giving the patient a solid bolus of barium and watching him swallow when lying horizontally or head-down. It is often helpful to see the patient eat or drink. In achalasia trick movements such as attempts to breathe out forcibly through a closed glottis may help to force food

scopy and biopsy are conclusive in most cases. Oesophageal perfusion with N/10 hydrochloric acid can be used as a provocative test to distinguish oesophageal from cardiac pain.¹

Carcinoma of Oesophagus

This is one of the most deadly cancers, the reason being not the type of neoplastic cell—most are squamous—but the surrounding anatomy of the oesophagus. As soon as the growth trespasses beyond its walls vital structures like the lung, the bronchi, or the aorta are invaded, either directly or by lymphatic spread. Hope of cure lies in early diagnosis.

Carcinoma of the oesophagus occurs particularly in men over the age of 65, though it may be a complication of chronic iron deficiency anaemia in women. Heavy smokers are slightly more prone to the disease, presumably because of the action of a swallowed carcinogen. Its incidence is high in certain races, notably among male Bantu—perhaps as a result of their drinking "cidivici," a native beer brewed illicitly—and among female Eskimos, probably because they chew edges of sealskins when making mukluks.² Chronic oesophagitis and oesophageal obstruction may predispose to neoplastic change, which would explain the slightly increased incidence of carcinoma in patients with long-standing hiatus hernia and achalasia.

The dysphagia, which is sometimes preceded by vague substernal sensations, is progressive and contrasts with the intermittent dysphagia of some benign conditions. It first affects solids, then liquids. A barium swallow may not show an early growth, so oesophagoscopy must be performed whenever the condition is suspected, and biopsies should be taken

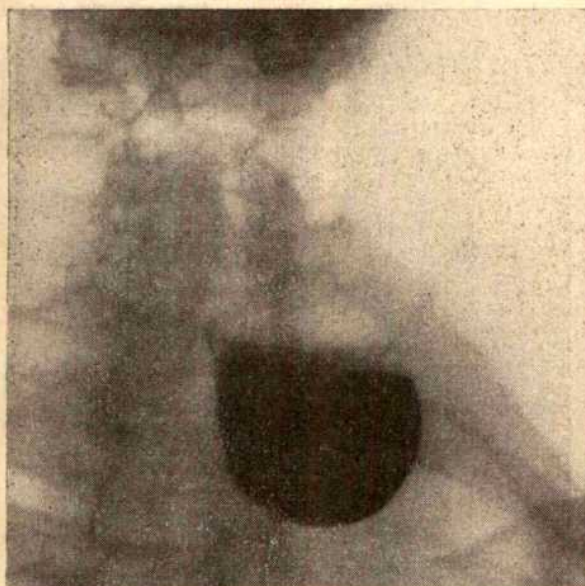


FIG. 1.—Pharyngeal pouch.

through the cardia. High oesophageal obstruction may cause the patient to eat with rabbit-like movements of the jaw for fear of letting food leave the mouth. One patient complained of a lump in the throat when drinking beer quickly, and he needed little encouragement to demonstrate this to us; later a barium swallow showed the pharyngeal pouch (Fig. 1). Special investigations such as cineradiography and manometry may be used to study disorders of oesophageal motility such as achalasia, diffuse spasm, and scleroderma. Some workers have found exfoliative cytology helpful in diagnosing carcinoma in conditions like achalasia, where the changes already present make detection of malignancy difficult. However, oesophago-



FIG. 2.—Adenocarcinoma of fundus of stomach invading lower oesophagus.

* Consultant Physician to the United Birmingham Hospitals and Lecturer in Clinical Medicine to the University of Birmingham.

from suspicious areas. Though the usual type of carcinoma is squamous, adenocarcinoma occurs in the lower oesophagus. This may arise in the cardia or fundus of the stomach and invade the oesophagus later (Fig. 2). Then the patient tells the story of dyspeptic symptoms for several months followed by dysphagia—an ominous sequence of events.

The radiological appearance of carcinoma of the oesophagus is frequently characteristic. There is a short narrowed segment and its irregular outline usually, though not invariably, distinguishes it from achalasia (Fig. 3). Occasionally there is a longer area of minimal narrowing, which is easily missed; this is caused by an extensive flat ulcerating carcinoma, in which the mucosal pattern is lost.

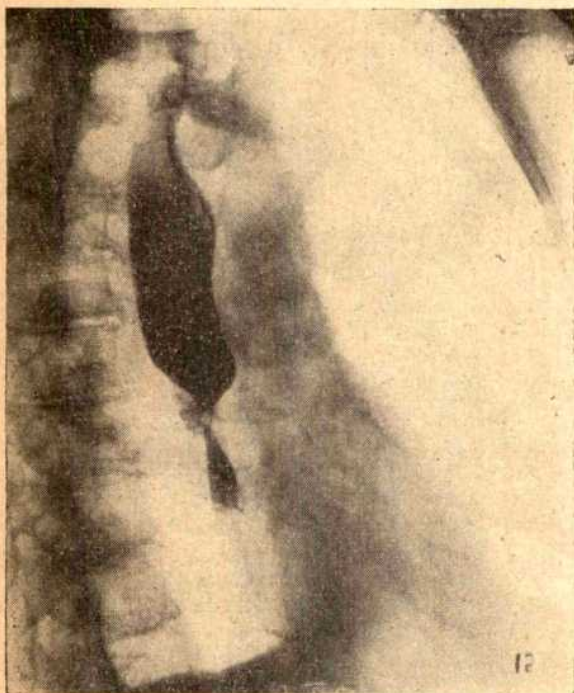


FIG. 3.—Carcinoma of oesophagus.

Radiotherapy may be the best treatment for growths in the upper third of the oesophagus because of their inaccessibility and the poor surgical results, but surgical treatment should always be considered for lesions elsewhere. If it is not possible to remove the growth some treatment is usually necessary to prevent the death of the patient from starvation. Gastrostomy has been abandoned, for it merely prolongs a miserable existence and for a short time only; the patient's inability to swallow saliva is pathetic. Palliative operations may be of great relief when resection is impossible. A bypass operation, such as oesophago-jejunostomy, may be feasible, though procedures of this type have a high mortality. It is often preferable to force some type of tube through the growth, either via an oesophagoscope or directly through a slit in the oesophagus above the lesion. A wide range of indwelling tubes has been devised for this purpose.

Achalasia

Achalasia of the cardia (formerly called cardiospasm) is a benign treatable condition caused by failure of the cardia to relax before the oncoming bolus of food, because of degeneration in Auerbach's plexus. Most patients are between 20 and 40 years old, though no age is exempt. The patient feels that food sticks behind the lower sternum; solids and liquids are equally affected and the dysphagia is usually painless. The patient has to eat slowly, and regurgitation of food may embarrass him and sometimes lead to lung complications.

Achalasia is a neuromuscular disorder of the whole oesophagus. Early diagnosis before obstruction has developed may be difficult. A patient occasionally complains of substernal pain from oesophageal spasm or discomfort, which may be attributed to "indigestion"; regurgitation may be mistaken for vomiting and a peptic ulcer may be diagnosed, the dysphagia being overlooked. In the early stages the barium swallow may be normal except for signs of disordered motility or persistent failure of the cardia to open; this is best shown by giving the patient a small breadcrumb soaked in barium to swallow, when it will lodge at the cardia. The methacholine test is useful: 5 to 10 mg. of methacholine chloride is injected subcutaneously, when in achalasia violent painful contraction of the lower half of the oesophagus will result which may obliterate the lumen when seen by x-ray. The test is positive in achalasia except in advanced stages, and it is usually negative in carcinoma, scleroderma, and diffuse spasm.

Barium swallow typically shows a cucumber-shaped oesophagus with a tapering lower end (Fig. 4). There is complete loss of the peristaltic wave, this being replaced by segmental and tertiary contractions. The cardia is eventually forced open by the column of food when it is about 20 cm. high. This column also acts as a trap, so that no gastric air bubble is visible (Fig. 4). Sometimes a mega-oesophagus flops into the right chest, when it is described as a sigmoid oesophagus; because of the sigmoid shape the direct effect of gravity on the sphincter is lost. Patients with untreated achalasia lose weight, though they seldom die from starvation.

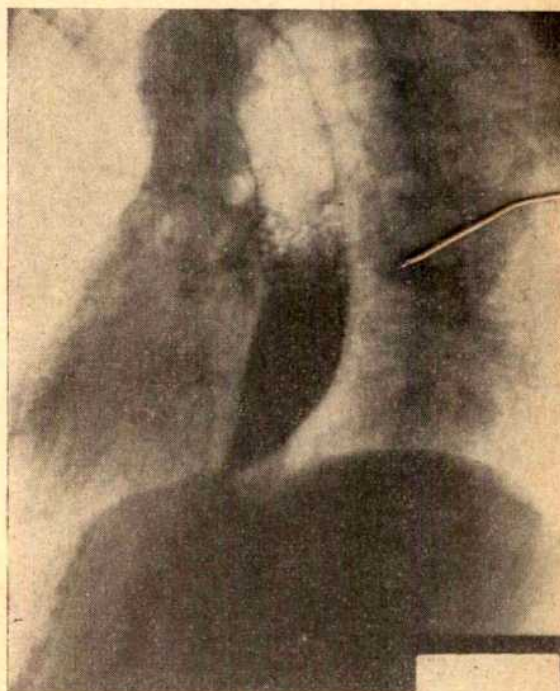


FIG. 4.—Achalasia of the cardia.

Oesophagoscopy is required, especially in doubtful cases, as carcinoma of the oesophagus can mimic achalasia (Fig. 3) and also complicate it. In addition to the methacholine test given with the barium swallow other drug tests may help in the diagnosis; inhalation of octyl nitrite relaxes smooth muscle transiently, and the oesophagus will empty in achalasia, though not in other conditions. To avoid unpleasant side-effects of this drug hyoscine-N-butylbromide (Buscopan), which has a similar effect, is preferable, and 20 mg. should be given subcutaneously or intravenously. Unfortunately these drugs are of little use in treatment. Heller's operation of myotomy should be advised as a curative procedure; it diminishes the hydrostatic pressure necessary to force food through the stomach. Alternatively, dilatation by the Negus hydrostatic bag can be

used. Whatever the treatment, the motility defect of the oesophagus remains and no patient with achalasia can swallow upside down.

Chagas disease (South American trypanosomiasis)—a parasitic disease especially prevalent in Brazil—causes destruction of ganglion cells in the bowel wall, leading both to achalasia and to megacolon.

Other Disorders of Motility

Sometimes the cricopharyngeal muscle fails to relax and leads to a feeling of food sticking in the throat, a symptom easily regarded as hysterical when the patient is highly strung. This incoordination of deglutition occurs with a pharyngeal pouch and may be the cause rather than the result of the pouch.³

Diffuse oesophageal spasm causes retrosternal pain and dysphagia and sometimes progresses to achalasia. Motility studies are usually required to show the motor dysfunction, though sometimes it may be seen during radiographic examination. As barium reaches the level of the aortic arch the lower half of the oesophagus suddenly becomes distorted and the outline is puckered into a series of pockets, giving it a beaded or corkscrew appearance (Fig. 5); these pockets are zones of lesser pressure into which barium is forced. A thickened oesophageal wall may develop and this hypertrophy may account for the high pressures which have been recorded. The diagnosis should be suspected in patients who have episodes of substernal pain unrelated to exercise and without disease of the upper alimentary tract, gall bladder, or pancreas. The pain may resemble angina, and caution is needed in making the diagnosis of oesophageal spasm, for these motility changes can be an incidental symptomless finding, especially in the elderly.⁴ Nitroglycerin may relieve this pain, for it also relaxes smooth muscle; relief has been given in severe cases by a long myotomy incision in the lower oesophagus.⁵ The case for regarding this condition as separate from achalasia is based on the motility pattern of the oesophagus and the normally functioning intrinsic sphincter, though the dividing line is by no means always clear.

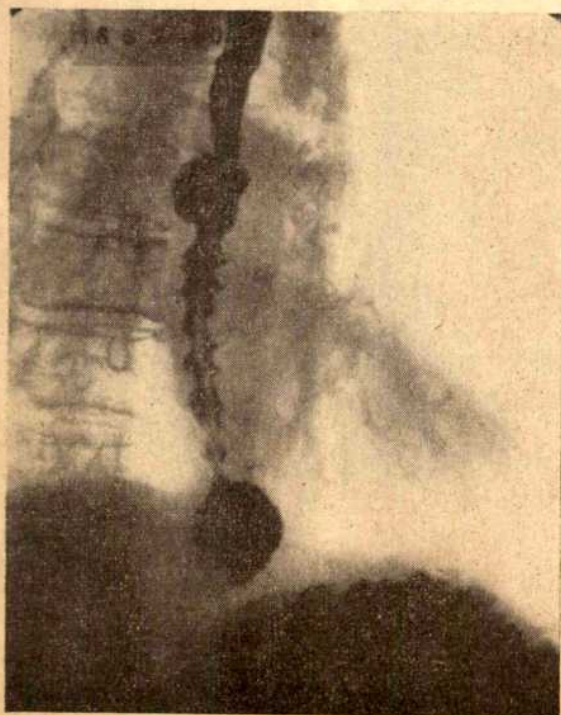


FIG. 5.—Oesophageal spasm producing the appearance of corkscrew oesophagus and pseudo-diverticulosis.

Hiatus Hernia

Hiatus hernia, which was described in detail earlier in this series of articles,⁶ is the commonest cause of oesophagitis. The oesophageal mucosa has no protection against peptic digestion from gastric juice. Reflux of gastric contents occurs especially in the sliding type of hernia, where an incompetent cardia lies in the chest, whereas the anatomy of the cardia may be retained in the paraoesophageal type and prevent reflux. The special symptom of reflux is postural heartburn. Patients may find bending down so unpleasant that they have special long-handled tools made for housework or gardening, and their night's rest may be spoiled. Sometimes they also complain of the mouth unexpectedly filling with partially digested food. This must not be confused with vomiting, which is usually preceded by nausea.

Stricture may be the sequel of long-standing oesophagitis. Heartburn and regurgitation may then cease as the stricture prevents reflux of gastric contents. These patients present a challenge to the surgeon. Some will back optimism and try the effect of repair of the hernia alone, as sometimes the oedema and inflammation around the stricture will subside; others attempt a more radical approach, using an isolated jejunal segment or gastric tissue to form a connecting tube between the lower end of the shortened oesophagus and the stomach itself.

Fortunately, a fibrous stricture occurs in only a few patients with hiatus hernia. Dysphagia in others is due to oesophageal spasm, and responds to treatment of the oesophagitis. The difficulty in swallowing then becomes intermittent and may be described as a feeling of a lump in the chest or temporary sticking of food.

Though hiatus hernia is the commonest cause of benign oesophageal stricture, all patients, except those with an obvious cause such as trauma or damage from corrosive agents, should undergo oesophagoscopy and biopsy to exclude carcinoma.

Other Causes of Oesophagitis

Bacterial or tuberculous infections of the mouth and pharynx may spread downwards and attack the oesophagus, when difficulty in swallowing will be caused by pain. Physical agents such as hot liquids or irradiation may cause similar symptoms. The heartburn, which may be the penalty for an alcoholic bout, is probably due to chemical oesophagitis. Additives to food or drink may be injurious. This was illustrated by the epidemic of cardiac and gastrointestinal disease among beer drinkers in Quebec during 1965–6. Necropsy showed that some had oesophagitis and severe gastritis with ulceration.⁷ The illness was caused by cobalt, which had been added to draught beer to improve the "head," as this was being increasingly subdued by detergents on poorly rinsed glasses. A iatrogenic cause of oesophagitis which may lead to heartburn and stricture is the prolonged use of the indwelling nasogastric tube, for it keeps the cardia open and allows acid reflux when the patient is nursed supine.⁸

Chronic oesophagitis also follows reflux of bile and pancreatic juice, which may be a sequel to gastric operations. The early morning "vomit" of the chronic alcoholic is usually oesophageal mucus which is secreted overnight. Chronic inflammation may be due to stasis from oesophageal obstruction. Antibiotics can cause dysphagia, especially in those weakened by prolonged illness and receiving corticosteroids. This is due to oesophageal candidiasis (thrush), which is usually present in the mouth or pharynx as well. Barium swallow may show an irregular filling defect in the oesophagus, which resembles the appearance of varices. The antibiotic should be stopped if possible and an antifungal agent such as nystatin given instead.

The ideal treatment of oesophagitis is removal of the cause; this may entail surgical repair of a hiatus hernia. Otherwise, simple mechanical measures intended to discourage reflux may

be advised: raising the head of the bed, avoiding constricting garments, and reduction of weight. Patients should be told to chew their food properly and their dentition should be adequate; roughage should be avoided during bouts of dyspepsia. Antacids pass rapidly through the oesophagus and have no permanent effect, though they afford temporary relief from the heartburn, as do solutions containing a surface anaesthetic, such as Mucaine. The constant sucking of antacid tablets (such as Nulacin or Prodexin) has been shown to keep the gastric acidity near pH 3.0,⁹ and some have advised a constant antacid drip through a thin polyethylene nasal tube lying in the mid-oesophagus; this, which is particularly useful at night, allows meals to be taken as usual during the day. Anticholinergic drugs are useless, for they are disappointing in their effect on gastric acidity and may cause more reflux by relaxing the cardiac sphincter.¹⁰

Other Forms of Obstructive Dysphagia

Foreign bodies must always be considered as a cause of dysphagia. There is usually a history of choking during a meal, though this may not be obtained in small children and in psychotic patients. For example, one patient of mine, a middle-aged woman with neurotic symptoms, complained to her general practitioner of dysphagia. He diagnosed globus hystericus and told her that it was "the change." He was in a way correct, for she had swallowed 2s. 4d., the change which she had received when shopping. Removal of a foreign body is an urgent matter, for it may lead to ulceration and cause fatal mediastinitis.

Dysphagia from pressure on the oesophagus in the neck or thorax may be caused by conditions such as enlarged lymph nodes, neoplasms of the lung or mediastinum, aneurysm, or a large retrosternal goitre.

Syndromes have a status denied ordinary symptoms or diseases, although their statistical basis is sometimes doubtful.¹¹ This may be the case in the syndrome of anaemia, glossitis, and dysphagia. Originally christened the Plummer-Vinson syndrome (although Vinson regarded it as hysterical), it should



FIG. 6.—Postcricoid pseudo-web associated with iron-deficient anaemia (by courtesy of Dr. J. S. Logan).

be named after Paterson and Kelly, for these workers noted it earlier and wrote a perfect description of the postcricoid web. Now, an epidemiological study has shown no evidence of a significantly increased prevalence of anaemia or latent iron deficiency in women with postcricoid dysphagia or with webs.¹² However, some women with long-standing iron-deficient anaemia do suffer from dysphagia, glossitis, and an atrophic mucous membrane of the pharynx and cricopharyngeal area. The accompanying loss of sensibility impairs the afferent side of the swallowing reflex, and if the anaemia is untreated a benign thin crescentic pseudo-web of the mucosa (Fig. 6) or carcinoma develops at this site. Webs, congenital, traumatic, or due to pemphigus, may occur elsewhere in the oesophagus and not give rise to symptoms until lumps of meat are eaten hastily. Webs are easily missed at barium swallow when situated just above the cardia unless a large bolus of barium is used. Patients can usually be encouraged to live with their difficulty, and surgery is rarely needed. The lower oesophageal ring (Schatzki's ring), which is often associated with hiatus hernia, is a similar harmless lesion and should not be confused with fibrous stricture.

Dysphagia lusoria (Fig. 7) is due to oesophageal compression by the arteria lusoria, an anomalous form of the right subclavian artery. Other congenital abnormalities may be present

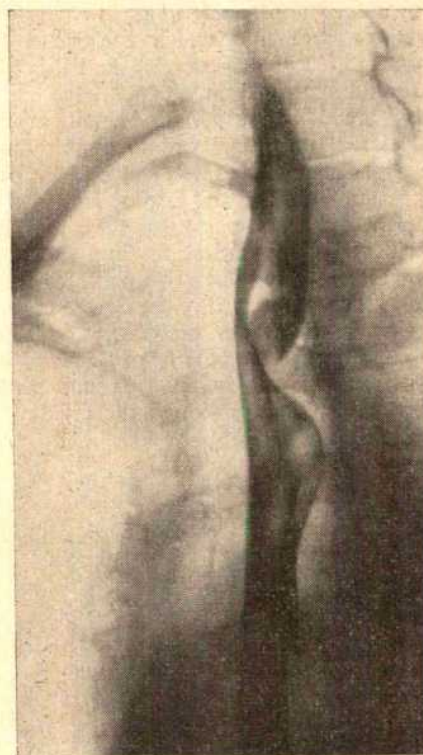


FIG. 7.—Dysphagia lusoria.

as well. Symptoms may appear in infancy or later in life, then perhaps being precipitated by arteriosclerotic changes in the artery. An explanation to the patient with reassurance is usually all that is needed.

Oesophageal Lesions in Systemic Disease

The oesophagus bears the main brunt when the alimentary tract is involved in scleroderma. It is dilated and transit through it so slow that barium is retained for half an hour or longer. A test for the detection of early cases is for the doctor to watch the patient swallowing barium against gravity, as when inclined head-downwards; barium hovers at the level of the tracheal bifurcation and enters the stomach only when the patient stands. Other connective tissue disorders also affect the alimentary tract. Dermatomyositis may lead to dysphagia

because of weak pharyngeal muscles or a motility defect in the oesophagus. The diagnosis is suggested by the dermatitis which is usually present and can be confirmed by muscle biopsy and enzyme tests. Some cases are due to malignant disease, either in the alimentary tract or elsewhere, and a search must always be made for this.

Neurological disorders may impair swallowing. Because of his mental state this may escape the notice of the patient as well as the medical staff, and he may die from aspiration pneumonia. Every patient with a stroke must be examined with this possibility in mind. The gagging reflex should be sought, and the patient should then be asked to swallow a mouthful of water. Dysphagia may also occur in patients with bulbar paralysis, myasthenia gravis, polyneuritis, and similar conditions.

Globus hystericus, though relatively common, has been left until last, and indeed should not be diagnosed unless serious disease has been excluded. An intelligent woman who can describe her symptoms clearly explains that she has a feeling of a lump in the throat but does not have difficulty in swallowing. Others are less precise. It is salutary to remember that probably every organic cause of dysphagia described here has at some time been mistaken as nervous, the patient then being labelled—and libelled—as hysterical.¹³

Figure 5 was taken from *Diseases of the Alimentary Tract* (1963) by C. F. Hawkins, by kind permission of William Heinemann Medical Books Limited.

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Stability of Ergometrine and Adrenaline

Q.—Is the yellow discoloration of ergometrine for injection after storage of any significance? How long can ergometrine injection and adrenaline for injection be kept before use?

A.—The stability of ergometrine preparations has been investigated by Foster and Stewart.¹ They showed that the official B.P. formula has satisfactory keeping properties. Samples stored at room temperature retained 90% of their activity after 33 months. In the discussion on this paper Eastland² reported that some ampoules with colours from a dark straw to blackish-brown had retained 86% of their activity. It seems likely that injections that are not more than a yellow colour will not have lost much activity.

The *United States Pharmacopoeia* states that ergometrine injection should be used within two years of preparation. A report of the Danish Academy of Technical Sciences,³ however, suggests an expiry date of three months. This is obviously a very conservative estimate of the shelf-life of the product, and the U.S.P. figure is probably satisfactory.

The stability of injections of adrenaline has been studied by West^{4,5} and by Foster, McDougall, and Thorp.⁶ They showed that solutions stored in ampoules are very stable, some samples retaining full activity after six years or more. West and Whitter⁷ showed that injections of adrenaline stored in rubber-capped vials are much less stable. The Danish report gives an expiry date of one year

for injection of adrenaline. This is probably advisable for samples in multidose containers, but those in ampoules could probably be kept for considerably longer periods.

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Erythromycin

Q.—What are the merits of the various esters of erythromycin that are available?

A.—The only commercially available ester is erythromycin estolate (Ilosone), which is the lauryl sulphate of the propionyl ester. Its merit is better absorption, the concentrations attained in the blood being considerably higher than those produced by the same dose of erythromycin base. It has also a drawback in that full doses given for more than a week sometimes have a reversible hepatotoxic effect. An ester of a related antibiotic, triacetyleandomycin, can also have the same effect. It has not been seen after administration of non-esterified forms of either antibiotic.

Erythromycin stearate, another form in which erythromycin is marketed, is not an

ester. Its advantage is resistance to gastric acid, whereas the base, which is acid-labile, has to be administered in enteric-coated tablets.

Children with Dyslexia

Q.—What is the treatment and what is the prognosis in a boy aged 7 suffering from dyslexia? Are there any special schools for children with this disability?

A.—Dyslexia means defective reading, and in a child aged 7 it might be due to a variety of factors, such as mental subnormality; sensory defects of vision or hearing; deficient or improper teaching by reason of insufficient or poor schooling, or frequent changes of school; poor motivation to learn, despite adequate opportunity; or it may be secondary to a primary emotional problem. In a smaller group it might be due to late development with slow learning, usually self-correcting, but this may progress to outright retardation in reading.

For these reasons, and because of the variety of teaching methods employed in different schools, many authorities are reluctant to talk of dyslexia in a child aged 7. In the smallest group, more often older children, the diagnosis of "specific developmental dyslexia" may be made in those who are unable to read with normal facility despite normal intelligence, intact senses, proper instruction, and normal motivation. These children are often competent in other subjects not dependent on reading skill.

Treatment and prognosis in the three groups differ according to cause. In the first two groups assessment via the school psycho-

logy service will define the majority of the causes and special medical examination the others, so that appropriate corrective and remedial measures can be taken. In the third group special techniques of remedial teaching are required over a long period of time and response may still be poor.

There are no schools at present dealing specifically with children with reading retardation, though different types of special education can be recommended, depending on the particular case. The Invalid Children's Aid Association's Word Blind Centre for Dyslexic Children, Coram's Field, 93, Guilford Street, London W.C.1, assesses and treats a variety of cases.

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Vitamin B₁₂ Absorption from Ileum

Q.—When it is necessary, in the presence of extensive adhesions, to perform an ileo-transverse colostomy for a faecal fistula of the terminal ileum can the megaloblastic anaemia of a malabsorption syndrome be prevented by prolonged parenteral administration of vitamin B₁₂? What length of terminal ileum absorbs vitamin B₁₂? What effects of malabsorption other than megaloblastic anaemia are produced by an ileo-transverse colostomy, and can they be prevented by subsequent medical treatment?

A.—In this situation, where the underlying process is almost certainly Crohn's disease, regular injections of vitamin B₁₂ will prevent or correct the megaloblastic anaemia. Vitamin B₁₂ is mainly absorbed in the terminal few feet of ileum, but the whole ileum has this ability to some extent. It is sometimes difficult to predict how disease will affect vitamin B₁₂ absorption, and a Schilling test is often valuable to assess this function.

An ileo-transverse colostomy is rarely accompanied by other evidence of malabsorption, but when there is extensive Crohn's disease, blind loops, or internal fistulae malabsorption may occur with steatorrhoea, hypocalcaemia, and hypoproteinaemia. When there is no other disease of the bowel and the patient has steatorrhoea a low fat diet with replacement of any deficiencies is the treatment of choice.

Desensitization to Wasp Stings

Q.—Is desensitization against wasp stings effective, and what is the best preparation to use? What emergency treatment should be given for an acute reaction to a wasp sting?

A.—Desensitization to the stings of insects, including bees and wasps, can be an effective form of treatment. Complete desensitization is rarely achieved and the effect is likely to be only temporary. Annual desensitization is therefore advisable, especially in those whose occupation brings them into contact with bees or wasps.¹

Extracts of whole bee or wasp are used, and in this country aqueous extracts are available. They may be given subcutaneously

or intradermally.² In America oily emulsions containing the active agent are sometimes employed and hyposensitization may be achieved with a few injections only.³ Such preparations are not available at present in this country.

The immediate treatment for a reaction to a wasp sting is adrenaline hydrochloride (1:1,000) 0.5–1 ml. subcutaneously. This may be life-saving. The sensitive patient may be provided with a syringe and an ampoule of adrenaline tartrate. Speed in treatment is essential, since collapse and death may occur within one minute. The injection may need to be repeated if symptoms recur after an interval. When the sting is on an extremity a tourniquet should be applied until the adrenaline has had time to act, and at the same time 0.5 ml. adrenaline hydrochloride may be injected into the site of the sting to slow up absorption. Phen-ergan (promethazine hydrochloride) may also be given intravenously, but it is less effective than adrenaline.

There is no place for corticosteroids in the first instance, but intravenous hydrocortisone may prevent recurrent attacks of urticaria and asthma when the effect of adrenaline and antihistamine has worn off.

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Ruptured Cruciate Ligaments

Q.—Is it possible to repair the cruciate ligaments of the knee joint eight months after rupture? Is there any other treatment of value?

A.—Late repair of the cruciate ligaments has been attempted by numerous operations, usually substituting strips of fascia or the meniscus for this important stabilizing ligament of the knee. The wide variety of technical procedures developed is the best indication that no one of them is satisfactory.

Though there would be much difference of opinion among orthopaedic surgeons, I have not seen results from any of these procedures that justify operative repair. The maintenance of an excellent quadriceps is the best aid to a patient that can be devised. Torn cruciate ligaments, usually the anterior, are very common, and relatively few people have disability except when attempting the most strenuous sports.

Cocaine in Asthma

Q.—Instillation of 1 ml. of 10% cocaine through the cricothyroid membrane into the lumen of the trachea is said¹ to terminate an asthmatic attack even in severe status asthmaticus. Does this mean that the bronchospasm of asthma is caused by the action of irritants on the tracheal or bronchial mucosa?

A.—The injection of 10% cocaine through the cricothyroid membrane in status asthmaticus is rarely employed and not devoid of risk. The way in which relief is obtained from it is uncertain, but it is probably from a vasoconstrictor effect as much as from the

action on nerve endings. It also potentiates the effect of sympathetically innervated organs to sympathomimetic drugs. There is evidence that it has an effect antagonistic to serotonin in animals.² Severe toxic reactions may occur after as little as 20 mg.,³ and allergic responses with sudden death are also recorded.⁴ Finally, when repeated there is always a possibility of addiction.

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Oral Candidiasis

Q.—What further treatment is there for a chronic monilial infection of the mouth which has failed to respond to nystatin, gentian violet, and dequalinium?

A.—Chronic monilial infection is usually extremely resistant to conventional treatment, but iodides, amphotericin B, and desensitization are other methods that have been recommended. Presumably underlying causes, such as poorly fitting dentures, diabetes, hypoparathyroidism, and chronic debilitating diseases, have been excluded.

Non-rubber Gloves

Q.—Is there any sort of rubber glove which may be worn by a person who is allergic to rubber, or is there any other way of overcoming the problem?

A.—In cases of allergy to rubber the allergen is never the latex itself but always a chemical additive. Several types of non-rubber gloves or gloves which do not contain these additives are available. They may be made of cellophane, polythene, or polyvinyl-chloride. A French company makes special gloves based on yet another type of plastic.

Notes and Comments

Muscular Spasms in Paraplegia.—Dr. T. K. DAVIDSON (Physical Medicine Department, General Hospital, Northampton) writes: With reference to this question ("Any Questions?" 28 October, p. 221), and particularly with reference to what I take to be flexor spasms, I have for some time now, on a wide variety of spastic muscles, used 5 ml. of 1% procaine and 5 ml. of 40% sterile ethylalcohol. This is injected in and around the motor point of the muscle in spasm.

In the case of flexor spasms in the hip injection into rectus femoris and/or sartorius will relieve the spasm to a considerable extent. If the main trouble is spasm of the hamstrings it may well be that semitendinosus is the main cause of it, and injection of this alone may give considerable relief. If it does not it may be necessary to inject both heads of biceps and semimembranosus—and even gracilis. This procedure can be repeated at 12- to 18-monthly intervals. It is said to act by knocking out the gamma fibres from the stretch receptors. Whatever the physiology, it is certainly a very useful and worth-while procedure.

Book Reviews

Mental Health Services in Many Countries

New Aspects of the Mental Health Services. Edited by Hugh Freeman and James Farndale. (Pp. 776 + xvi. £9 9s.) Oxford: Pergamon, 1967.

Observers of the new colossus of the medical publishing world, the Pergamon Press, have learned to nerve themselves against the shock of high prices, but this volume of collected papers, at nine guineas, is still astonishingly expensive. Relatively few clinicians, and fewer academics or research workers will be likely to buy a personal copy; but if it is available to them through a hospital or departmental library, will they want to consult it? The answer to this question is an unequivocal yes.

There are many papers here which are of the greatest interest to workers in all ranks of all the disciplines which contribute to the functioning of our mental health services. It should be noted, however, that the editors have cast their net even wider than the title suggests. More than 25% of the book is taken up by a section entitled "The International Scene." Some of the papers in this section, describing pioneer services in France, Denmark, Canada, Australia, and the U.S.A., are clearly relevant to the challenges which still face the British psychiatric services. Others, such as the account of the highly commendable but still quite rudimentary service which is being created in the teeth of formidable difficulties in Sarawak, and that of community psychiatry in Israel, are less

obviously relevant to our own circumstances; nor, indeed, are the rather extensive discussions of attributes of contemporary American and Soviet psychiatry which are clearly related to the socio-economic conditions and social philosophies of these two countries.

It is certainly arresting to learn that whereas in the U.S.A. nearly every other hospital bed is a psychiatric one, in the U.S.S.R. psychiatric beds account for only one in eight of the total; but this at once excites our curiosity about such unanswered questions as whether there is a lower prevalence rate for psychiatric illness in the latter country, and whether the emphasis on community care which the Russians have built into their treatment services makes a significant difference to the outcome of mental illness. The description of a new pattern of medical care is often interesting in itself, but it invariably provokes a desire for objective evaluation of its effectiveness. Enthusiasm is an admirable and perhaps necessary characteristic of innovators; the majority, but by no means all, of the contributors to this book have realized that self-congratulation is not an adequate substitute for a candid appraisal of results.

There are some particularly valuable reviews and essays among the book's 42

chapters. Both clinicians and research workers will mine with profit in the papers of J. K. Wing, E. M. Goldberg, and Douglas Bennett on the care of schizophrenics, and that by A. Kushlick on a comprehensive service for the subnormal. M. M. Glatt contributes an excellent chapter on alcoholism which is marred only by his failure to do justice to Scottish research and clinical reports of recent years. Two chapters on hospital administration (unaccountably placed in different sections of the book) discuss this topic respectively from the point of view of a clinician, Dr. B. M. C. Gilsenan, and an experienced administrator, Mr. T. D. Hunter: the latter chapter is particularly impressive in showing how thoroughly a lay administrator can grasp both the therapeutic aims of social psychiatry and the changes in administrative organization which may be required fully to achieve these aims.

One could continue to single out many more chapters for special mention: there are papers here which will be of particular interest to psychiatric nurses, to the hospital junior doctor, and to the sociologist. Above all, however, the volume is a valuable reference work for clinicians and administrators who carry the responsibility for conducting community mental health services and who wish to keep informed of the latest developments in this field.

G. M. CARSTAIRS.

Fungal Infections of the C.N.S.

Mycoses of the Central Nervous System. By Bernard F. Fetter, M.D., Gordon K. Klitworth, M.D., and Wilson S. Hendry, M.D. (Pp. 214 + vii; illustrated. £5 2s.) Edinburgh: E. & S. Livingstone, 1967.

This book throws a lot of light on an obscure corner of pathology. It is well organized into two introductory chapters, followed by chapters for each of eleven individual mycoses (arranged alphabetically)—a composite chapter covering 14 rare mycoses—and three appendices. The latter list a classification of fungi incriminated in disease of the central nervous system, a list of references to staining techniques, and a classification of fungal neuropathogens seen in histological sections and proved culturally.

Each of the chapters on an individual mycosis opens with a general account of the discovery and distribution of the fungus and its usual clinical presentation. Within the nervous system the incidence, source of involvement, clinical manifestations, cerebrospinal-fluid findings, course and treatment, tissue reactions, and practical identification in tissues are systematically presented. A comprehensive list of references (293 in the case of cryptococcosis), including non-English sources, concludes the chapters. There

are 157 black-and-white photographs. Fungi stained by silver methods lend themselves to this and are superb. Other illustrations showing microscopic, macroscopic, and radiographic appearances are of uniform excellence. The four coloured figures are sensibly used to show pigmented fungi and the fluorescence of *Cryptococcus neoformans* after staining with acridine orange.

The compilation of such data will contribute to further research into how fungi take advantage of altered immunity to invade the tissues. As the authors point out, the rise in incidence of some mycoses has coincided with the use of antibiotics, steroids, cytotoxic drugs, and deliberate immunosuppressive techniques. Inside the nervous system cysts, abscess formation and granulomata, meningitis, or thrombosis and infarction (following invasion of blood-vessel walls) are the range of reactions to the various fungi, but an interesting point mentioned is that patients with cryptococcal meningitis have been shown to have alcohol in the spinal fluid due to the presence of the enzyme alcohol dehydrogenase.

These members of the department of pathology at Duke University Medical Centre, North Carolina, have done a thoroughly competent job in collecting and presenting all the data at present available relevant to fungal infections of the central nervous system. Much of the material appears to be their own,

although their names do not appear among many references listed. In the foreword Dr. N. F. Conant remarks that the "identification of the specific fungal etiologic agent by its appearance in tissues demands experience that can be obtained only by having had long and intimate contact with both the clinical and laboratory aspects of fungus infections." With this not inexpensive but compact volume to hand the rather less experienced pathologist or clinician may hope to diagnose the case of central nervous involvement by fungi when it presents.

KENNETH R. HILL.

Help towards Solving Problems of the Disabled

Equipment for the Disabled. An Index of Equipment, Aids and Ideas for the Disabled. 2nd edition. Edited by Margaret Agerholm, M.A., B.M., B.Ch.Oxon. (4 loose-leaf volumes; illustrated. £7 7s.) London: National Fund for Research into Crippling Diseases, 1967.

The first edition of this manual appeared in 1960 and was well received, for it provided information both for disabled patients and

those professions concerned with their management or welfare which had been difficult to obtain elsewhere.

The success of this venture by the National Fund for Research into Poliomyelitis and Other Crippling Diseases can be judged by the appearance of this greatly enlarged second edition seven years later. The book is divided into the same 17 sections, covering house adaptations, beds, chairs, wheelchairs, hoists, bed-table, communications, upper-limb prostheses, aids for eating, personal toilet, clothing, household equipment, cooking, aids for the disabled mother in child care, hobbies, walking aids, and invalid transport.

The sections on personal toilet, household aids, beds, and transport have been greatly enlarged. The new binding with its four-ring looseleaf cover is an improvement on the spiral spring holder of the first edition, which tended to perforate the pages. The general layout is excellent, the illustrations, photographs, and descriptions of the aids being clearly presented and simply described. The prices, where relevant, are given at the end of each section, so that variations can be catered for without amending the original illustration, but an approximate idea of cost would be an advantage on each page. The section on bathroom facilities in "house layout" is disappointing—no mention is made of showers, and details of hoists suitable for getting severely disabled patients into a bath would be welcome.

This book is an essential text for anyone, medical or lay, who has to deal with disabled people and should have as wide a circulation as possible. In particular, it is hoped that the attention of local authorities will be drawn to it, to show what can be done and to remind them of the wide powers permitted them in solving the manifold and complex problems disability presents.

The medical editor is to be congratulated on what must have been a herculean task of assembly, and also all the hospital departments and firms that have provided details of their equipment. It is to be hoped that they will not be so exhausted by their labours as to rest too long before preparing the next edition, as new ideas are constantly being developed. Such a compendium will itself inspire others to renewed efforts to solve the outstanding problems of living with a disability.

C. WYNN PARRY.

Full Story of Cardiac Pacemakers

Cardiac Pacemakers. By Harold Siddons, M.Ch., F.R.C.S., and Edgar Sowton, M.D., M.R.C.P. (Pp. 331+xvi; illustrated. \$16.75.) Springfield, Illinois: Charles C. Thomas. 1967.

This monograph written by two of the world's leading authorities on cardiac pacing is one of the most up to date and complete reference works on this important subject available. The contents include a historical review of heart block and defects of the conduction system followed by the aetiology, clinical presentation, and drug treatment of this condition. Subsequent chapters deal with short- and long-term pacing and discuss in great detail the practical application and management of the various methods of electrical

stimulation of the heart. There are 896 references and a most excellent appendix with full particulars of commercial pacemakers with their circuit diagrams and electrical characteristics.

The first chapters contain a detailed description of the aetiology and clinical and haemodynamic changes associated with heart block. This is followed by a critical review on the values of drug treatment apart from pacing the heart in this condition. It is probably right to say that all centres responsible for treating patients following myocardial infarction should have available facilities for short-term pacing, should the occasion arise, and the chapters in this book describing this can be usefully used as a practical guide. Long-term pacing with implanted pacemakers has to be undertaken by specialist surgeons, but these chapters can be read by all cardiologists with profit.

The authors must be congratulated on producing this first-class monograph which will be of the greatest value to cardiologists and all those involved in any way with the treatment of heart block. No cardiac department can afford to be without it.

J. P. SHILLINGFORD.

Irrecoverable Renal Failure

Renal Transplantation. 2nd edition. By Roy Yorke Calne, M.A.(Cantab.), M.S. (Lond.), F.R.C.S.(Eng.). (Pp. 220+ix; illustrated. 63s.) London: Edward Arnold. 1967.

When the first edition of this monograph appeared four years ago the author could not claim much personal experience of human kidney transplantation. Indeed, at that time it was necessary to convince many internists and nephrologists, especially in the United Kingdom, that intermittent dialysis, usually haemodialysis, was not necessarily preferable for the management of patients with severe irrecoverable renal failure. The situation has since changed so that it has now been possible for Professor Calne to collate his own experience with that of others in Australia, Belgium, France, Great Britain, and the U.S.A. and for him to be reasonably able to state in his concluding paragraph that we are now in a position to offer patients a good chance, possibly years, of tolerable life.

At the present time the success rates in the most experienced centres, judged by effective function of the transplanted kidney after one year, are approximately 70% when living related donors are used. As yet, however, the success rates are generally not nearly as good when organs from unrelated or cadaver donors are used. But with practical advances in tissue typing, provision of facilities for adequate intermittent haemodialysis (and possibly peritoneal dialysis) before and, when required, after transplantation, and the development of more efficient and less toxic means of immuno-suppression such as anti-lymphocytic serum it should not be unreasonable to expect significantly better results both with living related and unrelated or cadaver donors.

Professor Calne provides clear and concise accounts of these and many other of the problems that have to be resolved before kidney transplantation becomes a straightforward and

common surgical exercise, and has omitted little of relevance. Any renal unit contemplating a transplantation programme would be well advised to have a copy of this volume readily available for use by its medical and surgical staff.

RALPH SHACKMAN.

Otolaryngology

A Synopsis of Otolaryngology. 2nd edition. By John F. Simpson, F.R.C.S., Ian G. Robin, F.R.C.S., John C. Ballantyne, F.R.C.S., and John Groves, F.R.C.S. (Pp. 529+xv; illustrated. 52s. 6d.) Bristol: John Wright. 1967.

Otolaryngology is a rapidly expanding subject, short of practitioners, and is neglected by many British medical school curricula. Consequently, not only are students and general practitioners ill-served in the diagnosis and management of many common disorders, but few are stimulated to undertake specialist training. This synopsis is not designed for non-specialists but contains much information that would be of value to them.

In my view, synopses are to be deplored, for only selected information is provided in note form which makes for difficult reading, and such a dogmatic standardized treatment of the subject merely encourages learning by heart and fails to interest the reader. Much interesting theory receives scant mention, and concepts cannot be fully and logically developed. The absence of detailed surgical technique and reference lists must limit the book's usefulness for the postgraduate student.

However strong the objections, synopses are frequently bought and used for quick reference and revision in preparation for examinations (in fact, examinations are the reason for these shortened texts). In this case the authors' primary intention is to provide information which is suitable for higher diplomas. They have done it within the limits of inevitable cataloguing, for the subject is comprehensively surveyed, well illustrated, and almost up to date in every respect. The frequent drawbacks of multiple authorship are minimized, for each author intrinsically belongs to one school of thought—namely, that of St. Mary's Hospital in the first instance and that of the Royal Free Hospital in the second.

For those postgraduate students requiring potted information this work will fulfil almost all the requirements, but in no way does it replace the larger texts, monographs, or careful reading of specialist journals.

J. D. K. DAWES.

Autoimmune Disease

Autoimmunity. Clinical and Experimental. By J. R. Anderson, W. W. Buchanan, and R. B. Goudie. (Pp. 485+xv; illustrated. \$19.50.) Springfield, Illinois: Charles C. Thomas. 1967.

As one would expect of these authors, this book is lucidly written, sound, and critical. It deals with the more clinically important and well-established examples of autoimmune disease, but omits, as the authors concede in their foreword, a number of con-

ditions, such as Crohn's disease, male sterility, exfoliative dermatitis, and so on, whose autoimmune basis is still in doubt. This unadventurous attitude, though it makes for brevity and practicality, also means that the treatment is a little staid and conventional.

The first section, after a rather breathless synopsis of general immunology, includes a clear discussion of autoimmunity and the mechanisms of its production; subsequent chapters deal with the thyroid, stomach, adrenal, nervous system, kidney, colon, muscle, heart, and liver. The last section includes rheumatoid arthritis and disseminated lupus erythematosus with allied conditions. The pathology in particular of all these conditions is admirably dealt with. It is unfortunate in so soundly written a book that it is not completely up to date. Although one cannot fault it as a background review of the subject, there have been advances and clarifications—which it would be both laborious and invidious to note individually—since early 1965, which (from a cursory search through the references) would appear to have been the time of going to press. Though the tribulations of editors and publishers are innumerable, this seems too long an interval in a subject developing as rapidly as autoimmunity.

The illustrations, almost all of histological sections, are well selected and reproduced. There is still some doubt in my mind whether even the best monochrome illustration is really more than something to break up the page; and these must clearly account to some extent for the rather excessive price of this volume. But for those who are less lukewarm about pictures, the ones in this book are superior to those of any other book of its kind which I know.

Readers would be well advised to read the general editors' foreword after the text (if at all), since it contains an uncritical and inaccurate account of many aspects of autoimmune disease—for example, the remarks on damage by antithyroglobulin antibody in thyroiditis and on sensitivity to immunosuppression as a criterion for an autoimmune disease, which are contradicted or modified by more sophisticated discussion in the text.

The controversy on whether "autoimmune" conditions should really be called

"autoallergic" conditions has not affected the writing of this book, which may or may not be a pity.

P. G. H. GELL.

New Work in Ophthalmology

Advances in Ophthalmology. Vol. 18. Edited by M. J. Roper-Hall, H. Sautter, and E. B. Streiff. (Pp. 248; illustrated. sFr./DM. 68.) New York and Basel: S. Karger. 1967.

The eighteenth volume of *Advances in Ophthalmology* contains several articles of considerable interest. The first, by I. H. Leopold and A. H. Barnert, of New York, is a long account of the value and dangers in the use of the corticosteroids in ophthalmic diseases. The effect of these hormones, used both topically and systemically, on inflammatory diseases is undoubted and frequently dramatic; but due attention is given not only to the systemic complications which may arise with their administration by mouth but also to the ocular complications which may result from their topical instillation, whether it may be the encouragement of an active infection or the development of a complicating cataract or glaucoma.

The second, by C. A. Stucchi, of Lausanne, is an assessment of the present position of keratoplasty, particular attention being given to the use of preserved grafts and the social value of eye-banks. Then follows an experimental assessment by J. Draeger and F. Becker, of Hamburg, of the electronic applanation tonometer introduced by Mackay and Marg in 1959 in California. It will be remembered that this useful instrument, which takes continuous readings for tonography, eliminates the small errors in this type of tonometry by the use of a small central plunger surrounded by a "guard-ring" in such a manner that the factors of surface tension and deformation of the cornea are effective on the outer guard-ring and not on the tonometer itself, so that the Imbert-Fick law is applicable. A final article by Elisabeth Meier, of Basel, deals

with the intracapsular mechanism of lenticular accommodation.

STEWART DUKE-ELDER.

Highlights in Surgical History

Great Ideas in the History of Surgery. 2nd edition. By Leo M. Zimmerman, M.D., and Ilza Veith, M.A., Ph.D. (Pp. 587+xii; illustrated. 24s.) London: Constable. 1967.

This is a revised edition of a book first published in 1961. Though the authors state that it is neither a complete nor a conventional history, it is certainly an excellent and readable survey of the progress of surgery from the dawn of history to the end of the nineteenth century.

It portrays "a gallery of great surgeons," ranging from Hippocrates, Galen, and Celsus, through the backward times of the Middle Ages, and giving interesting and instructive accounts of the outstanding surgeons of the eighteenth and nineteenth centuries. Some little-known surgeons are included, as, for example, Caspar Stromayr, who was the first to differentiate direct from indirect inguinal hernia in his *Practica Copiosa*, written in 1559. In the chapter on Marion Sims the authors include a short account of the most distinguished early American surgeons.

Interest mounts as we approach the Listerian era, and the book finishes with descriptions of the work of Victor Horsley and Ferdinand Sauerbruch. There are very brief accounts of more recent developments in neurological and thoracic surgery. One would have liked to see some mention of Owen Thomas, and Lawson Tait and William MacEwen deserve more than the very brief reference accorded them. However, one hopes that the authors may compile a similar volume dealing with the surgeons who have pioneered modern surgery through the last 80 years. Such a volume would surely be welcomed.

I cordially recommend this book to all young surgeons and to medical students, for it is a valuable volume and the price is very reasonable.

ZACHARY COPE.

Books Received

Review is not precluded by notice here of books recently received.

Psychology and Social Problems. By Michael Argyle. (Pp. 232. 25s. Paper 16s.) London: Tavistock. Methuen. 1967.

The Physical Management of Developmental Disorders. Clinics in Developmental Medicine No. 26. By Errington Ellis. (Pp. 50; illustrated. 18s.) London: Spastics Society Medical Education and Information Unit in association with William Heinemann. 1967.

Sarcoidosis. By J. G. Scadding, M.D., F.R.C.P. (Pp. 542; illustrated. £7 7s.) London: Byre & Spottiswoode. 1967.

Background to Migraine. 1st Migraine Symposium. Edited by Robert Smith, M.A., M.D. (Pp. 160; illustrated. 18s.) London: William Heinemann. 1967.

Cystic Fibrosis. Modern Problems in Paediatrics. Vol. 10. Proceedings of 4th International Conference on Cystic Fibrosis of the Pancreas, 1966. Part 1. Edited by E. Rossi and E. Stoll. (Pp. 404+xiv; illustrated. £8 14s.) London: Academic Press. 1967.

The Hereditary Haemolytic Anaemias. The Davidson Lecture. By J. V. Dacie, F.R.S., M.D., F.R.C.P.Lond. (Pp. 37. 7s. 6d.) Edinburgh: Royal College of Physicians of Edinburgh. 1967.

Patterns of Urban Mortality. Report of the Inter-American Investigation of Mortality. By Ruth Rice Puffer and G. Wynne Griffith. (Pp. 353+xiii. No price given.) Washington: Pan American Health Organization. 1967.

Artistic Possessions at the Royal College of Surgeons in England. By Sir Victor Negus, D.Sc., M.S., F.R.C.S. (Pp. 212; illustrated. £5 5s.) Edinburgh and London: E. & S. Livingstone. 1967.

The Auditory Pathway. By I. C. Whitfield, B.Sc., Ph.D.(Lond.), D.Sc.(Birm.), F.R.I.C. (Pp. 209+vi; illustrated. 55s.) London: Edward Arnold. 1967.

Evaluation of Drugs for Tropical Diseases. Proceedings of Symposium held at the Royal Society of Medicine, London, 1967. Edited by Dr. C. Wilcocks and Dr. E. L. Harris. (Pp. 95. 22s. 6d.) Horsham, Sussex: Association of Medical Advisers in the Pharmaceutical Industry. 1967.

Recent Advances in Anaesthesia and Analgesia. 10th edition. Edited by C. Langton Hewer, M.B., B.S.(Lond.), M.R.C.P.(Lond.), F.F.A. R.C.S. (Pp. 342+viii; illustrated. 60s.) London: J. & A. Churchill. 1967.

Exercise at Altitude. Based on Papers Presented at the International Symposium, Milan, 1966. Edited by R. Margaria. (Pp. 216; illustrated. £4 13s. 6d.) Amsterdam: Excerpta Medica Foundation. 1967.

Middle Articles

GENERAL PRACTICE OBSERVED

Extended Use of Nursing Services in General Practice

J. WESTON SMITH, M.B., CH.B., D.R.C.O.G., D.A.; E. M. MOTTRAM, S.R.N.

Brit. med. J., 1967, 4, 672-674

Nursing Services in a General Practice—An Experiment

Our practice comprises a partnership of two doctors with a list of about 5,500 patients during the first nine months of this year. The practice covers a radius of about 5 miles (8 km.). We were faced with a difficult situation at the beginning of the year, as it was obvious that a major outbreak of measles was imminent, in addition to the other common infections.

There seemed to be three main problems. Firstly, the practice is situated in a "designated" area which is rapidly expanding because of overspill. There are more new patients than can be comfortably accepted if a satisfactory standard of medical care is to be maintained. Secondly, there is a large rural area to be covered, but both the partners are also heavily involved with hospital work. Thirdly, there is a lack of suitably experienced doctors willing and able to undertake this wide spectrum of work.

It was thought that the scope of work, both in hospital and in the care of greater numbers of patients, could be done efficiently and properly provided that time was not wasted with minor problems, especially unnecessary visiting and revisiting and routine procedures in the surgery. Nevertheless, the ordinary patient is not in a position to know whether a particular situation needs the visit of a doctor or not. The Ministry of Health circular puts the onus of decision on the doctor, who often has only the verbal history of the patient, possibly second-hand from a neighbour or relative. Further, revisiting is desirable and necessary in certain cases where the progress of the patient needs to be assessed professionally and skilfully. There was one more disquieting factor; because of the good will in the practice, we found the patients, knowing we were working under strain, often helped by not asking for a visit but for advice and a prescription to be left; we felt that this was not a desirable practice.

Hence we decided to appoint an experienced nurse to help in the clinical work of the practice for about 20 hours weekly, with the following duties:

- (1) The reception and assessment of requests to visit and other messages, from 8.45 to 10.30 a.m.
- (2) Visiting new calls after consultation with the doctors in those cases where there was doubt about whether a visit by doctor was necessary.
- (3) Immunizations and desensitization procedures during surgery.
- (4) Assistance at the antenatal clinics.
- (5) Revisits and routine visits to elderly and disabled people.

It was obviously necessary for the nurse to have a fairly wide experience, preferably with outpatients, and to be a car driver. From the beginning we decided to employ her for three and a half hours in the morning and two afternoons a week, and to pay her top salary scale and a car allowance on a per mile basis.

Instructions to the Nurse

The nurse received all the incoming requests for visits and advised and recorded them. Our patients with problems have always been able to speak personally to the doctor; and in these cases, or when the nurse was in doubt, the nurse was instructed to put the call through to the doctor. After conferring with the partners she visited the requests for first calls. The doctors meanwhile went on to their hospital duties. If in her opinion any patient needed immediate attention the doctors could be contacted at the hospital.

All patients visited were to have their temperature and pulse recorded, together with a short clinical history, followed by the nurse's impressions and suggestions. This was all to be recorded in a report book which was to be kept in the surgery. The nurse would then deal with the request in one of the following ways:

- (1) In the nurse's opinion a doctor's visit was not necessary, nor was it necessary for the patient to visit the doctor at his surgery, and the household could be reassured.
- (2) A doctor's visit to the house was not necessary, but the patient was fit to visit the surgery and an appointment was arranged.
- (3) Common-sense measures were suggested or the nurse would recommend some mild medicine be prescribed by the doctor—for example, a simple cough linctus or antacid.
- (4) If a common infection was found or suspected—for example, measles—the nurse was usually able to make a provisional diagnosis and report it to the doctor, who would visit the patient when he was in the neighbourhood.
- (5) If pyrexia was present or other disquieting symptoms in the absence of a known epidemic condition, the nurse advised the household that the doctor would be calling later on.
- (6) The doctor was contacted urgently.

It was emphasized to the nurse that if the family in any way indicated they would like the doctor to call personally this must be done. In fact, in the course of over 700 calls this did not happen once, and in only three cases was a call later requested for the doctor personally to visit after the nurse had called. In each of these three cases no reason was found to disagree with nurse's assessment of the case, neither did the patients want anything apart from reassurance.

The numbers in Table I exclude all visits requested after 10.30 a.m. and all midwifery calls.

TABLE I.—Number of Visits Made

	Nurse	Doctor 1	Doctor 2
Total No. of visits January to October	744 + 41 (2 in 1 house)	800	285
Total No. of first visits	537	560	228
" " " revisits advised by nurse	86	10	57
" " " " " " doctor	111	230	No. of visits not recorded
Emergency visits during surgery	10	first revisits	

We found that if a conference was held at about 12.30 p.m. the cases could be discussed and action agreed on. Occasional checks were made by the doctor on families visited if further reassurance seemed necessary or where there was an element of doubt. This was found to be increasingly unnecessary as the scheme began to be known to the patients. It was soon found that there was a great preponderance of nurse calls to young children and revisits to elderly people. This is, of course, in line with the general visiting pattern of general practitioners, but the doctor visits proportionately increased in the age ratio of 10 to 60. It was our impression that, as the scheme became more widely known, the threshold at which a visit is requested has become lower and a visit of the nurse is specifically asked for.

The nurse's 785 visits were made up as follows: 485 to children under 10, 133 to patients over 65, and 167 to others. From the report book we were able to compile Table II, which shows the numbers of first visits performed by the nurse and roughly the type of case.

TABLE II.—*First Visits Made by Nurse*

Common infections, measles, mumps, chicken-pox, etc. . .	187
Rashes without pyrexia	19
Catarrhal colds and coughs without pyrexia	62
Infections with pyrexia	96
Diarrhoea and vomiting	66
Others—e.g., injury, social, oedema, abdominal pain, history taking	97
Emergency	10

The method of working of the two doctors differs. Doctor 1 is the elder, with a much larger proportion of older and chronic sick patients, and it is from him most of the revisit requests emerge. Doctor 2 has a number of hospital anaesthetic appointments together with the bulk of the practice midwifery (about 114 cases per annum); hence most children under the age of 10 years are in his care, and it is from him that the highest proportion of first nurse visits emanated. The proportion on a typical spring day would be: three first nurse visits requested by Doctor 2, one or two nurse revisits requested by Doctor 1, one nurse revisit, and one nurse routine visit. Thus a very high proportion of patients anxious about their own or their children's health do not actually appear to need a personal visit by the doctor. This is emphasized by the fact that there was not one complaint about the scheme. However, on many visits the nurse was asked to see other patients at the same time; she was able to do this without undue stress, though this may be a source of minor irritation to a general practitioner with a full visiting-list.

Of 440 first visits to children only about 10% required a doctor's visit that day. The period surveyed covered a parallel epidemic of measles and chicken-pox, and here the nurse's help proved invaluable. The confirmation of the condition with general common-sense advice, to settle with the later visit by the doctor, proved to be very popular with all classes of patients. Another fact was the early recognition and treatment of enteritis in infants and the institution of the standard regimen.

Questions to Patients

It was appreciated that many people who had been used to sending for a doctor might not accept the visit of a nurse, however well trained she might be. Hence it was thought essential

Replies to Questionary

	Yes	No
Did you find it a help for a nurse to advise you whether a visit by doctor was necessary?	179	3
Did you find the visit of nurse helpful?	185	2
Were you satisfied with the result of the visit?	186	2
Did you later visit doctor?	63	120
Have you any further suggestions?	33	congratulatory replies, 1 unfavourable

to find out the reaction of the various patients. A questionnaire was sent to every household visited by nurse. At its head was a letter outlining its purpose, and a dotted line underneath indicated that it could be torn off and returned anonymously if so desired.

A total of 260 copies of the questionnaire were sent out to all the households visited and we received 189 replies, although the postage was not prepaid.

The answer that exceeded our expectations was under the heading "suggestions." About 26% of the households visited had something to say on this subject, and their comments show there is a very definite demand for this type of service. There were many comments on the great help given; several people said that the National Health Service would be greatly improved if the practice were extended. In particular we found that there is a need among mothers of infants and young children for expert advice about when to summon the doctor, the opinions of neighbours and relatives being notoriously unreliable. We found that elderly patients are glad to be revisited, but like a doctor to see them the first time. One other fact emerged—families with problems appreciated the visits, as they knew they had time and opportunity to discuss apparently trivial matters with which they would not bother the doctor for fear of wasting his time. Nevertheless, knowledge of these factors often helped in assessing an individual patient. On the other hand, we found that problem families were best left to the county authorities, who have the machinery and time to deal with the many difficulties involved.

We strictly excluded nursing procedures on the district, as it was thought that the county district nurses might think that this was an unwarranted intrusion into their province. As a general rule, therefore, the nurse did not visit any family which was in the care of a district nurse. On the other hand, we found that she could complement the work of the health visitors, especially with premature babies and congenital defects; these she could weigh regularly at home and take prescriptions ordered by the hospitals; moreover, she could give courses of immunization at home.

Developments

As the scheme developed considerable changes were made. Firstly, we realized that the initial time allocated to the nurse was grossly inadequate, and this was increased to about 27 hours. Since 1 October 1967 we have acquired a new partner and over 2,000 new patients, and we envisage that there will be enough work for a full-time nurse. Secondly, we found the use of a trained nurse to assess incoming calls invaluable, and we soon found that patients were asking specifically for the nurse.

One of the more worrying happenings in general practice is the apparently urgent call during a busy surgery. During the period under review the nurse went out immediately to assess the situation with instructions to report at once in 10 cases. The final assessment of these was as follows: two coronary thromboses (doctor and ambulance were sent for); two falls (sent to hospital); one appendicitis (doctor visited after surgery); two fits (first aid, and doctor visited later); two epistaxes (first aid); and one sudden death (arrangements made).

Like many others, we also found that there are a surprising number of duties apart from immunizations and routine injections for a nurse to do during surgery—for example, routine blood pressures, skin reaction testing, detailed history taking, and ear syringing. Moreover, during antenatal clinics routine blood pressures, testing of urine, weighing, and the preliminary medical history could be done by nurse before the patient was seen by the midwives or doctor. We found that by restricting her duties to these items the relations between the different types of nursing staff were happily maintained.

We were anxious about a possible tendency to prescribe appetite suppressants without a careful follow-up. Accordingly we decided to prescribe only a week's supply, and that the nurse should do weekly weighings; further supplies depended on a gradual loss of weight. To our surprise, a weight-losing group soon developed, and we noted that patients in this group were voluntarily giving up taking the pills and often losing weight faster than those on suppressants. Two full clinics have now formed. We are also proceeding with the formation of an anti-smoking group, and the demand for this is already high.

Discussion

It is too early to evaluate all the implications of this project or to assess accurately the advantages and dangers inherent in its application. We think it is sufficiently important, however, to put our experience on record, realizing that there must be critical comment and observation. We think there is an opening in a practice such as we have described for a full-time nurse carrying out the duties we have outlined. This is no position, however, for the newly qualified State-registered nurse. At least four years' post-qualification experience is necessary, preferably up to the standard of staff nurse or sister in a casualty outpatient department or in a ward for acute cases, where not only ill people are encountered and have to be assessed but the problem of human relationships between the profession and the patient together with their relatives is of paramount importance.

We think that the scheme shows that there is a much wider field of work for the experienced nurse than has been thought possible in the past. The S.R.N. of today has a wide education and her training takes her a long way beyond the traditional nursing procedures; one of the criticisms of nursing today when a nurse leaves hospital is that a large amount of her time is occupied in nursing procedures which in hospital would have been left to nurses in their early training period. We think that the modern nurse is in a position to assess whether a patient is ill enough to need the visit of a doctor; in other words, we are placing her in the position of a sister with a responsible hospital position. It was noticeable during the nine months that the main calls fully dealt with by the nurse concerned patients at the extremes of age, and we found that in the nurse's opinion working men and women who requested a visit usually needed the visit of a doctor.

We have found in practice that the whole concept is acceptable to the majority of our patients. It is most important for patients to know that the nurse is not a substitute for the doctor, and in fact is trying to help the latter arrive at a decision. In fact we found that the nurse is far more apt to err on the patient's side than on the doctor's. Nevertheless, many people may query the possible dangers of using nurses for first visits. There is, on the one hand, always the possibility of the mistaken assessment of the case; on the other hand, this is so with any doctor, for no professional person is free from errors of judgement. Looking back over the past, we think that the incidence is not likely to be higher in the case of an experienced nurse. We have taken the attitude that the partners are responsible for all the acts of the nurse, but it is the view of the Royal College of Nursing that the nurse should be indemnified and protected in the event of litigation on her own account; this, we understand, is possible in a similar manner to the medical profession.

We would like to emphasize that we think the following points are essential:

(1) That the employing doctors satisfy themselves, by inquiry and personal assessment, of the ability of the nurse to undertake this type of work.

(2) That the written report *must* be entered of each patient visited, together with the temperature, pulse rate, full history, and the nurse's opinion.

(3) That there should be personal consultation and agreement between the doctor and nurse about the conduct of each individual case.

Unless the above criteria are strictly observed a disastrous situation may occur at any time. If this type of scheme is used as a form of cheap medicine, as a barrier between the patient and doctor, or is embarked on without careful thought and planning, we believe it a retrograde step. In practice it is our impression that far from lessening the amount of work done by doctor the amount of consultative work has actually increased; this, however, can be only a subjective impression owing to the increasing number of patients, but it is already apparent that the total travelling time by the doctors has already diminished.

We think it is essential for a full secretarial service to be maintained, and that the nurse has the same facilities as the doctors for documentation and dictation of letters. It is also extremely important that the correct relationship be maintained with the local health authorities, and for this reason no nursing procedures are undertaken on the district. The attendance of midwives at the antenatal clinic is encouraged by the local health authorities, and on these occasions the work of the nurse is restricted to initial documentation and history, urine tests, and blood pressure estimation. In our opinion the nurse in the circumstances described is best employed direct by the practice rather than by the county service. On the other hand, the nurse must make herself fully conversant with all the services available through the county.

At present nurses employed in this way would seem to forfeit their superannuation rights under the National Health scheme, and this would seem to merit critical attention. From the practical standpoint the hours worked are especially suitable to part-time nurses—that is, 8.45 a.m. to 4 p.m. from Monday to Friday—and may tap a source of nursing strength hitherto unavailable.

We feel certain that in this field of work there is a great future, and that the nurse entering it will at some time in the future have special training—in fact this would seem essential. We think that two months' instruction in the methods of general practice and the various forms used by the executive council, followed by four months' attachment to a suitable practice with an assessment at the end, might merit serious consideration.

Summary

Over a nine months' period a State-registered nurse has been used for helping in the clinical work of a general practice in a semirural area with about 5,500 patients. Provided a nurse with the right temperament and extensive clinical experience is obtained, and suitable safeguards are used, we think that she can be used for making first visits to patients, and the replies to a questionnaire sent to the patients showed that most patients agreed and welcomed the scheme.

Our thanks to Dr. C. H. Goodliffe, the senior partner, for his wholehearted co-operation in the study and the use of his figures, and to Mrs. Beryl Weston Smith for the preparation and typing of the paper.

CONTEMPORARY THEMES

Medical Partnership: Minister's Lecture at Glasgow

A Maurice Bloch Lecture was delivered by the Minister of Health at Glasgow University on 6 December.

Mr. ROBINSON's title was "Partnership in Medical Care." He began by referring to his recent statement in the House of Commons [*B.M.J.*, 11 November, p. 367] that the Government intended to review the administrative structure of the National Health Service and, if necessary, to reconstruct it. He emphasized that they did not in any sense feel that the National Health Service had "failed." Nevertheless, the statutory apparatus—which had been basically unchanged since 1948—had been outgrown by its service content. Medicine changed, evolved, and developed, and hence required an organization which not only permitted but actually promoted change.

"Phase I" of the N.H.S.

Discussing what he called Phase I of the National Health Service, Mr. Robinson said that the objective of the Service was firmly set forth in the wartime Beveridge Report, which aimed at producing a comprehensive blueprint for the Welfare State, and assumed that a National Health Service would be an essential part of this blueprint. Taking up the idea, the Government of the day produced a White Paper in 1944 which announced the intention to establish a comprehensive health service for everybody in Britain. Nevertheless, the founding of the National Health Service was evolution, not revolution; thus the White Paper spoke of a "comprehensive service for all regarded as the natural next development."

Organizationally speaking, what had happened in 1948 was that a uniform organization was imposed on services which were already there, though not all of them everywhere or available within the individual's means. The tripartite structure of the Health Service established by the Acts of 1946 and 1947 reflected a concept of three interdependent but separately managed streams of care for the community and an implicit assumption that relationships would not change. Looking back, Mr. Robinson continued, this was a curiously static conception, as if the new form of management need only attempt the organization of services as they then saw them.

Need for Co-operation

The need for co-operation had been reviewed as early as 1952 by a Committee of the Central Health Services Council. Its recommendation had been to establish standing joint liaison committees both for general and for special purposes, but again it had seemed unaware of the organic nature of the enterprise. Having no executive powers, the usefulness of these liaison committees was limited, and those few that were established took up a lot of time.

The committee set up to inquire into the cost of the N.H.S. (the Guillebaud Committee) had in the nature of things to consider the structure of the Service. In essence, its finding was that the organization had only just settled down in the eight years of its existence and that it was far too early to

make a change. This committee set the tone for most of the thinking about structure for many years. While it was perhaps unfair to criticize the committee now when circumstances had changed so radically, the fact remained that the doctrine "When it is not necessary to change, it is necessary not to change" had inhibited and perhaps stultified thinking. But people were not ready then to think of entirely new machinery, only permutations of the old. In respect of particular services, it became evident that there was a case for unifying the three branches, but the committees reviewing these particular services recognized that they should not be split off from the general Health Service structure and that, given that the general structure was tripartite, the particular service also had to remain so. Chapter and verse could be found in the Cranbrook Report on Maternity Services—of which the Scottish equivalent was the Montgomery Report—and the Report of the Royal Commission on the Law relating to Mental Illness and Mental Deficiency.

Continuing, Mr. Robinson pointed out that the question of an entirely fresh approach to administration of the Health Service had been reopened by the Porritt Report in 1962. This report had come out uncompromisingly for the principle of area health boards, which would deal with all aspects of the Health Services, but it had made no attempt to define the size of areas or the composition of boards. The reasons which had moved this committee were those of fulfilment: for the general practitioner to be able more fully to realize his capacity and his potentialities by extending his access to the specialized services of the hospital, though consultants were to remain responsible for hospital work.

The committee also wished to tap the special expertise of the medical officer of health and to give him a wider sphere in which to exercise his talents by making him a consultant in social health in an appropriately broadened department. This report was a turning-point, though he could wish that the committee had agreed on and said more about some very necessary changes in the organization of medical work in and out of hospital.

Among the many criticisms made of the Porritt Report it had been said that the report produced an idea and a philosophy, but in no sense a plan. "What was to be the geographical extent of the area health board? How was it to be governed? Was it not a self-defeating process to propose, as the report did, first unifying the administration of the services but then setting up three subordinate bodies under the area health board corresponding to the existing tripartite divisions?"

Is There an Alternative?

There was something in all of these criticisms of the Porritt Report, but they had missed the important point that the post-Guillebaud freeze had been thawed. Since then restructuring of the administration had been a frequent topic among those connected in any way with the Service. The medical profession had itself returned to this ques-

tion, and the *British Medical Journal* had produced a series of articles, now collected in book form under the title *Is There an Alternative?* The object of these essays, ranging widely as they do from almost pure organization theory to the possibility of a sweepstake to finance hospital services, seemed to have been to provoke people to think about the range of possible alternative structures. "If I may say so, this seems altogether helpful: there is not one, there are many possible ways of restructuring the Health Service."

Mr. Robinson then turned to what he called the realities of life for workers in the field which underlay this debate on the government of the Service. He pointed out that, firstly, a revolution had begun in general practice. Much of this had been carried out by the general practitioners themselves, and the changes had become so widely accepted that there was some danger of losing sight of their magnitude. Let it never be forgotten that group practices were a truly co-operative advance made by independent professional men of their own volition. They had come together to give better service to the public, and also to find a more satisfying professional and personal life. This was essentially a development which individual doctors must seek. The action of Government in such matters was necessarily limited.

Changes in General Practice

In the 1940s the general practitioner had often been isolated from professional contact and learned only from his own experience. Now, many of them were active in research, and far more eagerly took advantage of courses for postgraduate education. All were making increasing use of the diagnostic support facilities they could draw on from the hospitals. Secondly, the general practitioner was beginning to emerge as the leader of a team. Most local authorities had agreed that some at least of their health visitors, home nurses, or midwives should be attached to group practices rather than districts. This move had helped to make each member of the team more "productive" and to ensure a good two-way flow of information about cases in which both the general practitioner and the local authority department were interested.

Thirdly, there had been a quite remarkable upsurge of interest in the new opportunities offered by health centres. All these changes had been in the field; they had not been matched by any change in the structure. The conclusion was inescapable that the administrative apparatus must be clearly made to serve the needs of those who were actually doing the work.

A comparatively unnoticed development was the beginnings of a managerial revolution in health planning. The application of the principles of scientific management to the hospitals had raised some very big questions, and it had been realized that economy could often be best achieved by concentration. It was a very difficult matter to find the right blend between the managerial and the medical optimum; it must never be forgotten that good medicine must be humanely based on personal contact.

Best Features of N.H.S.

Mr. Robinson then turned to some of the best features of the Service which must be carried on into any new structure. The first and greatest of these was the partnership of the health professions. Despite all the demarcations of which he had spoken, a continuity in medical care had been preserved. The professions had never allowed their contract with one authority or the other to obstruct their acting together in the common cause. It was apt, he thought, that the President of the B.M.A. should have chosen for his text "One Profession, One Purpose." [*B.M.J.*, 15 July, p. 129.] These four short words reminded us that medicine was more than a science-based discipline: it was founded on the rock of an ethic.

One aspect of partnership which he hoped could be established on firmer foundations than in the past was the partnership between profession and Government. This relationship was critical for the success of any State-organized health service, but it had been bedevilled by the profession's suspicion of Government from the day more than half a century ago when the State had first entered the arena of comprehensive medical care. To-day the suspicion lingered, perhaps less among the rank-and-file members of the medical profession than among some of those who spoke for the profession in a representative capacity. There might have been sometimes partial justification for this, because suspicion soon became mutual, but he did not think that had been more than fleeting and occasional.

"The medical politician is expected, or believes that he is expected, to reflect the anxieties and frustrations, real and imagined, of those he purports to represent. In such a situation a politician, and I speak as one myself, is tempted to look for an easily recognizable scapegoat. To delve into and try to identify the root causes of frustration is an altogether more complex and possibly painful process. Furthermore, if such an exercise reveals causes that are internal rather than external the findings may not be too welcome. It is so much simpler to blame

the Minister and his department, or to suspect their motives."

The relations between the State and a distinguished profession could never be entirely smooth. Nevertheless, not only was the doctor's clinical freedom sustained as the inviolable rule of the Service but questions of remuneration (always a potential source of friction) had been handed over to independent bodies for consideration, subject to the Government's retaining, as it must, the ultimate right of decision. Despite these efforts, however, there was still not the relationship of mutual confidence between profession and State. Obviously they had failed to carry conviction, and he wished he could see why.

Many doctors might well recognize that the Minister's objectives were the same as their own—namely, to provide the best possible service the nation could afford and as quickly as a vast modernization programme permitted. Nevertheless, one looked almost in vain to see this attitude reflected in the official voice of the profession. To the public outside there appeared to be a state of antagonism towards Government. Every test of opinion, however, confirmed that the patients themselves simply did not share the misgivings of so many medical spokesmen. Hence in devising a new structure for the Service it was essential to do everything possible to promote the development of a genuine sense of partnership.

Health Service Management

Mr. Robinson preferred to think of Health Service management not as the place from which orders issued, but the forum where problems were thrashed out; where each point of view was put, the professional requirements, the needs of the community, and the financial restraints; where there was communication between the various groups concerned in sharing out resources; where information was gathered and pooled; where proposals could be framed in the light of every consideration; where agreed policies could be hammered out. The problems of the Service could be solved only if the pro-

fessions had a clear role in that process.

The planners they wanted in the Service were those who knew how to make common cause and partnership with the workers in the field. He would naturally like additional resources, but perhaps above all he would like 50 more men skilled both in medicine and the managerial sciences. More men were needed who were "health planners" as versed in that art as town planners were in their specialty. The Health Service needed some of the ablest men to come forward for such duties, centrally and locally, and to fill the group and divisional posts recommended in the two recently published reports on the organization of medical work in hospitals. They would find much scope for their talents, for the time was clearly past when individual skills sufficed for successful hospital work.

Concluding, Mr. Robinson offered a "friendly criticism" of the medical profession—that in their laudable concentration on "this patient here and this patient now," they had in general tended to neglect the question of general management of resources, and in particular what the businessmen called corporate strategy: "Where shall we be going in 5, 10, or 20 years' time, what kind of medicine will be practised, and what kind of environment shall we be working in?" He therefore applauded the setting up within the British Medical Association of a Forward Planning Unit under Professor Henry Miller. He hazarded a guess that fairly rapid moves would be made in the functional linking of the hospital and the community services. The general practitioner would give a new dimension to the concept of the all-round personal physician as group practice developed with nurses and doctors forming the group. Hospitals would become ever more sophisticated and intensive in their approach to treatment. Nevertheless, they would be places where people might go more often but would stay for a shorter time if they stayed at all. The hospital of the future was likely to function effectively only through its partnership with the group practices, with which it would form a complex for both curative and preventive work.

TOMORROW'S BUILDINGS**Thamesmead: First Phase of Community Health Service**

[FROM A SPECIAL CORRESPONDENT]

The overall proposals for the community health service at Thamesmead, the new G.L.C. development within the London boroughs of Greenwich and Bexley, have been described in other articles.^{1,2} A new stage in the project is marked by the current exhibition at the Building Centre, Store Street, London W.1, of the plans of Messrs. Derek Stow and Partners, architects and planning consultants for the health centres, of the first phase of the development.

The essential feature of the Thamesmead project is that medical planning should proceed step by step with overall planning from the very first stages. The aims of the medical plan are:

1. To provide the best possible health services economically feasible within the present structure of the N.H.S.

2. To enable medical, dental, and other students to see and partake in community health care.
3. To promote research and experiment into medical care and its organization.

"The original proposals" showed how these aims could be achieved by a network of health centres enabling doctors, dentists, nurses, and other health staff (whether under the local health authority or the executive council) to work effectively together and in association with the local hospital. The first two stages of Thamesmead, which are now under construction, will house about 10,000 people by the end of 1970 and lie entirely within the borough of Bexley. By 1981 a population of 58,000 is envisaged.

As it may be five years before any building can take place in the centre of Thames-

mead, it is necessary to provide comprehensive services as soon as possible. The proposals illustrated in the current exhibition are for a health centre to be built by the G.L.C. for the borough of Bexley under section 21 of the N.H.S. Act. As this may not be completed before the end of 1969, it is also proposed that a temporary mobile health centre be erected early in 1968; when the first permanent building comes into operation the latter could be moved to a new site in Thamesmead.

Principles of Buildings

The briefs for these two buildings were drawn up by the General Practice Unit at Guy's Hospital (Director, Dr. ROBERT SMITH) working in close collaboration with

the borough of Bexley and with the Medical Architecture Research Unit at Southend (Director, Mr. RAYMOND MOSS) and the General Practice Advisory Service (Architect, Mr. BRIAN BROOKES). None of the hospital services envisaged in the overall plan is now involved, but otherwise the brief reflects in miniature the ultimate aims of the project.

The design of the first building was influenced by a number of important factors:

1. The need to be self-sufficient, taking account of the possibility of some changes in function as the total pattern of health facilities grows.
2. The town-planning principle of segregation of pedestrians and vehicular traffic by means of a pedestrian deck at first-floor level: all traffic (but only a small number of pedestrians) will approach the building at ground level.
3. The site location (bordering on an artificial lake near one of the development subcentres) and size (rather less than the floor area required).

The architect's solution was to raise the main accommodation on a concrete deck to first-floor level (that is, pedestrian-deck level), leaving the ground floor for vehicle passenger entrance, service rooms, stores, and a pram park for the minority of pedestrians who approach from a near-by bus-stop and from the subcentre via the lake walk. Car park-

ing is provided at this level under cover of the pedestrian deck above.

Patients and staff arriving at this level can reach the main accommodation by means of lift or staircase, which discharges adjacent to the main pedestrian entrance at first-floor level. Immediately facing the patient on entry is the reception desk, which has visual control of the three sides of the square-ring corridor. After registering, patients wait in the adjacent general or dental waiting-rooms (which include a children's playroom) and are called down the east and west corridors respectively to consulting- and treatment-rooms.

Consulting-rooms

General consulting-rooms are served by a treatment room, specimen room, and laboratory; in addition, they share a supply store and disposal room with the dental suite. A small local waiting space is provided for patients passing from consulting- to treatment-room or—in the case of antenatal clinics—in the opposite direction.

Dental patients pass from the main waiting area, down the west corridor, where they are met by the dental nurse. After treatment they may return by way of the main entrance, or, if a general anaesthetic has been

necessary, they may use the exit adjacent to the dental suite, which is also used by the dental staff.

A separate exit for staff is provided by the escape stair in the north-east corner, allowing them to arrive or leave without passing the main waiting area (see plan).

It will be noticed that rooms around the perimeter are those requiring a view and natural light but no other special environmental requirements; rooms in the core of the building would not benefit from a view, but do require special ventilation of one sort or another. Neither the consulting-rooms on the east side, nor the dental surgeries on the north, are overlooked, since they face the lake.

The temporary mobile health centre has a demountable structure, consisting of four single-steroye timber units, each the size of a large caravan and containing part of the health centre accommodation, fully equipped. These units are simply carried to the site on a trailer, set down on their skids and connected by additional floor elements which form waiting and corridor spaces.

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CONFERENCES AND MEETINGS

Operating-rooms a Century after Lister: B.M.A. Symposium

[FROM A SPECIAL CORRESPONDENT]

A Lister Commemoration Symposium on operating-theatre design was held at B.M.A. House on 8 December, under the chairmanship of the President, Mr. R. V. COOKE.

Opening the symposium, the Minister of Health, Mr. KENNETH ROBINSON, referred to Lord Lister as one of the twelve people who had done most to relieve human suffering. At the present time new hospital buildings worth £230m. were under construction. In the interests of economy, speed of construction, efficiency, and good design his Ministry was now developing standardized plans for operating departments, but this would not mean stagnation. Alternatives were provided, and designs would be continually brought up to date.

Concluding the opening addresses, Professor Sir HEDLEY ATKINS, P.R.C.S., outlined Lord Lister's long association with the B.M.A.—extending from 1863, the year after his qualification, to his death in 1912. Within a month of Lister's publication of his second *Lancet* article, in 1867, the Association had invited him to address their Dublin meeting. He became president of the surgical section in 1870, and first described the famous carbolic spray at the Plymouth meeting of 1871. Although relations with the B.M.A. were subsequently less good for a time—largely owing to the activities of the then editor of the *British Medical Journal*—amity was later restored, and a special Lister issue of the *B.M.J.* appeared early in the present century.

Wound Infection

The first speaker in the symposium itself was Professor R. E. O. WILLIAMS (St. Mary's Hospital Medical School, London), whose subject was wound infection. The overall incidence of this was about 6.7%, but this figure concealed wide variations between different hospitals and operations—from 1.8% to 17%, according to hospital, and from 1% or less for orthopaedic operations to 15% for gall-bladder surgery. Infection acquired in the theatre probably accounted for about 20% of all wound sepsis, though the proportion might be as high as 50% for prolonged thoracic surgical procedures.

The source of infection varied with the type of organism. *Staphylococcus aureus* commonly came from the nose or skin of the patient or hospital staff, and the carrier rate in patients rose from 35% to 50% while in hospital. Two per cent. of patients carried penicillin-resistant strains on admission, but the proportion could rise to 20% or 30% during a prolonged stay. Probably post-operative wound sepsis with *Staph. aureus* was commoner in patients who were or had been carriers; during prolonged operations some bacteria almost inevitably fell into the wound, and many of these were the patient's own staphylococci.

Three other organisms—*Escherichia coli*, *Pseudomonas aeruginosa*, and *Clostridium welchii*—could also cause self-infection. The major source was intestinal, but *Ps. aeruginosa*

bred in moist environmental reservoirs such as sinks, sluices, and humidifiers; to a lesser extent this was also true of *E. coli* and perhaps *Cl. welchii*. A study of 20 patients with postoperative gas gangrene had shown that 18 followed lower-limb operations, 11 of them amputations. The antiseptics used had been ineffective against clostridial spores, and no prophylactic penicillin had been given. *Cl. welchii* was normally present in the intestine, and operations on the upper leg were readily contaminated from the anus. By contrast, *Cl. tetani* infection was almost always due to faulty sterilization—often of dressings or glove powder.

Preventive Measures

Professor Williams concluded by recommending preventive measures—proper sterilization for tetanus, suitable antiseptics and chemoprophylaxis for gas gangrene, and careful control of humidifiers and other moist areas for prevention of pseudomonas or *E. coli* infection. *Staph. aureus* presented more complex problems involving control of carriers and skin spread.

Some of these were covered by the second speaker, Professor R. A. SHOOTER (St. Bartholomew's Hospital, London)—speaking on dispersal of bacteria—who suggested that adoption of the measures proposed by Professor Williams would reduce the incidence

of operating-room sepsis to 1% or less. Showers did not control this dispersal from the skin; greater numbers of bacteria were shed for one and a half hours after a shower, and the effect of adding hexachlorophane was inconstant. Ordinary theatre gowns did not reduce the number of organisms put out, though the level was low and perhaps immaterial except in high-risk operations. Special operating suits made from very closely woven material and, worn with plastic bags enclosing the feet and trouser-bottoms were more successful; ultraviolet light could also help, though it was not fully effective when used alone. A combination of both methods was best, probably because dispersal of bacteria-laden skin scales was prevented, and individual organisms penetrating the finely woven material were killed by ultraviolet irradiation. The special suits and plastic foot-bags also cut down bacterial dispersion from nurses compared with conventional skirts and gowns.

Dispersal from inanimate objects was another danger. In the case of sterile packs, it had been found that opening a single-layered wrapper threw bacteria from the outside into the air; these landed on the instruments in 132 out of 250 packs tested. Substitution of a double-layered pack reduced contamination to 1 in 100. Finally, trials of paper sacks (sealed by stapling) for removal of all contaminated material from operating-rooms had shown that no bacteria escaped on handling or even when the bags were dropped. The special routes for removal of contaminated material now incorporated in many new theatres appeared to be unnecessary.

Ventilation

Dr. O. M. LIDWELL (Medical Research Council) said that operating-theatre ventilation systems had so often been to blame for wound infection in the past that they were now commonly made the scapegoat. In fact the number of pathogenic bacteria likely to reach an operation site by the airborne route was very small—perhaps one or two organisms—but even this might be enough to cause infection in the presence of sutures or other foreign bodies, or microscopic areas of dead tissue, or blood clots. Asepsis could be approached but never fully achieved.

Among measures to reduce airborne spread of infection, Dr. Lidwell emphasized the importance of doors. The airflow through an open doorway might be 1,000 cubic feet (25.5 cu. m.) per minute—and the doorless openings in some older theatres were a definite risk. Other important factors were reduction of temperature difference between the theatre and the neighbouring rooms, and the maintenance of positive air pressure in the operating-room so that air could leak only outwards around doors and other openings. This required a ventilation system delivering at least 1,000 cubic feet of air per minute, which could both prevent the ingress of airborne bacteria and help to remove those released in the theatre. To avoid the risk of pseudomonas or perhaps *E. coli* infection steam or spinning disc humidifiers could be used in ventilation systems. The incoming air was usually passed through a filter down to 5 microns and introduced at ceiling level, but attempts to direct it around the

operating area had met with only moderate success in reducing the number of airborne bacteria.

Concluding Dr. Lidwell showed that a good ventilation system could enhance working capacity by accurate control of temperature, but studies of comfort at different temperature levels had revealed some individual variation. Anaesthetists preferred to be about 4° F. (2° C.) warmer than surgeons, for instance, while a few of the latter felt too hot unless the temperature was reduced to the low sixties.

An aseptic operating enclosure for use in hip-prosthesis surgery was described by Mr. J. CHARNLEY (Wrightington Hospital, near Wigan, Lancs), who emphasized the need for absolute sterility in this type of operation. The use of a 7-ft. (2.1 m.) square transparent enclosure within a larger theatre had made possible the provision of a downward stream of sterile air at the rate of 300 air changes per hour without high cost or inconvenience. Only the surgeon, two assistants, and one sister worked within the enclosure, their expired air being withdrawn by suction appliances, worn under complete face and head masks, and removed by vacuum tubes down the back. The flow of 5 cubic feet (0.2 cu. m.) per minute under the mask had a markedly refreshing effect and reduced sweating, in addition to removing nose or throat bacteria. The patient's head was outside the enclosure, as were the anaesthetist and the rest of the theatre staff.

The ventilation system was situated immediately above the theatre and opened into the ceiling of the enclosure through an aperture 5 feet (1.5 m.) square. The lights were situated at the corners of this to avoid turbulence in the downward airflow, which was barely noticeable at a velocity of 1½ feet (45.7 cm.) per second. Deflection caused by the presence of the patient was beneficial, since the flow then tended to be away from the operation site towards the surgeon. Similarly there was always an outwards current of air through the instrument hatch and other openings. Other precautions were double gloves, separately sterilized instrument containers for each of the seven stages of the operation, and sterilization of the patient's skin with 2% iodine—after a skin test. This was followed by a varnish spray to fix potentially infected epithelial squames that might separate during operation.

Concluding, Mr. Charnley pointed out the simplicity of the method and the ease with which spectators could observe operations from outside the enclosure. He believed that such enclosures could be used in any room—several being supplied from a single autoclave by people in everyday clothes. This would be cheaper and better than expensive attempts at partial cleanliness, for there was nothing between totally sterile and dirty.

Operating-theatre Design

Mr. WALPOLE LEWIN (Cambridge) spoke on factors in theatre design and gave three reasons for failure to reduce the morbidity of operative infection. These were overconfidence in conventional aseptic ritual; complex procedures involving many people and prolonged exposure; and long waiting-lists. Bed turnover rather than quality had become

the criterion of surgical excellence. The load on theatre staffs was excessive, and there was a danger that the "dirty" cases at the end of one surgeon's list would be too closely followed by the important early cases of another surgeon using the same theatre. It took time to clean a theatre properly, and as Lister had said, "Asepsis in this imperfect world is not to be trusted."

It was the surgeon's duty to maintain theatre discipline and exclude infection. Attention had to be given to many factors, including postponement of operations on patients with colds or other infections, use of prophylactic antibiotics, and the wearing of double gloves and gowns covering back and front for all theatre staff. The patient's clothing and theatre trolley should be clean, and too much clutter of staff and apparatus should be avoided. Special equipment—often necessary nowadays—could perhaps be housed outside the theatre proper in adjacent rooms. Finally, humidity, ventilation, and temperature had all to be controlled, and a refrigeration plant was indispensable.

Mr. Walpole Lewin ended by suggesting that the best type of theatre to build at present might be *space*, in which functional areas could be adjusted to incorporate later developments. The accepted figure of 400 square feet (53 sq. m.) was too small for some operations, and there was a danger that all the work on theatre design since the war might be lost in Ministry standardization, if financial rather than surgical considerations were allowed to predominate.

Speaking as an architect, Mr. J. WEEKS (Bartlett School of Architecture, University of London) warned surgeons to be on their guard against architects' running away with ideas. The year 1963, the year of the Royal College of Surgeons' symposium on operating theatre design, had seen the peak of complexity, with every whim indulged, but since then two developments had taken place. Firstly, this complexity of design had become "frozen," and it was now enshrined by the Ministry of Health; and, secondly, accurate measurements had been made of the needs and functions of an operating-theatre. Some of the elaboration going into theatres at present was no longer necessary—though well adapted to intensive use and modern techniques, they were likely to be superseded. Micro-environments might prove more economical than large operating suites with porters hurtling up and down the sterile corridors. Detailed plans were always apt to become "dated"; and simpler suites with anaesthetic and recovery rooms and reserve space between the theatres should provide for future adaptation. If the original building was suitably constructed, later expansion could be on to different floors as well as on the same level. Concluding, Mr. Weeks said that architects and others thought in 1963 that they knew all the answers to operating-theatre design—in 1967 they were quite sure they did not.

The last speaker, Major IAN CAPPERAULD, R.A.M.C., described a portable tent-type operating-theatre with special lighting, ventilation, and electrical equipment, used recently at the Royal Herbert Hospital, Woolwich, while the theatres were temporarily closed for alterations. This theatre, together with many exhibits of modern designs for operating departments, was on show in the Great Hall during the symposium.

Correspondence

Letters to the Editor should not exceed 500 words.

Psychotropic Drugs

SIR,—Dr. J. T. Hutchinson's suggestion (2 December, p. 555) of using the suicide rate as a guide to the value or otherwise of antidepressant medication seems reasonable enough. However, the figures I have available do not appear to be encouraging. Assuming that the great majority of suicides are caused by depressive states, one would expect a significant drop in the overall rate for England and Wales. But the figure per 100,000 has been fairly constant¹ during the years 1954 to 1964 at 11 to 12—lowest 11.3 in 1960, highest 12.15 in 1963. Of course it may be that some deleterious factor other than depression has been increasing over the years and counteracting the preventive influences of antidepressant drugs. Or has the severity of depressive states become more intense? Or has the incidence of depression increased? I doubt whether there are reliable statistics to answer these questions. Practical psychiatrists are too busy to grade the severity of depressions accurately enough for research purposes; and not so long ago conditions which are now classified as "masked depression" were given all sorts of other labels.—I am, etc.,

Weybridge,
Surrey.

I. ATKIN.

REFERENCE

¹ Registrar General's Statistical Review of England and Wales for the year 1964, Part I, Tables, Medical, 1966. H.M.S.O.

SIR,—I could not agree more with your correspondent Dr. J. T. Hutchinson when he states in the *B.M.J.*: "It is time that clinicians ceased to be afraid of the dangers of these drugs" (2 December, p. 555). I am sure I speak for hundreds of general practitioners when I affirm that the use of antidepressant drugs (and this certainly includes monoamine oxidase inhibitors) has revolutionized the treatment of depressive illness in family practice.

My partner and I have about 150 patients suffering from various forms of depressive illness in our practice, and half of these attend intermittently for further supplies of antidepressant drugs. They are not asked to do so, but have found from their own experience that the various manifestations of depressive illness are helped by these drugs in a way no other treatment can equal. We have not had a single suicide in the past six years.

There is no doubt whatever that the use of these drugs has greatly added to the satisfaction that the family doctor can get from the management of a wide variety of illnesses that in the past were a source of continuing frustration and anxiety to him. In this context, as a family doctor long interested in psychiatric illness, I feel that the concept by Sargant and others of the wide anxiety-depression spectrum of illness¹ is one of great

interest to general practitioners and one with which they can wholeheartedly agree.

Amitriptyline and nortriptyline are increasingly used, but Parstelin and phenelzine are still very useful in general practice, reactions to them being very rare; and there remains a definite place for the use of a short-term liquid amphetamine preparation for "post-influenzal debility" and the like.—I am, etc.,

Leeds 17.

ALASTAIR U. MACKINNON.

REFERENCE

¹ Sargant, W., Walter, C. J. S., and Wright, N., *Brit. med. J.*, 1966, 1, 322.

SIR,—Dr. J. T. Hutchinson in his concern for the patient needs no support (2 December, p. 555). That he has seen only one death due to drugs in eight years may well depend on what drugs he has tried and in what dosage and combination; two of my patients on a pre-marketing drug trial fared badly: I abandoned this trial and the drug was later withdrawn.

Linking the suicide rate with the efficacy

of drugs is reasonable enough, but one must take account of the management of the patient, which includes the availability of lethal drugs and of clinical assessment, which needs to be reviewed repeatedly for each patient. It is not an overstatement that every depressed patient presents a suicidal risk which one might avoid by admission and full-time observation, but in general a calculated risk has to be taken during the whole course of the illness, particularly when initiative returns.

My own general approach is to separate patients suffering from depressive symptoms—unhappiness, guilt, unworthiness, and hopelessness—and to administer as a first choice convulsive therapy, which is still the most effective and the quickest mode of treatment. I use drugs first for those patients whose "depressive" state needs to be diagnosed and is not self-evident—for instance, preoccupation with spectacles and dentures, fatigability, impaired interests, various chronic somatic symptoms, and so on. These patients hardly ever constitute a suicidal risk, so that the manipulation of drugs until a suitable dosage or combination is found is valid and safe; if this is not achieved convulsant therapy is often effective. Of course by this time the natural history of the illness may also be a factor in improvement.—I am, etc.,

London W.1.

L. ROSE.

Clomiphene for Ovulation

SIR,—The letter from Dr. P. M. F. Bishop (9 December, p. 617) highlights the dilemma about the proper way to use clomiphene. On the one hand, there is much to be said for Dr. Bishop's view that as the drug appears harmless and as its sole purpose is to stimulate ovulation it should be freely used without elaborate scientific controls. Not many would agree with his implication that the main purpose of the steroid chemists is "to get on with their research work," but the central point is well taken. On the other hand, the induction of ovulation and subsequent fertilization is not a casual process or a frequent demand on the Health Service and it is not unduly fussy to treat the matter with some circumspection.

There are three good reasons for supporting the view taken in your leading article (25 November, p. 434) that accurate hormone assays should be used in connexion with clomiphene administration. The first is in selecting suitable women for the treatment; particularly in identifying those amenorrhoeic subjects with sufficient residual ovarian activity to respond to the treatment, or the women with regular but persistently anovular cycles. Dr. Bishop argues well for vaginal cytology as a compromise between no controls and proper hormone assays, particularly as he has himself done much to popularize these services, but few would deny that they are inferior to hormone assays, and they are inadequate for categorizing the women sub-

jected to the treatment or determining the nature and timing of their response.

The second reason for the use of hormone assays is that they make it possible to fix the day of ovulation with much more accuracy than by vaginal cytology. Indeed the most advanced laboratory services claim to be able to predict the day of ovulation from the rising oestrogen curve and usually advise about the timing of intercourse. At worst, one has valuable data about the pattern of response, which is likely to repeat itself in subsequent courses. The third reason is that hormone assays give quantitative information about the nature of the response. One can tell whether there was any ovarian response, whether the oestrogen excretion was equal to or much above that of the normal cycle, and whether or not it was followed by ovulation and how adequate the luteal phase was. The incidence of multiple pregnancy and of ovarian cyst formation appears to be related to the nature of the ovarian response, which in its turn is a dose-related phenomenon. Accurate information about the ovarian response enables the physician to regulate dosage in subsequent treatments.

I believe that these reasons are sufficiently compelling to justify some voluntary restriction of the freedom of the individual doctor to give his patient whatever treatment he chooses. It is a besetting fact of medicine in our time that it is passing from the individual to the team and from the man to the

institution. As laboratories cannot be brought to patients, patients must sometimes be brought to laboratories. On balance this seems to be a situation where this applies.—I am, etc.,

University of Aberdeen,
Aberdeen.

A. KLOPPER

Using Computers

SIR,—The paper by Mr. S. P. Watts and Dr. E. D. Acheson (25 November, p. 476) calls for two comments. Their study is not essentially a computer method in the accepted sense of the term. It has been done manually. It could certainly be done with business machines. Of course, it is easier with a computer. Hospital activity analysis can provide "treatments" or "persons." It is a matter of input organization (an identity-fix in particular) and programming. There is no "error" between one and the other. They are different things. For year-to-year comparisons "treatments" may be a sufficient indicator. For true morbidity measurements "persons" are inadequate, since they form only the hospital tip of the iceberg.

But, as in all statistics, it depends on what you want to use the rates for. If it is for hospital management—for example, the efficient use of resources—then the "spell" is the right unit. If for disease management—for example, for diagnosis symptom matrices—then the individual "person" record updated with the whole medical history (inside or outside the hospital)—that is, a full-blooded community health record system—is needed.

Hospital activity analysis is intended to lead into this,¹ and some experiments are already being made to extend hospital activity analysis in this direction. In the long run the unified record will pay bigger dividends than record linkage.—I am, etc.,

BERNARD BENJAMIN,

Director,
Research and Intelligence Unit,
Greater London Council.

London S.E.1.

REFERENCE

- ¹ Benjamin, B., *Proc. roy. Soc. Med.*, 1967, 60, 809.

Animal Reservoirs of Salmonellae

SIR,—I read with interest Dr. L. T. Newman's letter (4 November, p. 296) on the dangers of salmonella infections from pet tortoises and Dr. W. H. Parry's (25 November, p. 486) on the similar dangers from a pet terrapin. I am glad they have stressed the very real risks of animal reservoirs of intestinal infection which so often go unrecognized. Salmonella infections are far from rare¹ and thousands of new cases occur each year in Britain. In 1965 there were 832 cases of paratyphoid fever alone in England and Wales. The paratyphoid fevers may not always cause gastrointestinal symptoms and the carrier state is common and difficult to eradicate.² In addition to the typhoid and paratyphoid fevers salmonella infections may be far from minor illnesses,³ and a single outbreak in Sweden of *Salmonella typhimurium* was reported which caused 7,717 cases with 90 deaths.⁴

Certain preserved foods are universally recognized as potential sources of salmonella infections. It is not so well known that

nearly every animal in the world, both wild and tame, may carry salmonellae in its gastrointestinal tract, including dogs, foxes, horses, cattle, swine, sheep, goats, hedgehogs, pigeons, and even the ticks, lice, and fleas that feed on infected swine and other animals.⁵ Even the lion is not exempt,⁶ though it could hardly be classified as a pet except perhaps in Ethiopia.

Pet tortoises are a real hazard, but reported infections in iguanas, snakes, and lizards⁷ are more academic than real. As the festive season approaches, however, it is a salutary thought to remember that domestic poultry constitutes the largest single reservoir in nature and that turkeys are especially affected. Some 41% of turkeys in California were found infected with salmonellae.⁸ The canary may be affected⁹ and the dog is a frequent host. In 100 dogs examined in the U.S.A. 18 were found to have salmonella infections, most of which were pathogenic for man. In Norway an infected dog was found to be responsible for six cases of paratyphoid in human beings.¹⁰ In Florida greyhounds were routinely tested, and between 32% and 55% of all dogs were found to be carriers of salmonellae.¹¹ Dogs, after swine, were found to be the most important asymptomatic carriers and 40% of cases were due to *S. typhimurium*. Dogs and cats have been found to be responsible for *S. choleraesuis* transmission to children,¹² and 13.2% of healthy dogs in the U.S.A. were found infected with salmonellae and over 1% of cats in England.⁷

Obviously many salmonellae in animals are non-pathogenic for man. A number may be, however, and the possibility of an enteritis being spread by a pet should always be borne in mind, especially in young children with an undiagnosed gastroenteric infection.—I am, etc.,

R. L. HUCKSTEP.

Makerere University College,
Kampala, Uganda.

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Improving the Psychiatric Services

SIR,—There is a great deal of evidence indicating that readmission rates for discharged ex-psychiatric hospital patients are less among those provided with reasonably effective psychiatric aftercare.¹⁻⁴

Psychiatric patients can cause great disturbance and trial to others when left at home. Visiting can provide early warning that modification of treatment or persuasion to take tablets has become urgent. Thus in quite a number of these patients a relapse

can be averted. I find that a large number stop taking their tablets, and that a recurrence of symptoms within a few weeks follows. When there is no follow-up the patient will often not visit a doctor. Relatives are diffident about complaining. Maintenance of morale in many depressive patients does also appear to depend to some extent upon follow-up, and there being somebody, perhaps outside the immediate circle of the patient, giving disinterested help and caring. Dudgeon⁵ noted that as many as 23% of 471 patients seen a year after leaving mental hospitals had had no contact with a doctor or any other type of trained mental health worker since discharge.

The consequences of a significant number of schizophrenic patients stopping tablets have been outlined.¹⁻⁴ I have seen not one but a number of patients descend to further suicidal attempts following sudden cessation of antidepressant drugs. If in addition to cessation of drugs they are discharged from psychiatric outpatient clinics then it would seem vital that they be visited by someone from the mental welfare services.

In 1952 Dr. Arthur Pool initiated a six-week-in, six-week-out geriatric service in Oldham, with an associated day hospital. This alleviated the situation and did relieve many people with elderly relations as well as the patients. Spread of this system would appear to be well worth while and within the scope of numbers of existing institutions and staffs. As part of this scheme all relatives undertook to have their patients home at the end of the period so that everyone could benefit. They were made to realize that the scheme could only work widely if this was kept to. There was free use of admissions of the elderly, so that the relations who were doing their bit by keeping them at home could get off for needed holidays. Keystones in this system were the co-operation of geriatricians and of the ambulance department, which we had.—I am, etc.,

Colchester,
Essex.

HARRY JACOBS.

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Intussusception Due to Hamartoma

SIR,—A rare lesion of the base of the appendix may have initiated acute appendicitis and subsequent intussusception of the caecum, and is reported below:

A diagnosis of acute appendicitis was made on a 10-year-old boy, and at operation an acutely inflamed appendix was removed and the stump buried with a purse-string suture. Apart from oedema and local fibrinous exudate over the ileocaecal region no other abnormality was noted. The histology of the excised appendix showed acute appendicitis. After operation he made rapid progress, but on the sixth day complained of colicky abdominal pain. There was some tenderness elicited over the site of the scar, but the symptoms rapidly subsided and he was discharged home on the ninth day.

Two weeks later the patient complained of several brief attacks of colicky central abdominal pain, and during one of these his general prac-

itioner palpated an epigastric mass. On admission the child appeared well. He was afebrile and the pulse rate was normal. The abdomen was soft and the presence of a mass was not confirmed. Rectal examination was negative, and plain x-rays of the abdomen showed no evidence of fluid levels or dilated loops of bowel. He was therefore observed for 24 hours, after which time he complained of further abdominal pain. Examination during a spasm of pain confirmed the presence of a tender sausage-shaped mass in the epigastrium. A diagnosis of intussusception was made, and an immediate barium enema performed, which confirmed this. The apex lay in the epigastrium. This was readily reduced by the pressure from the enema, and filling was obtained to the caecum. No barium entered the terminal ileum, and a filling defect was demonstrated in the ileocaecal region (Fig. 1). It was not possible to be certain, therefore, that reduction had been complete.



FIG. 1.—Radiograph showing the caecum (C) with a persistent filling defect (D) at its base.

Laparotomy was undertaken through a right paramedian incision under general anaesthesia. It was found that the intussusception had been completely reduced, but there was a soft mass palpable through the wall of the caecum in the region of the healed appendix stump. This felt like a tumour of approximately 3 cm. in diameter and accounted for the filling defect seen in the radiograph and under the image intensifier. It was considered unwise to open the caecum, so a right hemicolectomy was performed and an end-to-side anastomosis made between the terminal

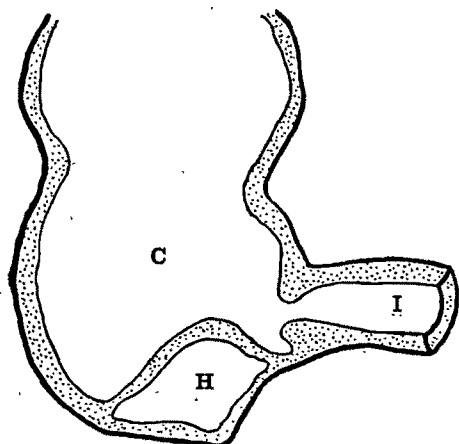


FIG. 2.—Diagram to show the position of the submucosal hamartoma (H) in the region of the appendix stump. I=terminal ileum. C=caecum.

ileum and colon. The abdomen was closed and the patient made an uninterrupted recovery. He was discharged home 12 days later, and has since remained well with a single bowel action daily.

The operation specimen was opened to reveal a small intramural tumour at the site of the appendix stump (Fig. 2). This was of soft rubbery consistence and measured 3 cm. by 2 cm. Histologically it was shown to be a benign hamartoma showing proliferation of vascular and nervous elements.

It is possible that in this patient obstruction of the appendiceal lumen by the hamartoma preceded the primary infection. The apex of an intussusception may be formed by the base of the appendix where this is unduly broad, or concretions, worms, a mucocele, or a polyp protrude from the lumen.

Although it is standard practice to bury the stump the chances of this acting as the apex of an intussusception are infinitesimal. In this case the hamartoma was missed at the first operation on account of the oedema caused by the inflammatory condition, and it is suggested that burying the stump had the effect of pushing the tumour towards the lumen of the caecum, which was unduly mobile. This created the apex of the intussusception. This complication is so rare that it should not prevent the surgeon burying the appendix stump routinely.

I wish to thank Mr. D. B. Craig for permission to publish this case, Dr. J. M. Burbury for the radiograph.

—I am, etc.,

DAVID P. GOODWIN.

Edgware General Hospital,
Edgware, Middx.

Prevention of Rh-haemolytic Disease

SIR,—Professor C. A. Clarke's answer (25 November, p. 484) necessitates further comment. He states that the number of cases in the various trials has increased considerably since his lecture. I have received the up-to-date figures, and although the total number of cases in the United States group has increased—for example, the controls from 347 to 503—surprisingly the number of immunizations has decreased from 40 to 36. The Liverpool and Edinburgh figures have not changed, but the German figures have actually decreased from 152 to 117, yet show one more immunization in the controls. Difficulties of this sort had made me confine my questions to the Liverpool series.

Regarding second pregnancies, as the initiative lies with the patient to notify when pregnant again one can guess that the response has been far from complete, and it could be that abortions would less likely be reported. An individual follow-up would give more true assessment.

Professor Clarke agrees that enhancement of immunization by IgM has not been satisfactorily explained and that it is not yet known whether suppression of D-immunization is specific. The mechanism of suppression with the use of gammaglobulin is equally ill-understood and much of the current literature on immunology¹ emphasizes this. As for the antigenicity of gammaglobulin, it may not be valid to compare the use of anti-D gammaglobulin in parturient normal women with gammaglobulin given to patients during

pregnancy, when there is a raised threshold to primary immunization,² or with gammaglobulin given to patients suffering from agammaglobulinaemia, who have a subnormal antibody response.

Gm antigens are transfused when whole blood or plasma is given and can stimulate anti-Gm, but when the gammaglobulin is fractionated, given intramuscularly, and without the competitive red cell antigens, its antigenicity may well be enhanced.³ Frequency of stimulation is probably important, and the incidence of anti-Gm may be greater if gammaglobulin is given to patients who have been previously transfused. Six per cent. of Professor Clarke's treated cases have developed anti-Gm antibodies, which warrants consideration of possible clinical reactions due to these in any further transfusion of these patients, and warrants also consideration of their implication in any further pregnancies and in possible long-term effects. The hypothetical causal relationship between anti-Gm and rheumatoid arthritis has been postulated by Fudenberg and Martensson,⁴ and in fact was mentioned by Professor Clarke himself,⁵ and although there is probably not a simple relationship the role of anti-Gm in rheumatoid arthritis and other immunological disorders is still much under discussion.⁶ Anti-Gm antibodies often display iso-specificity and can occur in the 7S globulin. One assumes that such antibodies could cross the placenta and therefore may have an adverse effect on the foetus. Indeed, the possibility that juvenile rheumatoid arthritis might have some such materno-foetal immunological relationship has also been raised by Fudenberg.⁴

Finally, differing Gm factors in different ethnic groups could also have some relevance when bleeding donors as a source of anti-D gammaglobulin. In view of these and other reservations I think there are "several" most important points requiring research, and that the challenge is

"How covert matters may be best disclosed,
And open perils surest answered."

Julius Caesar, Act IV, Sc. 1.

—I am, etc.,

SHEILAGH MURRAY,

Director,
National Blood Transfusion Service,
Region 1.

Newcastle upon Tyne.

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Intrauterine Transfusion in Rh-isoimmunization

SIR,—The paper by Professor D. V. I. Fairweather and others on intrauterine transfusion in Rh-isoimmunization (28 October, p. 189) calls for some comment. They state that the prolonged anaemia often seen in these babies is due to the depression of bone marrow consequent on the intrauterine transfusion.

However, our personal experience suggests that this might not be the only reason. We have seen three cases of prolonged anaemia occurring in babies who had had intrauterine transfusion, who at 2 months of age had a low reticulocyte count in the peripheral blood, while the bone marrow showed clear signs of erythroid hyperplasia. Coombs test in one

of these cases was strongly positive on the bone marrow, though only very weakly positive on the peripheral blood. The anti-D antibody titre was 1/1,024. Examination of this infant's blood showed that virtually only Rh-negative cells (that is, like those given by transfusion) were present.

This observation supports the hypothesis that the late anaemia seen in very severe Rh disease is due to the persistence of antibodies in the blood. This phenomenon has become apparently more common recently, since, because intrauterine transfusion is now performed, these infants do not require large exchange transfusion at birth, and also there is an increasing survival of severe cases.—We are, etc.,

University of Milan,
Italy.

G. MASERA.
A. MARINI.

Gastritis, Aspirin, and Alcohol

SIR,—We were interested in Dr. C. E. Astley's letter (25 November, p. 484), and particularly his last paragraph in which he suggests that regular beer drinking over a number of years eventually leads to duodenal ulcer. Our practices are in Middlesbrough and Redcar, the same area as Dr. Astley's consulting practice. Recently, together with Dr. G. R. Freedman, of Newcastle, and Dr. I. C. Fuller, of Sedgefield, we made a survey of cases of duodenal ulcer in our practices. In this survey various factors in our cases of radiologically proved duodenal ulcer were compared with ulcer-free controls selected by a statistically sound method using random numbers. The figures quoted below are from the Middlesbrough and Redcar practices only. Superficially, at least, our figures do not support Dr. Astley's contention.

In Middlesbrough there were 42 male cases of proved duodenal ulcer, of which 20 (47.5%) were beer drinkers. The average weekly consumption was 6.3 pints (3.6 l.) of bitter beer. Controls numbered 24, including 17 beer drinkers (71%), average consumption 6.5 pints (3.7 l.). In Redcar out of 34 proved cases 19 were beer drinkers (56%), average consumption 11.1 pints (6.4 l.), whereas 25 controls included 16 drinkers (64%), average consumption 11.0 pints (6.3 l.). The difference in the beer consumption between the two towns probably reflects different social patterns in the two practices, the Redcar practice having a higher percentage of steel workers, who have a long-standing tradition of beer drinking.

It is possible that some patients with duodenal ulcer have stopped drinking because of previous advice or adverse effects of alcohol upon their symptoms. In the combined practices, 17 proved cases admitted that alcohol aggravated their symptoms, but 10 were still drinking beer. If the 7 who were apparently deterred are added to the beer drinkers, then the percentage of beer drinkers in controls is still higher than in the cases of duodenal ulcer. The pattern of drinking among ulcer cases and controls in each practice is remarkably consistent, and suggests that if advice to stop drinking has been followed it has been on the all or none principle. This advice too would probably have included smoking in its restrictions. There were, however, in the combined practices

58% of smokers in the proved cases, compared with 45% in the controls.

This illustrates the difficulties which arise when environmental causes are attributed to duodenal ulcer, and more work must be done on a prospective basis before Dr. Astley's contention can be accepted.

With Dr. Astley's stricture on aspirin, particularly Alka-seltzer, we are in complete agreement.—We are, etc.,

Middlesbrough,
Yorks.

G. K. H. HODGKIN.
J. WHEWELL.

Alcoholic Content

SIR,—In 1961 I made a suggestion that it was time that the alcoholic content of beverages was properly described on the bottles in terms of approximate percentage by volume. Labels which refer to degrees of proof spirit convey precisely nothing to most people.

It is not only spirits, usually about 40% by volume of alcohol, which should be properly described: various beers and stouts can vary from 3% up to, in one case, 11%. Sherry, port, madeira, and marsala may contain 18%, and wines from 9 to 15%. These must serve as examples of the problem.

In view of new legislation, and a new sense of awareness of road dangers, surely the time has come when drivers, cyclists, and pedestrians are entitled to know just what they are imbibing, and have we not a duty to help the populace to educate itself by learning how and what to drink, and how not to?

To avoid over-elaboration in a letter, may I refer anyone interested to the summer and autumn editions of *Health Horizon* 1961, which go more fully both into the matter of per cent. labelling and alcohol and the driver? What seemed important then seems to be highly relevant today.—I am, etc.,

Broadbridge Heath,
Sussex.

GUY BOUSFIELD.

Endocarditis and the Mitral Valve

SIR,—In our paper "Prolapse of the Posterior Leaflet of the Mitral Valve: A Clinical, Familial, and Cineangiographic Study" (8 July, p. 71) we suggested that bacterial endocarditis was unlikely to be a complication of this lesion although other authors had suggested that these patients should receive penicillin prophylaxis for dental work. We now wish to report a case of *Streptococcus viridans* endocarditis in one of our patients who had previously been found to have prolapse of the posterior leaflet of the mitral valve.

The patient, a male aged 35 years, was investigated by means of left ventricular cineangiography in May 1967, after a systolic click and late systolic murmur had been found on routine examination. Investigation revealed the typical abnormality of prolapse of the posterior leaflet of the mitral valve into the left atrium with late mitral incompetence. The patient was seen again in October, with a four-week history of malaise and fever for which he had received several short courses of penicillin. (Shortly before the onset of this illness he had been bitten by a dog on the left calf.) On examination he

had a fever, but there was no change in his cardiac auscultatory findings and no other findings to suggest the diagnosis of bacterial endocarditis. E.S.R. was 34 mm. in one hour, white cell count was 8,000. Blood cultures were performed and *Str. viridans* was grown from three cultures. The patient was treated with 8 million units of crystalline penicillin intravenously daily for one month and made an uneventful recovery.

We therefore consider that prolapse of the posterior leaflet of the mitral valve may predispose to bacterial endocarditis and that patients with this lesion should receive prophylactic antibiotics for dental work and other conditions which may lead to bacteraemia.—We are, etc.,

MARY STANNARD.
ALAN J. GOBLE.

Cardiac Department,
The Royal Melbourne Hospital,
Victoria, Australia.

Jaundice in Pregnancy

SIR,—I was interested to read your leading article on jaundice in pregnancy (2 December, p. 499), with particular reference to recurrent intrahepatic cholestatic jaundice of pregnancy. Perhaps it should be emphasized more strongly that this is a benign condition, and the prognosis for mother and child are excellent. No special treatment is needed in the antenatal period, such as induction of labour or caesarean section, on account of the jaundice alone. There is an increased tendency for premature delivery in the 38th week, and some authors have noticed a tendency for the prothrombin level to fall and lead to postpartum haemorrhage if not promptly dealt with.

'Thorling' in 1955 produced the classical account of the disease, and he and other authors are agreed that the jaundice usually fades first in the puerperium and that the pruritus resolves within about a week or two after this—this point being at variance with your editorial view. Probably generalized pruritus without jaundice occurring in the last few weeks of pregnancy is part of the same syndrome, and Fast and Roulston¹ pointed out that these patients may have elevated serum bilirubin and alkaline phosphatase levels. They also thought that recurrences occur in at least 50% of cases. The condition is probably a great deal more common than realized, and the recent influx of case reports seems to suggest that obstetricians are becoming more aware of it.—I am, etc.,

J. E. A. ONI-ORISAN.

Stobhill General Hospital,
Glasgow.

REFERENCES

- ¹ Thorling, L., *Acta med. scand.*, 1955, 151, Suppl. No. 302.
- ² Fast, B. B., and Roulston, T. M., *Amer. J. Obstet. Gynec.*, 1964, 88, 314.

Massive Overdose of Adrenaline

SIR,—Dr. Michael A. Lewis (7 October, p. 38) speculates on the reasons for the prolonged period of hypotension and tachycardia displayed by his patient without reaching any firm conclusions. Is he able to say what volumes of fluid were administered to this

healthy young woman, and over what periods?

Prolonged hypotension and tachycardia, often accompanied by signs of inadequate cerebral oxygenation, are quite frequently due to overhydration by intravenous therapy. When given orally, excess fluids are rejected by the onset of nausea or active vomiting, but this defence mechanism cannot operate when fluids are administered intravenously. The protocol of Dr. Lewis's patient suggests that considerable volumes of fluid were injected, for he speaks of a large catheter inserted into the saphenous vein and the use of a pressure-pump. It is sometimes forgotten that infused fluids (water) leave the intravascular compartment as rapidly as possible, taking with them a measure of diffusible molecules. The presence of an increased bulk of extravascular fluid in turn retards and even interferes with oxygen and carbon-dioxide molecular diffusion between blood plasma and protoplasm. Where extracellular fluid volume is increased, the intercapillary distance is also increased, and if this exceeds the critical distance discussed by Scharrer¹ cellular ischaemia may progress to a point of irreversibility. The target areas for such a development will depend upon the circumstances, and where intense peripheral vasoconstriction has been produced these target areas are more likely to be myocardium, brain, and lung, where survival dictates that perfusion should be maintained as long as possible.

To me there is one other point of great interest in this report. One has seen so many patients unharmed by prolonged and sometimes profound hypotension that, as I have suggested elsewhere,² we need to realize that blood pressure does not really indicate the extent of the circulation to peripheral tissues. The gross hypertension which operated here and the peripheral vasoconstriction to my mind underlines this generalization, and highlights a need to reappraise our concepts of the practical value of blood-pressure measurement in the clinical practice of medicine.—I am, etc.,

Worcester, C.P.,
South Africa.

C. S. JONES.

REFERENCES

- ¹ Scharrer, E., *Quart. Rev. Biol.*, 1944, 19, 308.
- ² Jones, C. S., *Postgrad. Med.*, 1966, 40, 499.

Homonymous Hemianopia after Oral Contraceptives

SIR,—Permanent homonymous hemianopia has been recognized for many years as a rare aftermath of a migrainous paroxysm.¹

I have seen two such cases within a few days of each other. In both patients this incident occurred shortly after commencing the contraceptive-pill regimen, which also had the effect of causing severe recrudescence of migraine dormant for some years. Both patients were otherwise fit women in their forties. One of them discontinued the oral contraceptive of her own accord four months ago, and she has remained free from headaches since. The time that has elapsed since the second patient stopped taking oral contraceptives is too short to warrant any conclusion as yet.

These cases may perhaps betoken a migrainous causation of the otherwise unexplained hemiplegia occurring during contraceptive-pill medication, especially since

these drugs have been shown not to produce any abnormality of the coagulation pattern.²—I am, etc.,

London W.1.

SIMON BEHRMAN.

REFERENCES

- ¹ Adie, W. J., *Lancet*, 1930, 2, 237.
- ² Haeger, K., Nilsson, I. M., and Robertson, B., *Brit. med. J.*, 1967, 3, 493.

Abortion and Conscience

SIR,—Dr. P. Darby (2 December, p. 549) puts forward the pregnant woman's "well-being" as a medical consideration for abortion. He appears to have forgotten that the "well-being" clause which was included in an earlier stage of the Medical Termination of Pregnancy Bill was withdrawn by its sponsors and is not in the new Abortion Act. That the W.H.O. includes such a phrase in their definition of mental health does not give it legal validity. Neither does it give it medical sanction, for W.H.O. definitions are notoriously unstable and liable to change, as is evidenced by those on alcoholism and drug addiction.

There is no agreement on a definition of "mental health" in spite of national associations, institutes, and research funds devoted to its cause. At a conference in 1956, sponsored by the World Federation for Mental Health and the International Association of Universities, which lasted for 10 days, the delegates agreed they could not define mental health in a simple, universally acceptable manner. What they were able to do was to say what it was not, and the following are the negative statements they produced:

- (1) It is not characterized by adjustment under all circumstances.
- (2) It is not characterized by freedom from anxiety and tension.
- (3) It is not characterized by freedom from dissatisfaction.
- (4) It is not characterized by conformity or constant happiness.
- (5) It does not imply the absence of personal idiosyncrasies.
- (6) It does not imply a lessening of accomplishment or creativity.
- (7) It does not imply the undermining of authority.
- (8) It is in no way opposed to religious values.

These points should be borne in mind when the pregnant woman's "mental health" is being considered.—I am, etc.,

Edgbaston,
Birmingham 15.

MYRE SIM.

Body Building on Drugs

SIR,—May I comment upon the letter (11 November, p. 353) and your leading article (p. 310) concerning the use of anabolic steroids in sport.

The use of these drugs for increasing bulk and strength in power events has been going on since at least 1963. The practice is widespread in the U.S.A., Australasia, and probably Eastern Europe. It is not yet so common in Britain, but it is on the increase. Several Olympic and Commonwealth Games titles and world records have been won and set up by athletes who have influenced their training with anabolic steroids.

The International Amateur Athletic Federation laws are loosely worded on the

definition of doping. They specifically ban the use of drugs which stimulate muscle and nerve (this by my interpretation includes anabolic steroids) and are against in principle all drug-taking in sport. The penalty is banishment from competition for both athlete and accomplice for an indefinite period.

The British Amateur Athletics Board officially recognized this problem in the autumn of 1966. They issued a statement categorically condemning the use of these drugs to influence training.

The International Olympic Committee decided in the spring of 1967 that all athletes taking part in future Olympic Games should sign a declaration stating that they have not used drugs (specifically mentioning anabolic steroids) for influencing their sporting ability.

The problem of detection is real. Even if it should become possible to detect biochemically whether or not the drug has been used, the testing is likely to be a complicated and expensive procedure. This in itself will tend to limit testing in amateur sport. The only ways I see of limiting their use is by (1) making supply of the drug difficult—that is, by all doctors being aware of the abuse—and (2) by the introduction of body weight gain limits into the sports particularly affected.—I am, etc.,

St. Annes-on-Sea,
Lancashire.

M. T. LUCKING.

Restrictions on Doctor in South Africa

SIR,—The recent banning order served on Dr. R. Hoffenberg has rightly been commented on in your columns (26 August, pp. 512 and 556). On 6 September 1967 I sent a letter of resignation to Dr. Burger, Superintendent of Groote Schuur Hospital, Cape Town. This letter was also submitted to the *South African Medical Journal* for publication. Its journal committee decided that all correspondence on the matter would be delayed pending a decision between a deputation from the University of Cape Town and the Minister of Justice. Attempts to obtain such a meeting lasted several months. When the meeting finally took place a few weeks ago the Minister indicated that he was not willing to make concessions on anything other than minor details. The decision of the journal committee in fact meant that, over a long and crucial period, South African doctors were denied the right to protest in their own organ against the banning of their colleague. Immediately after I heard of the meeting between the deputation and the Minister I cabled the *South African Medical Journal* asking whether they would publish my letter. This was refused.

In my letter to Dr. Burger I stated that the major consideration that prompted my resignation was political and was crystallized finally by the ban on Dr. Hoffenberg. To continue to participate in academic activity, to be stimulated by social and intellectual contact with colleagues, and to publish and to teach when a fellow doctor was precluded from doing so was intolerable. I felt that original and critical thought could not survive in academic life in a politically suppressive atmosphere and that freedom of thought was essential.—I am, etc.,

Lemuel Shattuck Hospital,
Boston,
Massachusetts, U.S.A.

S. SHAPIRO.

Overseas Registration and Seniority Payments

SIR,—I was interested to read the letters of Drs. A. M. Poornan (19 August, p. 500) and G. Murtaza (28 October, p. 239) about the rejection of their claims for seniority allowance by the Ministry of Health. The ruling of the Ministry is incompatible with the spirit and principle with which the Review Body introduced this payment.

In para. 159 of the Report¹ it states that this payment "will recognize the development of experience in the general practitioner, and will provide him with the prospect of maintaining the level of his remuneration at a time when he may wish with advancing age . . . to curtail his responsibilities or reduce his work load."

The present ruling of the Ministry will mean that doctors registered overseas will qualify for the payment late in their lives, and some may even retire before getting any increments. It will also delay the recognition of their experience in general practice (the minimum laid down in the Report for allowance is five years), as they will be in practice for more than that time before their claim is accepted. It will also prevent them from reducing their work load with advancing age, should they wish to do so, without a serious financial loss.

Thus it is evident that the Ministry's ruling is quite contrary to the intentions with which these payments were introduced. May I also point out that nowhere in the Report has the registration body been specifically mentioned to be the General Medical Council. Para. 215(4)(c) of the Report says only the *Medical Register*.

Those of us who qualified and registered overseas should be treated in the same manner as doctors qualified and registered in the Irish Republic, or has the Ministry two sets of rules?—I am, etc.,

Manchester 16.

G. J. DRABU.

REFERENCE

¹ *Review Body on Doctors' and Dentists' Remuneration*, Seventh Report, Cmd. 2992, 1966. H.M.S.O.

Seniority Payments

SIR,—I feel that one must take issue with Dr. S. Stowe (2 December, p. 557), who feels strongly on matters of principle and practice that seniority payments should not be tied to a stipulated amount of postgraduate training.

The principle of linking seniority payments with a small postgraduate training requirement seems to me to be reasonable and enlightened. However, it is really the question of practicability that has caused me to write. I found it difficult to imagine that the letter was from a colleague working in the same conurbation as myself. Are there not week-end rotas in Wolverhampton? Do the doctors still live and work in isolation? Is it not possible to ring up a friend in the vicinity and get him to cover for the odd Saturday morning? Will no locum work in the area? Are there no hospital staff who would undertake to come in at times? The use of any or all of these simple methods would enable Dr. Stowe to get away for postgraduate training, and he is fortunate to be in an area served by the University of Birmingham Medical School and the Midland faculty of the Royal College of General Practitioners. He has on offer a plethora of

week-end courses, together with the possibility of individual attachment in virtually any specialty he cares to study. In Birmingham itself there are excellent postgraduate facilities available at most of the major hospitals, and I would imagine that the same applies in the Wolverhampton area.

The need for postgraduate training is being increasingly recognized, and for many the stipulation linking this with seniority payments is accepted without any apprehension, for it is really rather pleasant to revert to being a student again.—I am, etc.,

Handsworth,
Birmingham 21.

K. G. DICKINSON.

Thirteen-week Certificate

SIR,—A number of my patients who have long-standing chronic illness such as disseminated sclerosis, chronic bronchitis, and ankylosing spondylitis are likely to survive for many years but will be quite unable to resume work. Many are unable to attend the surgery and require a home visit on fixed dates for the purpose of insurance certification.

It is my practice to visit such patients only when a change in their medical condition demands such a visit, and this rarely coincides with the timing of certification. It therefore becomes necessary to make home visits for a purely non-medical administrative procedure.

Would it be possible for one of the following alternative measures to be given consideration?

(1) Arrangements for a medical board to review such cases at yearly or less frequent intervals, thus dispensing with certification by the general practitioner altogether.

(2) That it be required for the general practitioner to certify that he has seen the patient in the interval between the regular 13-week periodic dates, rather than on a fixed day.—I am, etc.,

Oldham,
Lancashire.

G. LLOYD.

"Mediflash"

SIR,—The usefulness of the "Mediflash" was proved recently during the Hither Green train disaster.

Having heard the news on the radio a local doctor drove towards the scene of the accident only to find the traffic completely at a standstill and blocking his way. However, the police recognized his "Mediflash" and he was directed to pull out to the right-hand side of the road and was waved on by the police to the actual disaster area.—I am, etc.,

MARTIN F. HYATT,

Hon. Secretary,
Lewisham Division, B.M.A.
London S.E.12.

First Fellows of the Royal College of General Practitioners

SIR,—Whatever one may think of the main burden of Dr. B. I. Kohlinsky's letter about the list of new Fellows of the Royal College of General Practitioners (2 December, p. 557) his last statement demands flat repudiation, the more so because it seems to be a view held, erroneously, by many other doctors.

If these doctors had read the documents that really matter instead of the giveaway medical journals, they would have found in the Second Report¹ of Joint Discussions between General Practitioners' Representatives

and the Ministry of Health, paragraph 19: "... the Government propose that the ... recognition of ... experience and special qualifications ... should be furthered by way of additions to the basic practice allowance."

Later in the same document there is a paragraph head "Special Experience and Service to General Practice." It contains the following words: "The profession's representatives made it quite clear that no such proposal appeared in the charter and that they had no mandate to agree."

At no time did the negotiators accept the principle of merit awards. Of this anyone who has read the documents mentioned above or listened to or read the negotiators' statements on the subject can be in no doubt whatsoever.

It should be further noted that the negotiators are elected by and responsible to the G.M.S. Committee only, and through it to all general practitioners. It is notable that of the 71 new Fellows of the R.C.G.P. from the United Kingdom, only one is a member of the G.M.S. Committee and one other has recently been so.

It only remains to make the obvious point that the Royal College of General Practitioners has absolutely no power over the G.M.S.C.—I am, etc.,

Clarendon,
Warwick.

B. D. MORGAN WILLIAMS.

REFERENCE

¹ *Brit. med. J. Suppl.*, 1965, 2, 153.

Points from Letters

Nicotinic Acid in Acne

Dr. N. ISLAM (Dacca, E. Pakistan) writes: Acne vulgaris most commonly develops during puberty, a period during which people are very conscious of their appearance. . . . Various treatments have been suggested from time to time. . . . It was a chance finding that nicotinic acid is effective against this condition and I have treated 20 cases. The age range was from 15 to 35 years.

The patients who develop facial flush do better with this treatment. Initially a dose of 100 mg. thrice daily was advised. Then the patient was instructed to go on increasing the dose by 100 mg. daily till a facial or a generalized flush was observed. Subsequently it was advised to continue this "flush dose" for two to three weeks. It was interesting to note that the dose varied from patient to patient and ranged from 100 mg. to 1,000 mg. a day. Duration of treatment varied from 10 to 30 days, depending on the severity of the lesion.

Medical Science—Master or Servant?

Dr. M. S. ROSE (Experimental Haematology Research Unit, St. Mary's Hospital Medical School, London W.2) writes: Scanning the *B.M.J.* today (2 December) I wondered whether Lord Platt was disappointed at apparently evoking no controversy with the publication of his Harveian Oration (25 November, p. 439). Your editorial "Cui Bono?" (p. 433) appeared to assert that Lord Platt's views should concern us because of who he is rather than because of what he says, which was a pretty crazy way of introducing otherwise creditable comment. . . . I wonder whether the departure of so many graduates overseas and the loss of others from general subjects in medicine into ancillary fields is not in part an expression of frustration at not finding a purposeful framework in which to become involved. On graduating the vast majority are on their own. "Ars gratia artis" is fine for Metro-Goldwyn-Mayer but can hardly do credit to such an intrinsic service as medical care of the sick.

Obituary Notices

J. W. LINNELL, M.C., M.D., F.R.C.P.

Dr. J. W. Linnell, a former consulting physician to the Metropolitan Hospital and to the Mildmay Mission Hospital, London, died at his home, the Retreat, at Pavenham, Bedfordshire, on 2 December. He was 89.

John Wycliffe Linnell, a son of the Rev. J. E. Linnell, vicar of Pavenham, was born on 31 October 1878, and was educated at Bedford Modern School and St. John's College, Cambridge. For his clinical studies he went to the London Hospital, graduating M.B., B.Chir. in 1907. After house appointments he carried out research work in tuberculosis at the Hospital for Diseases of the Chest, Ventnor, Isle of Wight, at the Mount Vernon Hospital, Hampstead, and as Gibbons research student at St. George's Hospital, London. He proceeded M.D. in 1913. During the first world war he served with distinction as a regimental officer in Gallipoli, France, and Egypt, attaining the rank of major. He was awarded the Military Cross and was mentioned in dispatches. After demobilization he took the M.R.C.P. in 1921, and was appointed medical registrar at the London Hospital. Subsequently he acted as assistant to Sir James Mackenzie, and later to Sir John Parkinson in the cardiac department of the hospital. He was then appointed physician to the Metropolitan Hospital and to the Mildmay Mission Hospital, continuing on the staff of both hospitals until he reached the statutory retiring age. He also became consulting physician to the endocrine unit of New End Hospital, Hampstead. In 1940 he was elected F.R.C.P.

Dr. Linnell was chiefly interested in cardiac and pulmonary diseases, and especially in disorders of the thyroid gland. His contributions to medical literature mainly concerned these subjects. He was also co-founder of the Thyroid Club. Dr. Linnell never married but lived at Pavenham with his brother and widowed sister, both of whom predeceased him.

C. W.-D. writes: Jack Linnell was a charming personality who will be very much missed by a wide circle of friends and colleagues. He was an admirable raconteur, and it was always a pleasure to meet him both professionally and socially and enjoy his conversation. Apart from contributions to medical literature he wrote a most interesting book entitled *Old Oak*, a story of a forest Northamptonshire village. Not only in London but also in Bedford he carried on consulting practices, both of which could have been more extensive had he wished, and one could always rely on him for a sound opinion. With his kindly disposition the question of fee never seemed a matter of interest in him. During the many years we were colleagues I never heard him say a really unkind word about anybody. His recreation was mainly that of taking long walks—"tramping," as he termed it—in Switzerland and Germany, usually accompanied by his schoolmaster brother. As a result of what he saw in Germany in the 1930s he told me before the second world war that he was quite certain that the Germans were

preparing for war, and I believe he conveyed his views to the authorities concerned. He was an enthusiastic supporter of rugby football, and very seldom missed attending the Oxford and Cambridge match and the internationals at Twickenham. One must be thankful that Jack Linnell was spared to us for so long.

G. M. S. writes: With a wicked twinkle at times in his intensely blue eyes J. W. Linnell belied the austere evangelical rectory atmosphere in which he, his three brothers, and one sister had been reared. Although prepared to mock at any sign of pomposity or self-aggrandizement that crossed his path, he paid the highest tribute to integrity, to loyalty, and to devoted service whatever the cause. Many are the students, the housemen, and the registrars who breathed their thanks for help given at the right moment, for an uncanny insight into their difficulties, and an unaccountable effort to solve them. From the rectory at Pavenham, Bedfordshire, to the aptly named "Retreat" near by, the spirit built up collectively by the Linnell family permeated the neighbourhood and beyond. Visitors from London were encouraged to come for week-ends and to enjoy especially the Sunday teas which were such a feature of the Retreat for so many years. A genius for friendship, kept up by letters all over the world, contributed to the width of knowledge which illuminated discussions whenever a few congenial people met. Jack, as he was known to all his friends, was an uncompromising Christian and an ardent supporter of the Bible Society and its associations, but to his many friends he was the kindly ever-helpful physician who spared no effort to assist in any way. He always maintained that the right attitude was not "to turn the other cheek" but to "fight the good fight with all his might."

B. A. MEYER, M.B., CH.B.

Dr. B. A. Meyer, who was engaged in general practice in the West End of London, died suddenly at his home on 21 November after a long illness. He was 66.

Benjamin Arnold Meyer was born in Cape Town on 25 December 1901, and from his earliest days determined to study medicine. He won a bursary to the University of Cape Town, and from there obtained permission to take his medical course in the United Kingdom. He chose to attend Edinburgh University, and graduated M.B., Ch.B. in 1925, taking the Scottish triple qualification in the same year. After a distinguished undergraduate career he took an additional course in midwifery at the Rotunda Hospital, Dublin. He became assistant to a general practitioner in a country district in Scotland whose firm view it was that they should be able to perform all the surgery in the practice themselves. This delighted Bobby Meyer and stimulated his interest in a branch of medicine which already had a marked attraction for him. After two years he went home

to South Africa, meaning always to return to Great Britain. After five years spent in resident surgical appointments and general practice near Durban he achieved his ambition, first taking a resident post at the Royal Sussex Hospital in Brighton, and then a partnership in general practice in the same town. He subsequently set up practice on his own account in Streatham, and then in central London, keeping alive his interest in surgery with clinical assistantships and for a period a part-time surgical registrarship at the National Temperance Hospital. He revisited South Africa many times to stay with his relations and his many friends there.

Bobby Meyer was a man of great kindness and personal charm. He knew life, and loved it. These qualities, together with his wide medical experience, made him the ideal general practitioner and family physician. He had other gifts besides—a powerful memory, a facility for friendship, and a sense of humour which was characteristically evident to the day of his death. He was a fascinating raconteur, and among other achievements he wrote a play for radio which was performed a few years ago.

The passing of Bobby Meyer is mourned alike by his patients, colleagues, and friends. His devoted wife, his son, and two daughters provided a background of complete happiness and pleasure for him, and we extend our deep sympathy to them.—S. M.-D.

N. J. NICHOLSON, M.B., CH.B.

F.R.C.S.ED., F.I.C.S.

Mr. N. J. Nicholson, emeritus surgeon, County Hospital, Louth, died at his home on 30 October. He was 65.

Neville Jennings Nicholson was born on 13 November 1901, and received his early education at Durham School. He entered the University of Edinburgh, and graduated M.B., Ch.B. in 1927. Keen on rowing and football, he was captain of both boats and rugby football in 1920 at Durham School, later rowing for Edinburgh University as well as being a member of the university rugby team. After holding early resident appointments he took the F.R.C.S.ED. in 1935, and from 1936 to 1938 he was surgeon and deputy superintendent of the Municipal Hospital at Birkenhead. In December 1937 he was appointed surgeon and superintendent of the newly opened County Hospital at Louth. He was active in building up the new hospital, which played an important part in the second world war in providing a treatment centre for large numbers of Service men. On his retirement in 1966 he was given the title of emeritus surgeon. He was also surgeon to Alford, Skegness, and Louth district hospitals.

Mr. Nicholson was a former chairman of the Lincoln Medical Society, a member of the British Medical Association, and chairman of the Grimsby Division in 1957-8. He had been a member of Louth Borough Council for eleven years, and was mayor of Louth in 1963.

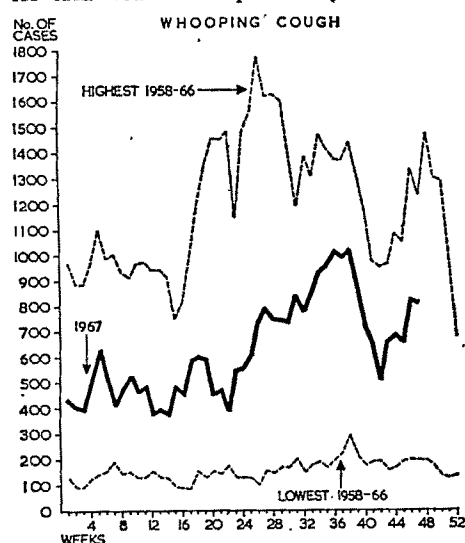
He married in 1939, and had a son and four daughters.

News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graph below shows the uncorrected number of cases of whooping-cough in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

		Week Ending	
		24 Nov.	1 Dec.
Dysentery			
Berkshire	...	17	15
Wokingham R.D.	...	15	13
Durham	...	20	53
Blaydon U.D.	...	7	29
Essex	...	11	16
Braintree R.D.	...	0	11
Greater London	...	34	58
Ealing	...	5	15
Redbridge	...	12	11
Hampshire	...	22	17
Portsmouth C.B.	...	22	15
Lancashire	...	55	103
Liverpool C.B.	...	5	13
Manchester C.B.	...	0	11
Ashton-under-Lyne M.B.	...	3	26
Irlam U.D.	...	22	15
Worsley U.D.	...	2	10
Warwickshire	...	101	111
Coventry C.B.	...	84	99
Yorkshire West Riding	...	60	38

		Week Ending	
		24 Nov.	1 Dec.
Dysentery (contd.)			
Leeds C.B.	...	19	11
Sheffield C.B.	...	17	11
Glasgow	...	45	59
Edinburgh	...	29	17

Diphtheria

Manchester C.B.	...	1	3
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Food-poisoning

Greater London	...	31	25
Lancashire	...	14	25
Liverpool C.B.	...	0	11
Yorkshire West Riding	...	9	27
Glasgow	...	2	13

Blind People in Scotland

Last year the number of registered blind people in Scotland fell by 46 to 10,341, according to the Scottish Home and Health Department. Of this total 52% were aged 70 or over.

New registrations during 1966 totalled 1,271. Of these, 66% were over 70, while 20 persons were children under 16, six being under 5 and one under 2.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 25 November (No. 47) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	1	0	0	0		1	0	0	0	
Dysentery ..	407	34	100	2	4	458	68	159	7	3
Encephalitis, acute ..	2	0		0		1	1		0	
Enteric fever: Typhoid ..	1	0	0	0	2	3	2	0	0	
Paratyphoid ..	4	2	0	0	0	3	1	0	0	
Food-poisoning	91	31	11	3		126	22	18	1	
Infective enteritis or diarrhoea under 2 years				33	42				23	52
Measles*	1,271	47	32	12	92	11,581	1727	496	206	76
Meningococcal infection ..	7	1	1	2		9	2	1	2	
Ophthalmia neonatorum ..	5	0	1	0		13	0	0	0	
Pneumonia† ..	141	10	111	4	4	137	30	108	9	2
Poliomyelitis, acute: Paralytic ..	0	0	0	0		3	0	0	0	
Non-paralytic ..	0	0	0	0		0	0	0	0	
Puerperal fever§	67	18	1	1		95	48	2	0	
Scarlet fever ..	398	50	28	14	13	441	72	38	11	13
Tuberculosis: Respiratory ..	181	36	29	7		242	55	46	4	
Non-respiratory ..	38	0	0	2		34	6	7	0	
Whooping-cough	817	95	38	12	62	621	91	80	5	19
DEATHS	1967					1966				
	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute ..				0						0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	1	0	0	2	7	2	1	0	1
Influenza ..	13	3	0	1	0	9	2	2	0	1
Measles ..	0		0	0	0	0		0	0	1
Meningococcal infection ..			1					0		
Pneumonia ..	831	131	20	12	14	784	131	26	20	6
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	39	5	3	1	1	32	7	1	0	0
Non-respiratory ..				0	0				0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	297	57	18	9	17	270	48	19	7	8
Deaths (excluding stillbirths)	11,337	1765	556	141	213	10,902	1797	609	135	189
LIVE BIRTHS	14,565	2427	801	256	490	14,933	2572	916	259	389
STILLBIRTHS	245	42	15			244	29	21		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.

PARLIAMENT

Qualified Support for Health Services Bill

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The second reading of the Health Services and Public Health Bill on 7 December produced no significant opposition, but much questioning of the intentions of the Minister of Health in exercising the powers the Bill gives him. This will be carried further during the committee stage after the Christmas recess, and will examine more closely several sections of the Bill which received only preliminary attention. These include, for example, executive council powers to supply goods to doctors and others, and the health and welfare work of local authorities; also policy towards pay-beds and private practice. (See *B.M.J.*, 2 December, p. 562.)

This Bill is concerned mostly with subsidiary changes in the administrative structure of the Health Service. Major changes must await the full examination which the Minister has begun, and on which he is to publish in due course some tentative proposals.

No Reduction in Pay-beds

Mr. KENNETH ROBINSON began his exposition of the Bill by explaining that the purpose of Clauses 1 and 2, which had aroused some misunderstanding, was not to reduce or abolish the number of pay-beds. The main changes, which followed the review of pay-beds he announced a month ago, were to introduce a degree of flexibility in the use of accommodation by private patients, and to enable charges to be determined on a national basis for different classes of hospitals, instead of by reference to the cost at the particular hospital. The Bill also enabled him to dispense with regulations in determining charges for private outpatients, and for amenity beds. Apart from this the clauses merely repeated provisions which had been in force nearly 20 years.

To those Labour M.P.s who disliked private practice on principle he gave an assurance that he had no intention of using these powers to extend the area of private practice in hospitals. He equally assured the medical profession that the clauses did not enable the Minister to abolish their right to treat private patients, nor was this his intention. But the powers would, he believed, make possible a more rational use of all hospital beds, public and private.

University Hospitals

The most significant administrative change, he thought, was the power taken in Clause 5 for a new designation of hospitals—"university hospitals."

The Government had approved the creation of medical centres at the Universities of Nottingham and Southampton. At both places facilities for clinical training would be needed in hospitals which did not now provide them. The creation of new medical schools provided an opportunity to link more closely the regional boards with the new centres of medical education. The universities, however, should be assured of a voice in

the planning and administration of such hospitals, and that was not provided for in the normal constitution of management committees.

Clause 5 required him to consult the university concerned before designating a university hospital. Such a hospital would be managed by a management committee appointed by the regional board, but with a special constitution which would ensure that the university had adequate representation.

The clause was not confined to hospitals associated with new medical schools. It would also give latitude in devising suitable administrative arrangements where, to accommodate larger numbers of students, a second main hospital was to share the responsibility with the existing teaching hospital. It was not the present intention, he stated, to use the clause to effect sweeping changes in the administration of teaching hospitals already controlled by boards of governors.

Ophthalmic Services

Dealing with the provisions affecting executive council services, the Minister said the hospital ophthalmic clinics had not developed along the lines envisaged in 1946. Instead, the hospital eye service had in the main dealt with the more specialized requirements, while the supplementary ophthalmic services, far from becoming redundant in any area, had been the normal means under the Health Service of meeting the ordinary optical needs of the population. The Bill recognized this by making the services permanent and renaming them "general ophthalmic services." The membership of the executive councils was being altered to reflect the three groups of practitioners involved—ophthalmic medical practitioners, ophthalmic opticians, and dispensing opticians.

Practice at Health Centres

Originally only National Health services were to be provided in health centres, but since 1949 doctors had been able to practise privately there, and this had made some health centres more attractive to doctors and patients alike. There would be localities where similar extensions to the other services provided in health centres could be beneficial to patients attending them, and the Bill made it possible for dentists, opticians, and pharmacists to engage in private practice at health centres to such an extent and subject to such conditions as the Minister might determine.

He also had proposals to improve the arrangements which could be made for the postgraduate education of family doctors, dentists, pharmaceutical chemists, and opticians concerned with providing family practitioner services. Clause 25 accordingly conferred somewhat wider powers than those in section 48 of the 1946 Act. It would not only apply to those who were actually engaged in family practitioner services but also to those who were thinking of doing so, and would enable a wider range of instruction to be given.

Inadequate Consultation

Mr. MAURICE MACMILLAN, the Conservative spokesman on health legislation, assured the Minister that there was no intention on their part to delay or obstruct the passage of the Bill, but he pressed for time for full consultations before the committee stage. Some of the bodies concerned had informed him that there had been no consultation prior to the publication of the Bill, and were unaware only a month or two ago of any possibility of legislation affecting them being brought forward.

Mr. ROBINSON asked him to be more specific, because there had been extensive consultations over "vast areas" of the Bill. If there had been a particular failure to consult he would like to know about it, and would express his regret if it was so.

Mr. MACMILLAN replied that both the doctors and the pharmacists had publicly stated that they had not been fully consulted. The fact that there had been such widespread misgivings over pay-beds and the clauses dealing with the manufacture and supply of drugs was an indication that consultation was not sufficient.

He asked for an assurance, on rising costs, that the Minister would not economize simply where economies were easy. There was a danger that economies were effected at the expense of freedom of choice of treatment and might militate against the use of prophylactic drugs.

Private Practice

The clauses on pay-beds would require time for consultation. The Opposition were glad of the Minister's assurances, and accepted that the Bill was neutral in its approach to private practice. But he asked what effect this greater flexibility would have on waiting-lists, and how adjustments would be made now that beds were not to be designated. It was important that there should be no question of private patients jumping the queue, and equally that there should be no question of their being prejudiced, or of the Bill being so administered as to lessen the freedom of choice of the consultant and militate against part-time consultants. They would be asking the same sort of questions about charges. It was obviously sensible that charges should be regularized according to the nature of the care provided. It was equally obvious that the Minister could price the private patient out of the market, although, Mr. Macmillan added, he was not saying that he wished to do so.

He indicated that while the Opposition welcomed Clause 5 they would be happier if it was so drafted as to indicate that it was experimental and subject to review, and that they would like some assurance about the future of teaching hospitals and about the use of funds to initiate work or research not being undertaken by regional boards.

Occupational Health Service

Mr. K. LOMAS (Huddersfield, West, Lab.), having deplored the omission of provision for an occupational health service, went on to voice what he called the deep-rooted suspicion

of pay-beds, not solely confined to Labour Party supporters, and to demand a still further reduction in their number, the adoption of a salaried service, and the abolition of the part-time consultant.

Dr. M. S. MILLER (Glasgow, Kelvingrove, Lab.), a practising doctor until recently, regretted that 20 years after the inauguration of the Health Service the family doctor system was still based on the concepts of the 1920s or even earlier. He was worried that the nation was not making proper use of its 23,000 general practitioners. The family doctor, working from a health centre, should be the head of a health team in which he carried out the highly skilled work and the clerical and less highly skilled routine was carried out by ancillary staff.

Dr. M. P. WINSTANLEY (Cheadle), who speaks for the Liberal Party in these debates, fully endorsed the idea of the general practitioner as the leader of a welfare team. If the Minister put more emphasis on the clauses dealing with health centres and facilities he would find the doctors would stay in Britain. Postgraduate education was another means of keeping doctors here.

Dr. J. DUNWOODY (Falmouth and Camborne, Lab.) said he had been opposed to private practice since he was a medical student; it was morally indefensible and medically inefficient. Unoccupied private beds in hospitals should be used for Health Service patients. He welcomed the fact that more attention was to be paid to postgraduate medical education. There was a great need for this. The average doctor would during his working life see a complete transformation in the medical scene, and the need for regular refresher courses was increasing.

Lack of Confidence

Mr. P. GRIEVE (Solihull, Con.) asserted that there was a great lack of confidence

between the medical profession and the Minister. It was the use that the Minister would make of the new flexibility that worried the doctors. He quoted the reported remarks of Mr. Robinson's Bloch Lecture at Glasgow University the previous day, and commented that if there was an impression of antagonism between the Minister and representatives of the profession the fault was not all on one side, but lay very much with him.

He went on to argue that the new flexibility must be properly used, and that the demand for private practice was increasing, not decreasing.

Dr. DAVID KERR (Wandsworth, Central, Lab.) interjected, "Shame," and explained: "I do not deny the patient the right to private treatment. What I cry shame about is that there is thought to be a need for an extension of private practice, and that there should be an attempt to justify it as the kind of practice that ought to be followed. I think it should diminish, as the kind of practice that ought not to be followed."

Mr. GRIEVE replied that people were entitled to go to their own doctor and pay him if they wished. This was recognized in the Health Service Act. The complaint was that the Minister had been whittling it away.

Mr. ROBINSON here intervened, to state that over 18 months ago he discussed with the leaders of hospital doctors a package deal in connexion with pay-beds. There were features they liked, and features they did not like. They acquiesced in the total package, and part of it was that he would review the total numbers of pay-beds to adjust the pressure on them to something like the pressure on non-pay beds.

"Another part of the package," he continued, "was to do what no Conservative Minister was ever willing to do. I lifted completely the ceiling on fees which private consultants could earn from private patients in Health Service hospitals. You might take

the whole package together, instead of one aspect of which you complain."

Mr. GRIEVE said the aspect he was taking concerned the availability of something for which there was a demand. The figures of B.U.P.A. for insurance for private medicine spoke for themselves. At Glasgow the Minister sought to draw a contrast between representatives of the profession whom he criticized and the younger doctors. Was it the middle-aged or the elderly who had been emigrating? The answer to the Minister's completely false point lay in the emigration of thousands of young doctors who were not prepared to work in the Service under the conditions imposed by the Minister.

For the Record

In a short survey of progress in the Health Service which the Minister gave as a prelude to the debate he claimed that the new deal for general practice, in spite of setbacks resulting from the prices and incomes policy, had been fully in operation since last April, and he believed they had turned the corner.

There had been a remarkable upsurge of interest in health centres; 23 had been opened in the past three years, 38 were being built, 50 more had been approved, and 71 were being actively planned.

There was an intake of 2,431 students in the medical schools this autumn term. By 1970 the total would have risen to an estimated 2,800.

This year no less than £100 million would be spent on new hospital building in Great Britain. During the Government's three complete years in office the total would be £262 million.

In 1966 the number of hospital inpatients was nearly 4,900,000, a rise of almost 1,500,000 over 1953, the earliest year for which there were reliable figures.

MEDICAL NEWS

Emeritus Professors

The title of Professor Emeritus in respect to their posts has been conferred on the following:

Professor C. P. BEATTIE, Professor of Bacteriology at Sheffield University since 1946.

Professor E. STENGEL, Professor of Psychiatry at Sheffield University since 1956.

Professor J. M. YOFFEY, Professor of Anatomy at Bristol University since 1941.

Medical Research in Scotland

The Scottish Hospital Endowments Research Trust has made a grant of £11,730 over three years to Mr. J. HUGHES, University of Strathclyde, for research into body-powered lower limb prostheses. Others to receive support for projects are: Dr. H. W. SUTHERLAND, Aberdeen University, intravenous tolerance tests, £1,156 for one year in the first instance; and Professor L. L. ENGEL, Macfarlane Chair of Experimental Medicine, Glasgow University, biochemistry of endocrine neoplasms, £2,000.

Study of Insect Carriers

A new centre for the study of insect carriers of tropical diseases is to be built. It will be the headquarters of the Government's service for this study. The Ministry of Overseas Development has made a grant of £45,000 to cover the cost of the building and the work of the service over the next three years. Until recently the work was done at the Lister Institute of Preventive Medicine, Elstree. The new centre will be at the Imperial College of Science's Field Station, Silwood Park, near Ascot.

U.S. Immigration Policy

The American Embassy in London confirmed last week that it would become increasingly difficult for a British graduate to obtain an immigrant's visa. Referring to the new immigration laws, which come into effect on 1 July next, the spokesman said: "Anyone who has not filed a petition at least three months before 30 June will probably have to wait two to three years. It will be a case of first come, first served, based on the date on which a petition is filed."

Under the new amendments the present system of national quotas is replaced by a

world-wide system of "preference categories." Medical graduates are in the third category, which includes members of the professions and people with exceptional skills. The number of immigrants entering the United States from this category would be 17,000 each year.

Maccabean Prize and Medal

Entries for the 1968 Maccabean Prize (25 guineas) and Medal are invited for an essay of 5,000 to 7,000 words on some aspect of the history of medicine or pharmacy. Candidates must be under 30 years of age on 15 March 1968. Further details can be obtained from Dr. F. N. L. POYNTER, Wellcome Historical Medical Library, Wellcome Building, Euston Road, London N.W.1.

James Mackenzie Prize 1967

Dr. M. B. CLYNE, Southall, Middlesex, has been awarded the James Mackenzie Prize 1967 in recognition of his studies of diseases common in practice and of present-day conditions of general practice and the operational problems facing the family doctor. Dr. Clyne is the third recipient of this prize.

New Chair at Dundee

Dr. P. D. GRIFFITHS has been appointed to the new chair of clinical chemistry at the University of Dundee. He is at present the senior lecturer in the department. Dr. Griffiths, who is 40, was educated at Guy's Hospital Medical School. He graduated B.Sc. in physiology with first-class honours in 1953, and proceeded to M.B., B.S. in 1956. Following house appointments at Guy's and New Cross General Hospital he entered the department of physiology at Guy's, and later moved to the department of clinical pathology. He was appointed a consultant pathologist to the Harlow Group of Hospitals in 1964, and took up his present post in Dundee last year. He holds the M.D. (Lond.) and is a member of the College of Pathologists. His research interests include muscle enzymology, genetics, and the medical uses of computers.

**Career in Hospital Administration**

Opportunities for training in hospital administration are announced by the Ministry of Health. Details and forms of application can be obtained from the National Staff Committee, 16-19 Gresse Street, London W.1; in Scotland from the Scottish Hospital Administrative Staffs Committee, Woodburn House, Canaan Lane, Edinburgh 10.

Medical Directory for Nigeria

The *Nigerian Medical Directory 1967-8* provides lists of doctors, dentists, and opticians throughout the Federal Republic. It also records hospitals, medical schools, and drug and equipment centres. A feature is a symposium, "Progress in Medicine," which describes advances made in the specialties during the year. The editor is Dr. V. O. AWOSIKA, whose address is P.O. Box 70, Ikeja, Nigeria.

People in the News

► Professor MICHAEL ABERCROMBIE, F.R.S., has been appointed to succeed DAME HONOR FELL, F.R.S., as director of the Strangeways Research Laboratory, Cambridge.

► Professor L. VANDENDRIESSCHE, professor of the faculty of medicine of the University of Ghent, has been appointed Belgian visiting professor for the session 1967-8. He will work in the biochemistry department at University College, London.

► Professor H. ORISHEJOLOMI THOMAS has been appointed provost of the College of Medicine, University of Lagos, Nigeria.

► Dr. MERVYN GOTSMAN has been appointed to the chair of cardiology at the University of Natal in Durban.

Grants and Awards

Professor J. A. ROPER, of Sheffield University, has received a grant of £3,218 from the Medical Research Council for research into genetic instability.

The Wellcome Trust is to make a grant of £2,200 to the physiology department at Univer-

sity College, Dublin, in support of special studies into the action of the heart.

Recent Publications

Notes on the Law Relating to Experiments on Animals in Great Britain (third edition) issued by the Research Defence Society, 11 Chandos Street, London W.1, 1s. 6d.

The *B.S. Yearbook for 1967* provides a reference to all British standards published up to 31 December 1966 (15s.). It forms a companion volume to the *Annual Report*, which covers the period 1 April 1966 to 31 March 1967 (10s.). British Standards Institution, 2 Park Street, London W.1.

Coming Events

Institute of Diseases of the Chest.—Clinical demonstrations, open to medical practitioners without fee, will be held in the Lecture Theatre of the Institute (in the grounds of the Brompton Hospital, Fulham Road, London S.W.3) on Fridays at 5 p.m. from 12 January to 15 March inclusive.

King Edward's Hospital Fund for London.—Conference, "Hospital Bed Usage," 16 January, Hospital Centre, 24 Nutford Place, London W.1. Fee £1. Completed application forms by 5 January. This conference is the third of a series of three on making better use of hospital resources.

International Union Against Cancer and Swiss Cancer League.—Conference on thyroid cancer, 8-10 May 1968, Lausanne. Details from Professor G. CANDARDJIS, Institut Universitaire de Radiologie Médicale, Hôpital Cantonal, 1005 Lausanne, Switzerland.

18th Congress of the International Association for Bronchial Studies.—13-16 June, Uppsala, Sweden. Details from Congressus Bronchologicus, Lungkliniken, Akademiska sjukhuset, Uppsala 14, Sweden.

1st International Symposium on Metabolism and Membrane Permeability of Erythrocytes and Thrombocytes.—17-20 June 1968, Vienna. Details from the Secretariat, Wiener Medizinische Akademie, Stadiongasse 6-8, 1010 Vienna, Austria.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 18 December

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., combined staff consultation clinical meeting.

MANCHESTER MEDICAL SOCIETY: SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Manchester University Medical School, 9 p.m., Dr. L. Watt: Control of Venereal Infection.

Tuesday, 19 December

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. R. H. Franklin: Hiatus Hernia.

Wednesday, 20 December

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

WHITTINGTON HOSPITAL.—At Academic Centre, Archway Wing, London N., 11.30 a.m., Professor T. A. J. Prankerd: Haemorrhagic Diseases and their Treatment.

Universities and Colleges**LONDON**

Dr. S. Gnessen has been nominated for appointment or reappointment as a representative of the university on the governing body of Dalston and Mount Pleasant Secondary Schools.

SHEFFIELD

Appointment.—Dr. K. G. Wormsley (senior lecturer in the Department of Surgery with the title of senior lecturer in gastroenterology).

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

On 4 December the following were admitted Fellows *qua* Physician:

J. W. Affleck, T. B. Begg, I. A. Boyd, W. I. Card, A. Dunn, W. S. Gardner, B. R. Hillis, J. G. P. Hutchison, K. G. Lowe, A. Lyell, G. P. McNicol, M. W. McNicol, W. A. Parker, D. A. Seaton, J. Smith, J. MacL. Smith, M. B. Urs, R. S. Walker, D. H. Wallace, W. G. Whyte, G. Will, G. M. Wilson, R. B. Wilson.

Members *qua* Physician:

C. S. Cheung, D. L. Davies, A. I. E. Bey, M. E. E. Sarraj, J. B. Familul, P. K. Ghatak, A. K. M. B. Karim, C. K. Narain, K. A. Paulsen, F. M. Pope, T. H. Sia.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

At a meeting of the College held on 1 December, with the President, Professor Alan Thompson, in the chair, the following were admitted to the Membership:

R. A. Erinjery, R. S. Matthews, M. X. M. MacGeralt, J. A. O'Sullivan, J. J. Robb.

The following candidates were admitted to the Licence in Medicine and Obstetrics:

R. Bhaggeerutty, R. W. Charles G. A. J. Fernandes, H. Govind, E. E. Hansrod, E. O. E. Isong, A. H. M. Jiwan, M. J. Khetani, S.-L. Lau, M. A. Molake, L. A. Mosuro, D. K. Naidoo, A. O. Ogunola, B. M. Sandy.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council held on 25 November the following awards were made for 1968: *Edgar Gentili prize*, Dr. R. A. Diamond (Oxford); *William Blair-Bell Memorial lecture-ship*, Dr. R. J. Hunter (Belfast); *Eden Fellowship in obstetrics and gynaecology*, Dr. Mary G. Coyle (Dundee).

The following were admitted to the Membership *in absentia*:

K. H. Atkinson, G. C. Bird, L. J. H. Butterfield, G. J. Dennerstein, J. A. Hill, S. G. Kovacs, R. Lawrence, J. Ludlow, R. Luthra, P. N. McGuire, P. M. Renou, D. M. Saunders, J. E. Scott, A. Singer.

Notice to Authors

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 23 DECEMBER 1967

Pointers

Urinary Bacteriology in Children: Standards suggested for cell and bacteria counts for diagnosis of clinically unrecognized urinary tract infection in childhood, using plastic bag and midstream specimen methods of collection (p. 697). Accuracy of diagnosis with methods of collection just described compares favourably with catheter specimens when aforementioned criteria are used (p. 702). "Clean catch" method for neonates appears to be a reliable method of sampling (p. 705). Leader at p. 691.

Contraception and Anaemia: Compared with a control group and group using intrauterine devices, women taking the "pill" had on the average higher haemoglobin and haematocrit levels. Increased blood viscosity may be related to thrombotic phenomena (p. 708).

Emotion and Ileitis: Nineteen patients with regional ileitis did not show the emotional factors usually considered to be related to psychosomatic illness (p. 711).

Community Health Screening: Evaluation of survey undertaken to assess anaemia in non-pregnant women indicated that high-risk groups are unlikely to attend selectively to any large extent (p. 714).

Criterion of Fibrinolysis: Test for estimating fibrin degradation products in serum showed a measurable level of these in majority of a group of apparently healthy subjects (p. 718).

Case Reports: Malignant tumour of brown fat in Turner's syndrome (p. 720). Mumps nephritis (p. 721).

Haematemesis: Diagnosis and management of bleeding from the upper gastrointestinal tract (p. 723).

Today's Drugs: Epsilon aminocaproic acid (p. 725).

Peritoneal Dialysis: Sterilization of dialysate by filtration (p. 728).

Metabolic Studies: Special cot for newborn infants described (p. 729).

"The Queen's": Queen Elizabeth Hospital for Children (London) celebrates its 100th anniversary (p. 733).

Renal Disease: R.C.P.'s views on training of specialists (p. 735).

Teaching in General Practice: Aims and methods discussed at conference (p. 736).

Computers: B.M.A. symposium on use of mathematics in medicine (p. 737).

Test Your Knowledge: Christmas quiz at p. 740.

G.M.S. Committee: Minister's intentions on pay-beds discussed (*Supplement*, p. 81).

Diagnosis of Pyelonephritis in Children

Pyelonephritis is a potentially serious condition in childhood, the diagnosis is apt to be missed, and delay in reaching it can be harmful.^{1 2} In infants and small children it is rare to find symptoms which point directly to its diagnosis. Therefore microscopy and culture of the urine should always be undertaken when there is no obvious explanation for their illness.

It is generally accepted that a diagnosis of pyelonephritis should be based on the finding of an increase of both leucocytes and living pathogenic bacteria in the urine. But the situation is not so simple. For example, though an excess of leucocytes may be found in the urine in acute nephritis, a significant number of pathogenic bacteria may occur in genuine pyelonephritis without an increase in the number of leucocytes. Interpretation of the cell count may be difficult if the urine contains large numbers of epithelial cells: the small cells from the tubular epithelium are often particularly difficult to distinguish from leucocytes unless special stains are used. Moreover, the bacteriologist must decide whether the growth of organisms is due to contamination or a genuine infection.

As a routine method of obtaining urine for cell count and culture, catheterization has been abandoned and the mid-stream or "clean-catch" specimen is generally used in adults and older children. But for infants and young children who cannot pass their urine to order other methods have to be used. In some centres percutaneous aspiration of the full bladder is done on newborn babies to obtain an uncontaminated specimen, but this technique has not found universal acceptance. In Britain most paediatricians use a plastic urine-collecting bag. An additional complication in the neonatal period is that during the first week of life there is a higher proportion of epithelial cells from the renal tubules in the urine than at any other time of life. Consequently it is not possible to use as standards of normal the results obtained for older children or adults.

In the *B.M.J.* this week three papers from Edinburgh describe attempts to define acceptable limits of normal for cell and bacterial counts at various ages and by different methods of collection. Dr. Gillian Cruickshank and Dr. Elizabeth Edmond (page 705) studied the cell and bacterial counts of midstream specimens of urine taken from a group of infants during the first week of life. There was little difference between the males and females except that in the females the number of squamous epithelial cells was higher than in the males. The excretion of renal tubular epithelial cells was highest on the first day and fell gradually until the sixth day. By using a special peroxidase stain³ these cells could be easily distinguished from leucocytes. Their results suggest that bacterial counts fewer than 10^5 organisms per ml. are usually due to contamination when a count of more than 10^5 is obtained the examination should be repeated on one or more occasions. Of the cell counts, 96% of fewer than 10 leucocytes per cu. mm. in uncentrifuged urine. The

gations may be used as a standard against which other methods can be assessed, but it seems unlikely that the individually supervised midstream specimen, as collected in this study, is suitable for routine purposes.

In another paper in this issue (page 697) Dr. H. Braude, Professor J. O. Forfar, Dr. J. C. Gould, and Dr. J. W. McLeod have examined cell and bacterial counts in a large series of normal infants and children, from the newborn up to the age of 14 years. They compared the results obtained using the adhesive plastic bag and taking a mid-stream specimen; and these two groups were further subdivided into those in which the skin received simple cleansing without antiseptics or antibiotics and those in which the skin was not cleansed. In every age group the cell count was higher in the female than the male, irrespective of the method of collection. In the females the bag specimens gave considerably higher cell counts than did the midstream urines, and it would seem that many of the cells counted as leucocytes were actually epithelial cells or possibly leucocytes derived from the urethra or vulva. The bacterial counts did not show a great difference between the males and females at any age. An important observation was that bacterial counts were higher

in those specimens collected after skin preparation than when no preparation was used. The bag specimens gave higher bacterial counts than the midstream urines. In another paper the same group (page 702) report using a slightly different approach by comparing paired catheter and non-catheter specimens in children suspected on clinical grounds of having pyelonephritis. A special technique of catheterization was used, similar to that described by J. W. McLeod and colleagues⁴ in paraplegics. They showed that the risk of a false positive diagnosis with the non-catheter specimens (plastic bag or midstream specimens) was much reduced by making a suitable adjustment to the limits of normal for cell and bacterial counts.

These data can now be used as a basis for reporting quantitatively cell and bacterial counts in infants and young children in the same manner as has become accepted practice in adults.

¹ Smellie, J. M., Hodson, C. J., Edwards, D., and Normand, I. C. S., *Brit. med. J.*, 1964, 2, 1222.

² *Ibid.*, 1964, 2, 1215.

³ Prescott, L. F., and Brodie, D. E., *Lancet*, 1964, 2, 940.

⁴ McLeod, J. W., Mason, J. M., and Pilley, A. A., *ibid.*, 1963, 1, 292.

Substitutes for the Mitral Valve

Mitral incompetence is a clinical entity, but the variation in anatomical deformity found by the cardiac surgeon has prevented a uniform surgical solution. When mitral incompetence is due to destruction of tissue by subacute bacterial endocarditis or rupture of the chordae tendineae tethering the cusp edges the leaflets of the mitral valve remain relatively supple. This type of deformity is correctable by a plastic procedure such as plication of the cusps, narrowing the valve ring, or adding pericardial patches to deficient leaflets. Rheumatic mitral incompetence, though sometimes associated with supple leaflets, more commonly is due to rigid, fibrotic, or calcified cusps, and it can be corrected only by replacement of the entire valve mechanism.

Prosthetic valves of many types have been used for replacement of the mitral valve, but the only models to stand the test of time have been those embodying a ball or disc (Starr, Kay-Shiley) moving freely in a metal cage in systole and diastole. Relief of incompetence is immediate and the operative mortality is now low, but the incidence of thrombosis on the valve with embolism of fragments has been a continuing problem, and every patient has to have anticoagulant treatment with all its attendant complications. Thrombosis is known to begin where the metal parts of the prosthetic valve join the cloth ring that is used for stitching the valve into the heart. One development has been to cover all the metal with a plastic velour cloth, which becomes coated with endothelium and reduces the incidence of thrombosis and embolism dramatically.¹ The second approach has been to avoid metal cages altogether by replacing the destroyed mitral valve with a graft of human or animal valve. The technical problems of transplantation of a mitral valve from a cadaver into the mitral ring of a patient can be surmounted, but rejection of the homograft causes erosion and rupture of the chordae tendineae.²

The aortic valve has no chordae to rupture and attention has turned to inserting cadaver aortic valves upside down into the mitral area. The problem of maintaining the correct tension on the cusps has been solved by surrounding the homograft valve with a rigid or semi-rigid cloth framework and allowing it to project into the left atrium rather than into the ventricle. Homograft aortic valves from cadavers, however, are not easy to obtain and are always smaller than the dilated mitral valve rings into which they are to be inserted. These two objections do not apply to heterograft aortic valves from pigs and calves, and it has been shown by G. H. Wooler and his colleagues in Leeds that these can be used clinically with a low operative mortality and satisfactory maintenance of competence at the present interval of follow-up.³

Enthusiasm for putting human and animal aortic valves into the mitral ring has been stimulated by their successful insertion into the aortic area by D. N. Ross, B. G. Barratt-Boyes, J. P. Binet, and A. J. Gunning.⁴⁻⁷ This enthusiasm has been tempered by recollection of the history of homograft and heterograft replacement of the abdominal aorta, which had to be abandoned because of the frequency with which the grafts calcified and ruptured. Hopes that aortic valves would not behave similarly have been based on the fact that valve cusps are nourished from the blood stream and do not become infiltrated by the host tissue—like that which invades the dead aortic wall and becomes calcified. Longer term

¹ Braunwald, N., delivered at American Association for Thoracic Surgery, New York, 1967.

² Ross, D. N., *Lancet*, 1967, 2, 956.

³ Ionescu, M. I., Wooler, G. H., Smith, D. R., and Grimshaw, V. A., *Thorax*, 1967, 22, 305.

⁴ Ross, D. N., *Lancet*, 1962, 2, 487.

⁵ Barratt-Boyes, B. G., *Brit. J. Surg.*, 1965, 52, 847.

⁶ Binet, J. P., Duran, C. G., Carpenter, A., and Langlois, J., *Lancet*, 1965, 2, 1275.

⁷ Duran, C. G., and Gunning, A. J., *ibid.*, 1962, 2, 488.

⁸ Gunning, A. J., personal communication, 1967.

follow-up, however, suggests that history may be repeated; Ross and Gunning have now reported calcification extending from the aortic wall on to the valve cusps, producing stenosis of the graft.^{2,8} The present incidence of thrombosis and embolism associated with prosthetic valves may, it seems, be being avoided only at the cost of eventual stenosis of a graft.

A further development in this field is the use by Ross of the patient's own pulmonary valve to replace his destroyed mitral valve.² Such an autograft should persist as living tissue and so avoid the hazard of eventual calcification. The problem then becomes how best to replace the excised pulmonary valve.

It is not easy for a cardiac surgeon to decide which of the artificial mitral valves he should use today, and this explains his reluctance to advise mitral valve replacement unless the patient's disability is severe. Time will probably narrow his choice of valve to an improved prosthesis or a pulmonary autograft.

Amines and Migraine

Like its predecessor,¹ the second migraine symposium, which was held in London on 24 November, was a useful review both of the clinical and of the biochemical and pharmacological aspects of the condition. Once again the role of amines in migraine was one of the principal topics discussed. Tyramine and dopamine, which are present in certain foods, were reported to be able to induce severe headaches in patients taking monoamine oxidase inhibitors.²⁻⁴ Moreover, it was pointed out that many patients with migraine exclude from their diet foods such as chocolate and cheese, which contain varying amounts of tyramine and other amines. Patients who were apt to develop migraine if they ate these foods had been shown⁵ to develop a migrainous headache within 24 hours if given tyramine by mouth. Normally tyramine is prevented from gaining access to the general circulation by the action of monoamine oxidase in the gut and the liver. Hence a possible explanation for the production of migraine by dietary factors might be a relative lack of monoamine oxidase in these sites. There is no evidence of this, however, and histochemical staining of temporal artery biopsy specimens in an attack of migraine show a normal content of monoamine oxidase in the vascular wall.⁶ On the other hand, in-vitro studies on the adventitial layer of temporal artery taken from patients during an attack of migraine have shown a greater uptake of catecholamines than with temporal artery

removed from other patients undergoing craniotomy for cerebral tumours.

When catecholamines and ergotamines are added to human cerebral arterioles removed at craniotomy there is no response, though when either of these agents is added to somatic arterioles definite vasoconstriction occurs. This finding does not support the accepted idea that the aura of migraine is due to ischaemia as a result of vasoconstriction⁷—unless vasoconstriction is a property of migrainous cerebral arterioles and not of normal ones. The therapeutic effect of ergotamine, however, is still thought to be due to its vasoconstrictor activity on the extracranial arteries,⁸ and the development of new compounds for the treatment of migraine is based on their in-vitro effects on blood vessels. Other important properties of any new drug are that its effects on non-vascular smooth muscle, such as the uterus, should be minimal and that it should not induce nausea.⁹

The relationship of migraine to menstruation and to pregnancy suggests that hormones may also play a part in the condition, directly or indirectly. The results of treatment with oestrogens have been disappointing,¹⁰⁻¹² and androgenic steroids have also been unsuccessful.¹²⁻¹⁶ Parenteral injections of progestogens are sometimes more effective, though the effect is of short duration. Giving progestogens by mouth, on the other hand, has had disappointing results,¹⁷ despite some benefit having been reported previously.¹⁸ Migraine remains an enigma, but further work on these biochemical and pharmacological aspects may help in its elucidation.

Life after Death

Man's response to the approach of death has a perennial fascination. In part this may rest in a false hope that by understanding its immediate antecedents we may come to know something of the nature of death. Sometimes the threat comes from outside—for instance, earthquake, battle, falls from great heights—and can be apprehended clearly. Men vary in their response to these experiences¹: some remain calm and can continue to perceive their predicament in detail, while others develop fear of such intensity that awareness becomes clouded and behaviour incoherent, and yet others develop amnesia and other hysterical symptoms.

Illness is a threat to life which comes from within. The patient who has a serious heart disease is in a psychological as well as a physical predicament. He is aware of his heart to a greater extent than any of his other vital organs; he is aware of it as something which moves and thus epitomizes life. This internal threat to life cannot be countered as can many threats to life from outside, but at the same time the patient has not the reassurance that matters are entirely out of his hands, since he recognizes that intemperate activity endangers him.

R. G. Druss and D. S. Kornfeld² have recently described the psychiatric sequelae of cardiac arrest and compared these with the response of patients to other forms of heart disease. The only difference found was that patients whose hearts had stopped subsequently experienced nightmares of violence—as do those who have been wounded in battle. The significance of these nightmares is not yet known. They may be an

¹ *Brit. med. J.*, 1966, 2, 1340.

² Blackwell, B., *Lancet*, 1963, 2, 849.

³ ———, Mabbitt, L. A., *ibid.*, 1965, 1, 938.

⁴ ———, Marley, E., paper read at 5th International Congress of Collegium Internationale Neuro-Psychopharmacologicum, Washington, March 1966.

⁵ Hanington, E., *Brit. med. J.*, 1967, 2, 550.

⁶ Adams, C. W. M., Orton, C. C., and Zilkha, K. J., *J. Neurol. Neurosurg. Psychiat.*, 1968, in press.

⁷ Thorne, J., and Whitty, C. W. M., *Proceedings Second Migraine Symposium*, 1968. Heinemann, London. In press.

⁸ Wolff, H. G., *Headache and Other Head Pain*, 1963, 2nd edition. New York.

⁹ Cerletti, A., and Berde, B., *Proceedings Second Migraine Symposium*, 1968. Heinemann, London. In press.

¹⁰ Blumenthal, L. S., and Fuchs, M., *Amer. Practit.*, 1951, 2, 755.

¹¹ Lanzarot, M. M., *Rev. cli. esp.*, 1953, 51, 155.

¹² Roberts, S. E., *Arch. otolaryng.*, 1955, 61, 401.

¹³ Jönsson, B., von Reis, G., and Sahlgren, E., *Acta psychiat. scand.*, 1951, Suppl. No. 74, p. 102.

¹⁴ Keil, C., *Rev. méd. Liège*, 1953, 8, 521.

¹⁵ Moehlig, R. C., *J. Mich. med. Soc.*, 1955, 54, 577.

¹⁶ Als, E., and Jacobsen, J. J., *Ugeskr. Læg.*, 1964, 126, 1355.

¹⁷ Hudgson, P., Foster, J. B., and Newell, D. J., *Brit. med. J.*, 1967, 2, 91.

¹⁸ Lundberg, P. O., *Acta endocr. (Kbh.)*, 1962, 40, Suppl. No. 88, 1.

¹ Jaspers, K., in *General Psychopathology*, 1963, 7th ed., translated by J. Hoenig and M. W. Hamilton. Manchester.

² Druss, R. G., and Kornfeld, D. S., *J. Amer. med. Ass.*, 1967, 201, 291.

³ *The Times*, 13 December 1967.

adaptive process—a catharsis—which enables the patient to adjust to his experience; or the distorted, fragmentary, and purposeless appearance of recent memories which emerge when repression is in abeyance during sleep; or the result of a subtle organic disturbance, with their content derived from recent experience. Neurotic reactions were found in almost all the patients with grave heart disease whether or not they had suffered cardiac arrest, but as the criteria of abnormality were not clearly defined any comparison with the incidence found in other studies is difficult.

These problems are likely to become more common as apparatus is developed which can take over other vital functions in patients who are seriously ill. Victims of accidents can be maintained alive by respirators³ until it becomes clear, whether or not the brain is going to recover. In these cases the borderline between life and death is becoming blurred.

The atmosphere of an intensive care unit heightens suggestibility. The patient is anxious, and he is in the presence of others, both staff and fellow patients, who are also likely to be anxious. He is surrounded by equipment to which contemporary mythology attributes magical powers. Druss and Kornfeld advise that patients should be allowed as much privacy as is feasible, that monitoring equipment should be placed inconspicuously, and that patients should not be aware of the monitor signal. Patients gain relief from talking about their worries and they should be given the opportunity to do this while they are in hospital and their experiences are still fresh. Druss and Kornfeld also advocate that: "the patients should be told that their bodies were alive during the time their hearts had stopped." Many would disagree with this advice. The fantasy of having been dead may arise spontaneously, but it may also be suggested by the doctor's attitudes and by this type of comment. Confronting the patient with the information that his heart stopped beating or that he stopped breathing could do harm. The physician's detailed understanding of the emergency has served its purpose if it has helped the patient to get better; it is not part of treatment that this knowledge should be shared.

Doctors in Court

The protection of a doctor's professional confidence must sometimes conflict with the interest of justice in discovering the truth. The law resolves that conflict in all except a few special cases by giving the trial judge power to use the ultimate deterrent of committal for contempt to enforce disclosure of the confidence, while enjoining the judge to be sparing in the use of that deterrent.

In a report published last week the Law Reform Committee recommended¹ no change in the law so far as it affects doctors in civil cases. The Criminal Law Revision Committee is apparently thinking along similar lines in its consideration of the criminal law. The only change at present envisaged might arise out of the deliberations of Lord Justice Winn's Committee on Personal Injury Litigation, which is considering whether the "privilege in aid of litigation" should continue to apply to certain classes of hospital and other medical reports. At present a medical report prepared at the request of the legal advisers of a litigant for the purpose of litigation need not be disclosed to the court.

Much can be said in favour of the present state of the law.²

Difficulties of definition alone make it almost impossible to set out the cases in which the professional man should be permitted to refuse to answer questions. The Committee's report shows how difficult it is to describe broad principles to cover this point. When considering how the court should exercise its discretion on the issue of compelling medical witnesses the Committee states:

"Where a doctor is called, not in his capacity as a medical adviser to testify as to the physical or mental condition of his patient, but as a witness of another fact not related to the health of his patient, we are confident that any judge would protect him from being questioned upon information obtained by him from his patient in his capacity of medical adviser."

The Committee suggests, for example, that a doctor should not be compelled to give evidence of an admission of adultery if the admission had no bearing on the patient's mental or physical health. The reverse of this proposition is probably more attractive to doctors. One can see the public interest in preserving secrecy about disclosures which are of assistance to a doctor in his care of his patient. There is much less (if any) public interest in protecting those disclosures made as incidental conversation at the time the patient sought treatment.

What is plain is that if the law is to remain in its present fluid state some better system of appeals from the ruling of the court should be considered. Since the right of confidence belongs to the patient and not to the doctor, the medical witness cannot be sure of his position until the patient's absence of consent to disclosure and the mood of the judge are revealed when the doctor is in the witness-box. It is not until the witness is in contempt of court by refusing to comply with an order to answer that he acquires any standing before the court to test the ruling on appeal. An adjournment for an immediate application to the Court of Appeal for a second ruling could probably be obtained even under the present Rules of Court, but it would require a firm advocate to persuade most judges to accede to such a course in the middle of a trial. It is a pity that the Law Reform Committee did not consider the procedural problems of ensuring that there are adequate means of appeal from the exercise of the existing wide judicial discretion.

Foot-and-mouth Disease

Few can fail to be shocked at the slaughter of nearly 300,000 animals in the current outbreak of foot-and-mouth disease. But this is the price that must be paid to keep Britain free from endemic infection with it. The disease is endemic in most countries of the world, and though Australia, New Zealand, North America, and Britain are normally free from it¹ the most rigorous measures of control must be employed to prevent the introduction and establishment of infection.

Foot-and-mouth disease is an extremely infectious viral disease of animals. Very rarely it also attacks man.^{2,3} It has a high attack rate in susceptible animals and a capacity for rapid spread comparable to human influenza. It affects cloven-footed animals such as cattle, sheep, pigs, and goats. The incubation period is from three to eight days, and the main route of infection is the respiratory tract. The virus causes a generalized infection, with vesicles on the tongue, mouth, and hooves, so that affected animals have increased salivation and lameness. Virus is excreted in large quantities in the saliva, and is present—though not in such large amounts

¹ *Sixteenth Report of Law Reform Committee, 1967, Cmd. 3472. H.M.S.O., London.*

² *Brit. med. J.*, 1964, 2, 955.

—in milk and urine also. Mortality is low in adult animals, but survivors take a long time to recover condition and show a high incidence of abortion and mastitis. In the high-production livestock industry in Britain such animals would be uneconomic. Surviving animals carry the virus for 15 to 18 months after infection.⁴ The virus is hardy and can survive for 14 days on wool and for about three months on boot leather, rubber boots, and hay,⁵ though it is rapidly inactivated by heat, sunlight, or by treatment with formaldehyde, sodium hydroxide, or—more slowly—sodium carbonate. It remains viable in frozen liver, kidney, glandular tissue, and bone, but is inactivated in muscle during rigor mortis.

The sources of importation of the virus into the country often remain obscure. Most outbreaks in Britain have been attributed to contaminated meat imported from countries where infection is endemic, but birds migrating from Europe were thought to have been responsible for introducing infection during the extensive outbreak in Britain in 1951–2, since it coincided with a large-scale epidemic in Europe and with mass bird migration to this country.⁶ When an outbreak starts it may spread from farm to farm through movement of infected animals, contaminated equipment, and products, or possibly by airborne dissemination of the virus.

The difficulties of controlling such a disease are obvious, and ruthless measures must be adopted. These include isolation with restriction of movement to and from farms in a wide area surrounding a focus of infection, together with disinfection and the elimination of susceptible animals which may have been in contact with infection. Unfortunately, vaccination, though successful in so many human infections, is fraught with difficulties when applied to the control of foot-and-mouth disease. For example, the protection conferred by primary vaccination in cattle is short-lived—from about two to six months—and even after revaccination immunity cannot be depended upon for more than a year.⁷ In pigs it is even more difficult to get a satisfactory immunity by vaccination. The second problem is the diversity of serological types of virus. There are seven main viral types, subdivided into at least 40 different subtypes or strains, and immunity to one strain within a type may not give complete protection against other strains within the same type.⁴ The most serious drawback, however, is that though vaccinated animals are protected against clinical disease they may acquire symptomless or masked infection and become carriers of the virus.⁸ This would greatly increase the difficulties of eradicating the disease. If vaccination were introduced here it might mean having to accept endemic infection in Britain.

Over the years the compensation paid to farmers in Britain as a result of the slaughter policy has been far less than the cost of vaccinating the 40 million susceptible domestic animals. So in 1967, as in 1952, the price of freedom from endemic infection is a heavy one. To medical men foot-and-mouth disease serves as a timely reminder that, despite striking advances in our knowledge of micro-organisms in recent years, infectious disease can still pose a threat not only to health but to a nation's economy.

Symposium on Thyrotoxicosis

The proceedings of an international symposium on thyrotoxicosis held in Edinburgh in May 1967 are now published.¹ The editor, W. J. Irvine, who also organized the symposium, is to be congratulated on the speed at which publication has been achieved. Many new developments in thyrotoxicosis are discussed.

The concept of the long-acting thyroid stimulator (L.A.T.S.) and its role in the pathogenesis of Graves's disease dominated the conference. L.A.T.S. is a member of the IgG class of serum proteins, most of which are antibodies. D. S. Munro and his colleagues reported that the thyroid-stimulating properties of L.A.T.S. are inherent in the IgG molecule. J. M. McKenzie, following on his previous demonstration that L.A.T.S. can be produced by the lymphocytes of patients with Graves's disease, showed that a long-acting thyroid stimulator could be produced in rabbits immunized with human thyroid. Like human L.A.T.S., this rabbit antibody increased the thyroid uptake of iodine-131, and the rate of release of thyroid iodine-131 was not suppressed by thyroid hormone. D. J. El Kabir and his associates showed that L.A.T.S. could be completely absorbed by thyroid tissue (but not by kidney) and subsequently eluted by techniques known to dissociate antigen-antibody complexes. It is likely that L.A.T.S. is an antibody produced by lymphocytes to some thyroid-specific antigen and is a major factor in the pathogenesis of Graves's disease. But indirect evidence discussed by R. Hall and his colleagues of the absence of L.A.T.S. in some patients with the ophthalmic form of Graves's disease is further evidence that some other factors, perhaps immune globulins as yet unrecognized, may be primarily responsible for the ophthalmopathy. Work on an exophthalmos-producing substance assayed in fishes² was discussed by P. J. der Kinderen. It is known to be distinct from L.A.T.S.

Conventional laboratory tests for the confirmation of a diagnosis of hyperthyroidism are often interfered with by drugs, especially those like the contraceptive pill, which affect the level of thyroxine-binding globulin (T.B.G.). Further simple methods of estimating the degree of saturation of this substance in the patient's serum were described by Irvine and his colleagues and by A. W. G. Goolden. These techniques, when combined with estimation of the protein-bound iodine, allow calculation of a free thyroxine factor which is independent of any changes in T.B.G. capacity. This type of test is particularly useful in the diagnosis of hyperthyroidism during pregnancy.

Important advances in the treatment of hyperthyroidism were reported. W. D. Alexander and R. McG. Harden found that patients treated with antithyroid drugs could be divided into two groups on the basis of their response to triiodothyronine. If this work is confirmed it may be possible to predict which patients will respond to a short course of antithyroid drugs and which will require alternative treatment such as surgery or radioactive iodine. With regard to surgery for thyrotoxicosis, Irvine and A. G. Stewart showed that patients with moderate to high titres of antibody to thyroid microsomes before operation stand about a one-in-four risk of developing hypothyroidism. Their conclusions are that such high antibody titres are a relative contraindication to

¹ Brooksby, J. B., *Advanc. Virus Res.*, 1958, 5, 1.

² Armstrong, R., Davie, J., and Hedger, R. S., *Brit. med. J.*, 1967, 4, 529.

³ *Ibid.*, 1967, 4, 503.

⁴ Brooksby, J. B., *Nature (Lond.)*, 1967, 213, 120.

⁵ Graham, A. M., *Vet. Rec.*, 1959, 71, 383.

⁶ *Report of the Departmental Committee on Foot-and-Mouth Disease 1952–1954*, 1954. H.M.S.O.

⁷ Hyslop, N. St. G., in *Veterinary Annual*, 1966–7, p. 140.

⁸ Henderson, W. M., *ibid.*, 1966–7, p. 136.

¹ *Thyrotoxicosis: Proceedings of an International Symposium, Edinburgh, May 1967*, ed. W. J. Irvine. 1967. E. and S. Livingstone, Edinburgh. 50s. net.

² Dobyns, B. M., and Wilson, L. A., *J. clin. Endocr.*, 1954, 14, 1393.

partial thyroidectomy, but that if thyroidectomy is carried out careful follow-up is obligatory. R. N. Smith and G. M. Wilson reviewed their long-term experience of radioactive iodine therapy for thyrotoxicosis. Using half the conventional dose of iodine-131 (about 3,500 rads) reduces the hypothyroid rate to 7% after five years but by itself is insufficient to control hyperthyroidism within a year in the majority of patients, who require additional therapy with antithyroid drugs. S. C. Werner described the use of prednisone in the treatment of the severe eye changes of Graves's disease. There appears to be a critical dosage which must be exceeded before benefit ensues, and it varies from patient to patient. Total thyroidectomy, a procedure difficult to achieve, did not arrest the progression of active severe eye changes in five patients.

The symposium embodied much that is new in relation to the pathogenesis, diagnosis, and treatment of thyrotoxicosis, but the enigma of Graves's disease remains to stimulate research worker and clinician alike.

Polycythaemia and Chorea

The clinical manifestations of chorea are pathognomonic and often florid, but paradoxically the underlying pathological changes in the central nervous system are often inconspicuous and non-specific. Patchy cellular infiltrations, diffuse loss of nerve cells, and mild endarteritis may be present in the cortex, basal ganglia, brain stem, and cerebellum, but obvious macroscopical changes are usually lacking. Chorea is usually associated with rheumatism or degenerative disease of the brain when it is refractory to treatment; but recently P. C. Gautier-Smith and T. A. J. Pranker¹ have drawn attention to the uncommon association of chorea and polycythaemia. Their experience suggests that both the neurological and the haematological response to appropriate treatment may be gratifying. One polycythaemic patient who had had Sydenham's chorea as a child developed transient cerebral ischaemic attacks and chorea. Initial treatment by venesection and intravenous ³²P induced a neurological remission and lowered the level of haemoglobin. When the involuntary movements and polycythaemia recurred they again responded satisfactorily to treatment. In a second polycythaemic patient, however, bilateral chorea of sudden onset improved spontaneously before the haematological diagnosis was established.

Cerebrovascular symptoms and lesions are common in polycythaemia but the occurrence of chorea is very rare. In one necropsy study² of polycythaemia distended and thrombosed veins with areas of demyelination were found to be scattered diffusely throughout the brain with no predilection for the basal ganglia. The pathogenic mechanisms causing cerebral dysfunction are usually considered to be the increased viscosity of the blood leading to raised vascular resistance and sometimes thrombus formation; but the

apparent reversibility of cerebral symptoms, including chorea, suggests that anoxia secondary to a sluggish circulation may be as important as multifocal irremediable infarctions. Though the critical combination of diffuse lesions responsible for the release of choreic movements remains obscure these case reports serve to remind clinicians that polycythaemia should not be overlooked in the investigation of cerebrovascular disease.

M.I.A. Jubilee

While the excellent service the Medical Insurance Agency renders the medical profession needs no embellishment, many doctors may be surprised to know that its support of medical charities is on as grand a scale. As a profession we are thus doubly grateful to note that the M.I.A. has now completed its first sixty years, an occasion celebrated by a diamond jubilee dinner held at B.M.A. House last week (see p. 755).

This non-profit-making agency has contributed more than £600,000 to charities over the years. The main recipients have been the Royal Medical Benevolent Fund, the Royal Medical Foundation of Epsom College, and the B.M.A. Charities Fund. Through them countless doctors and their families have been tided over desperate circumstances and their children often enabled to continue their education. In the present year alone the M.I.A. has contributed over £50,000 to medical charities.

The origin of this remarkable organization lies in a lunch-time conversation between Dawson Williams and Squire Sprigge, then the editors of the *B.M.J.* and *Lancet*. From experience of life assurance policies being effected by medical men they concluded that an organization should be set up to obtain the best possible terms, and that the whole of its surplus should be devoted to medical charities. This idea was put to the B.M.A., which, after investigating it further, agreed in 1907 to give the proposed scheme every assistance. The friendliest relations between the B.M.A. and the Medical Insurance Agency have continued till the present day and assuredly will for at least the next 60 years.

Return to Britain

A hard-pressed profession will welcome the Minister of Health's statement (see p. 753) that arrangements for the return of some 50 British doctors now in North America are well in hand. These doctors could ill be spared when they left and the need for them since has if anything increased. What experiences abroad or arguments by the Ministry's interviewing board¹ have decided them to come back are yet to be learnt. One thing, however, is certain: prompt news of home vacancies is essential for anyone contemplating this move. Doctors so placed will find helpful the *B.M.J.*'s air-mail lists of appointments. Details of this service, which started in 1953, are given at p. 756 of this issue.

¹ Gautier-Smith, P. C., and Pranker, T. A. J., *Acta neurol. scand.*, 1967, 43, 357.

² Kotner, L. M., and Tritt, J. H., *Ann. intern. Med.*, 1942, 17, 544.

¹ *Brit. med. J.*, 1967, 3, 128.

Papers and Originals

Cell and Bacterial Counts in the Urine of Normal Infants and Children

H. BRAUDE,* M.B., CH.B., M.R.C.P.ED., D.C.H.; J. O. FORFAR,* M.C., M.D., B.SC., F.R.C.P., F.R.C.P.ED., D.C.H.
J. C. GOULD,† M.D., B.SC., F.R.C.P.ED., M.C.PATH., F.R.S.ED.; J. W. MCLEOD,† O.B.E., M.B., CH.B., F.R.S.

Brit. med. J., 1967, 4, 697-701

Unrecognized urinary tract infection in infancy and childhood may have serious long-term effects, and chronic adult pyelonephritis may originate undetected at this time. The accurate diagnosis of urinary tract infection in the infant and child is thus important. It is usually based on assessment of the number of pus cells or bacteria in the urine, or both. In the case of cells, contamination from the urethra and periurethral area can increase the number falsely, and in an alkaline urine the rapid disappearance of cells can result in a falsely low count. With bacteria, contamination may occur from the perineal skin during collection; and multiplication will occur in a urine left standing. Antibiotics or chemotherapeutic agents may invalidate bacterial counts as diagnostic tests.

The object of the present study was to determine the cell and bacterial counts on urine collected from normal children by commonly used methods and to contrast the findings.

Material and Methods

Seven hundred and ten specimens of urine were examined from 553 infants and children aged 0-14 years who were without any suggestion of urinary tract infection and who had not received antibiotics during the previous six weeks (Table I). Most had not had any antibiotic.

The series included normal newborn infants in a maternity unit, medical and surgical inpatients in a paediatric department, and outpatients attending the same department.

Cell counts on the urine were carried out immediately after voiding, a few drops of homogenized urine being introduced into a Fuchs-Rosenthal counting-chamber. Where the identification of leucocytes was difficult one drop of acetic acid was added to a few millilitres of urine before introducing the urine into the counting-chamber, and further evidence of the presence of granular leucocytes was obtained where necessary by staining the sediment with Leishman's stain after centrifugation. In the neonatal period small non-squamous epithelial cells could significantly influence the cell count and were very difficult to differentiate from granular cells. Because of this, leucocytes and small non-squamous epithelial cells were counted together in the first 10 days of life.

For quantitative bacteriological examination a standard 3-mm. loopful of well-shaken unspun urine was plated and counted as described by Urquhart and Gould (1965).

pH was determined with wide range indicator papers.

Methods of Urine Collection

Bag Method.—Adhesive plastic bags obtainable commercially were used in the collection of specimens from infants in the 0-10 day and 11 days-2 years age groups (Table I). In some

infants the bag was attached without any previous skin cleansing (unprepared bag) and in others the perineum and external genitalia were well washed with sterile water beforehand (prepared bag). Antiseptics were not used. The bags were kept in position until the child passed urine and removed immediately or within a few minutes, the contents being transferred to a sterile wide-mouthed screw-capped universal container. Faecally contaminated urine was, of course, discarded. In a special group of 10 children aged 1-2 years 10 ml. of sterile water was introduced into the bag before it was applied and the bag removed at intervals ranging from 5 to 30 minutes for bacteriological examination of the contents before any urine had been passed into it.

TABLE I.—Specimens of Urine According to Sex of Patients, Age Groups, and Method of Collection

	0-10 Days		11 Days-2 Years		2+-14 Years		0-14 Years
	M	F	M	F	M	F	
No. of patients	95	89	80	79	110	100	553
Unprepared bag	38	30	24	24	—	—	116
Prepared bag	33	26	18	27	—	—	104
Total bag	71	56	42	51	—	—	220
Unprepared M.S.U. ..	25	20	42	37	67	68	259
Prepared M.S.U. ..	23	20	20	28	66	74	231
Total M.S.U.	48	40	62	65	133	142	490
Total bag and M.S.U. ..	119	96	104	116	133	142	710

Midstream Urines (M.S.U.s) or "Clean Catch" Specimens.—Midstream specimens were collected from patients in the 0-10 days, 11 days-2 years, and 2+-14 years age groups. The patients in these groups were further divided into those in whom no previous skin preparation had been carried out (unprepared M.S.U.) and those in whom previous to collection the perineum and external genitalia had been well washed with sterile water (prepared M.S.U.) (Table I). So far as was possible all specimens were caught in mid-air after allowing the initial few millilitres of urine to pass uncollected. With boys there was no serious difficulty, but there was with girls. When female infants void, the urine often wells up, forming a lake in the vulva and perineum. Sometimes the urine will be passed as a spray or drip off the posterior perineum. A strong jet may pass obliquely, striking the inner aspect of the thigh. Proper collection requires patience and time, but even with these, perfect collection is often not possible and in some cases specimens could not be obtained without bringing the mouth of the sterile container into contact with the skin. This was thought preferable to allowing the urine to flow over the

* Department of Child Life and Health, University of Edinburgh and Western General Hospital, Edinburgh.

† Central Microbiological Laboratories, Edinburgh.

perineal skin before collection. Young girls are often unable to pass urine on demand, and, particularly after any cleansing procedure, an hour or more may elapse before they will do so. Embarrassment commonly appears to be the dominant cause. Thus in the female infant and child many factors militate against the avoidance of contamination in the collection procedure.

Comparison of Methods of Collection on Same Patient

In 28 patients (11 males, 17 females) in the 0-2 year age group an unprepared bag specimen of urine was collected and then from the same patient on the same or following day a prepared specimen. In a further 58 cases (28 males, 30 females) in the same age group a bag specimen was collected followed on the same or the next day by a midstream specimen. In 33 patients (13 males, 20 females) in the 2+-14 year age group an unprepared M.S.U. was collected followed on the same or on the next day by a prepared M.S.U.

Bacterial Flora of Anterior Urethral Area

In 30 patients ranging from 0 to 14 years the anterior urethra was swabbed just before urine collection. Any organism isolated was considered in conjunction with any isolate from the urine specimen. Only organisms potentially pathogenic to the urinary tract were considered—namely, *Escherichia coli*, non-lactose fermenting coliforms, *Proteus*, *Streptococcus faecalis*, *Klebsiella*, *Pseudomonas pyocyanea*, and *Staphylococcus aureus*.

Results

Cell Counts

First 10 Days of Life.—Cell counts from 215 infants are shown in Tables II and III. In males some counts showed a moderate increase above 10 cells/cu. mm. for the first three days but thereafter fell well below this figure. In females the position was different. Throughout the 10-day period the counts tended to be high, 21% being above 10 cells/cu. mm. and 11% above 50 cells/cu. mm. The incidence of raised cell counts was higher in bag than in midstream urines. In bag urines from 56 females 27% were over 10/cu. mm., including 18% over 50/cu. mm. The corresponding figures for 40 M.S.U.s were 13% (P of difference=0.08) and 3% (P =0.01). In bag urines from 71 males 6% showed counts of over

TABLE II.—Cell and Bacterial Counts (Potentially Pathogenic Organisms) on 215 Specimens of Urine During the First 10 Days of Life (127 Bag; 88 M.S.U.)

Day	Sex	No.	Range of Cell Count	Cell Count > 10/cu. mm.		Cell Count > 50/cu. mm.		Bact. Count 10^5 or Over/ml.	
				No.	%	No.	%	No.	%
1	M	19	0-136	2	11	1	5	3	16
	F	15	0-100	2	13	1	7	5	33
2	M	14	0-150	1	7	1	7	5	36
	F	27	0-250	5	19	2	7	9	33
3	M	18	0-15	1	6	0	0	6	33
	F	19	0-1,000	5	26	4	21	9	47
4	M	19	0-10	0	0	0	0	7	37
	F	14	0-150	4	29	2	14	5	36
5	M	15	0-1	0	0	0	0	8	53
	F	7	0-300	1	17	1	17	4	57
6	M	13	0	0	0	0	0	8	62
	F	3	0	0	0	0	0	2	67
7	M	5	0-2	0	0	0	0	3	60
	F	5	0-42	1	20	0	0	4	80
8	M	5	0-2	0	0	0	0	3	60
	F	1	0	0	0	0	0	1	100
9	M	2	0	0	0	0	0	1	50
	F	1	25	1	100	0	0	1	100
10	M	9	0-2	0	0	0	0	3	33
	F	4	0-125	1	25	1	25	3	75
0-10 days	M	119	0-150	4	3	2	2	47	40
	F	96	0-1,000	20	21	11	11	43	45

10/cu. mm., including 4% of over 50/cu. mm. None of the cell counts for 48 male M.S.U.s was above 10/cu. mm. (P =0.03 and 0.08).

TABLE III.—215 Specimens (119 Male, 96 Female) First 10 Days of Life. 127 Bag Specimens (B) and 88 Midstream Specimens (MS)

Cells/ cu. mm.	Bacterial Count—Potentially Pathogenic Organisms/ml.												
	N.G.		10 ³		10 ⁴		10 ⁵		10 ⁶		10 ⁷		
	M	F	M	F	M	F	M	F	M	F	M	F	
201-1,000						1		3		2			B MS
151-200													B MS
101-150						1		1	2	1			B MS
51-100								1 1					B MS
11-50			1 2			1 3	1 1	1 1	1				B MS
0-10	18 18	10 9	12 5	2 7	7 13	8 6	22 12	9 12	6	7 1		2 5	B MS

Cell count > 10/cu. mm.	{ Bag urines M.S.U.	..	Male	Female
			6%	27%
Bacterial count > 10 ⁴ /ml.	{ Bag urines M.S.U.	..	0%	13%
			47%	54%
			25%	38%

11 Days to 2 Years.—From 104 males none of the cell counts in urine collected either by bag or midstream specimen was above 5/cu. mm. Cell counts in the 116 females were higher. With 51 bag urines 24% exceeded 10 cells/cu. mm., including 6% above 50/cu. mm., while with the 65 M.S.U.s the corresponding counts were 5% (P =0.01) and nil (P =0.07) (Table IV).

2+ to 14 Years.—Only two of the cell counts in the 133 males (all M.S.U.s) exceeded 5/cu. mm., including 1 above

TABLE IV.—220 Specimens (104 Male, 116 Female) 11 Days-2 Years. 93 Bag Specimens (B) and 127 Midstream Specimens (MS)

Cells/ cu. mm.	Bacterial Count—Potentially Pathogenic Organisms/ml.												
	N.G.		10 ³		10 ⁴		10 ⁵		10 ⁶		10 ⁷		
	M	F	M	F	M	F	M	F	M	F	M	F	
201-1,000										1			B MS
151-200													B MS
101-150													B MS
51-100				1				1					B MS
11-50		3 2		1		1		5		1			B MS
0-10	6 18	5 11	5 14	5 12	12 7	11 15	16 21	15 20	2 2	3 3	1		B MS

Cell count > 10/cu. mm.	{ Bag urines M.S.U.	..	Male	Female
			0%	24%
Bacterial count > 10 ⁴ /ml.	{ Bag urines M.S.U.	..	0%	5%
			45%	51%
			37%	35%

TABLE V.—275 Specimens (133 Male, 142 Female) 2+-14 Years. All Midstream Specimens

Cells/cu. mm.	Bacterial Count—Potentially Pathogenic Organisms/ml.											
	N.G.		10 ³		10 ⁴		10 ⁵		10 ⁶		10 ⁷	
	M	F	M	F	M	F	M	F	M	F	M	F
201-1,000		1								2		
151-200										2		
101-150		2				1		1				
51-100						1						
11-50	1	2						2				1
0-10	105	81	11	10	5	12	9	14	2	5		5

Cell counts > 10/cu. mm.	..	..	Male	Female
			1.5%	11%
Bacterial counts > 10 ⁴ /ml.	..	..	8%	23%

10/cu. mm. Of the 142 females (all M.S.U.s) 11% exceeded 10/cu. mm., including 7% above 50/cu. mm. (Table V).

Bacterial Counts

First 10 Days of Life.—The incidence of bacterial counts for potentially pathogenic organisms in 215 specimens is shown in Tables II and III and contrasted in the former with the corresponding cell counts. The incidence of counts of 10^5 /ml. or over was high (40% male and 45% female) and unlike cell counts showed no significant sex difference. The overall incidence of 50% in 127 bag urines was higher than the 31% in 88 M.S.U.s ($P<0.01$).

First 2 Years of Life.—Apart from the comparison with cell counts in the first 10 days of life, bacterial counts in the first 10 days and in the remainder of the first two years need not be considered separately. There was no significant difference between them at these two periods. Table VI thus shows

TABLE VI.—Bacterial Counts (Potentially Pathogenic Organisms) per ml. on 710 Specimens of Urine from Children Aged 0–14 Years

			No. of Specimens	No Growth		10 ¹ –10 ⁴		10 ⁵ or Over		10 ⁶ or Over		10 ⁷ or Over	
				No.	%	No.	%	No.	%	No.	%	No.	%
0–2 years	Bag	M	113	24	21	37	33	52	46	14	12	3	4
		F	107	19	18	32	30	56	52	20	19	5	5
		Total	220	43	20	69	31	108	49	34	15	8	4
	M.S.U.	M	110	36	33	39	35	35	32	2	2	0	0
F		105	24	23	43	41	38	37	4	4	0	0	
Total		215	60	28	82	38	73	34	6	3	0	0	
2+–14 years	M.S.U.	M	133	106	80	16	12	11	8	2	2	0	0
		F	142	86	61	24	17	32	23	15	11	6	4
		Total	275	192	70	40	15	43	16	17	6	6	2

bacterial counts for potentially pathogenic organisms for the whole of the first two years divided according to sex and method of collection. There was no significant sex difference in either bag urines or M.S.U.s. The incidence of bacterial counts of 10^5 or over/ml. was high, 49% for 108 bag urines and 34% for 73 M.S.U.s—a statistically significant difference ($P=0.001$). At 10^6 or over/ml. the incidences were 15% for bag urines and 3% for M.S.U.s ($P=0.03$) and at 10^7 /ml. 4% and nil ($P=0.001$). In the 58 cases in which a bag specimen was followed by an M.S.U. 66% showed a lower bacterial count with the M.S.U. (average difference= 10^2 organisms/ml.); 15% a lower count with the bag (average difference= 10^2 /ml.), and 19% similar. This is a significant difference ($P<0.00001$). The effect of the time interval between the application of the bag and the voiding of urine into it is shown in Table VII. Longer intervals made little difference, suggesting that contamination was already pronounced at less than half an hour. Where, in 10 children, bags containing sterile water were applied for periods of 5, 15, and 30 minutes all specimens of water produced a pure growth of *E. coli*, the average count at 5 and 15 minutes being 10^5 and at 30 minutes 10^6 .

TABLE VII.—Effect of Time Interval (Application of Bag to Passage of Urine) on Bacterial Count (All Organisms) (219 Children Aged 0–2 Years)

	< ½ Hour	½–1 Hour	1–2 Hours	> 2 Hours
No.	82	52	43	42
No. 10^5 or over	53 (65%)	28 (54%)	26 (61%)	30 (72%)

2+ to 14 Years.—The incidences of raised bacterial counts in 275 specimens are shown in Tables V and VI. Counts of 10^5 or over/ml. were significantly less frequent than in the 0–2 year group, 16% compared with 34% ($P<0.00001$), and the incidence of specimens in which there was no growth was significantly greater, 70% compared with 28% ($P<0.00001$). Paradoxically the incidence of bacterial counts of 10^6 or more/

ml. was significantly higher in females in this group than in M.S.U.s in the 0–2 year group. There was a significant sex difference within the group, 23% of females showing counts of 10^5 or higher/ml. compared with 8% of males ($P=0.001$).

Effect of Preparation on Bacterial Counts

Table VIII shows that with bag specimens in the 0–2 year group skin preparation with sterile water resulted in a significantly higher incidence of bacterial counts of 10^5 or over, 65% compared with 34% ($P=0.0001$). This applied to both sexes.

In the 28 cases in the 0–2 year group in which in the same patient a bag urine was collected without, and then with, previous preparation, the former showed a lower count in 46% of specimens (average difference= 10^3 organisms/ml.) and the latter in 14% of specimens (average difference= 10^2 organisms/ml.). This difference is significant ($P<0.01$) and was seen in both male and female children.

With M.S.U.s similar bacterial counts were obtained from unprepared and prepared specimens in the 0–2 year and 2+–14 year groups though at lower incidences in the latter. The similarity was evident in both sexes.

TABLE VIII.—Effect on Bacterial Count (Potentially Pathogenic Organisms per ml.) of Previous Preparation

			No.	No Growth		10^5 or Over		10^6 or Over		10^7 or Over	
				No.	%	No.	%	No.	%	No.	%
0–2 years	Bag	Unprep.	116	26	22	40	34	12	10	2	2
		Prep.	104	17	16	68	65	23	20	6	6
	M.S.U.	Unprep.	124	42	34	44	36	4	3	0	0
		Prep.	91	18	20	29	32	2	2	0	0
2+–14 years	M.S.U.	Unprep.	135	95	70	21	15	9	7	4	3
		Prep.	140	97	69	22	16	8	6	2	1

In the 33 cases in the 2+–14 year group in which in the same patient unprepared and then prepared M.S.U.s were examined, 6% of unprepared specimens had lower counts than prepared (average difference= 10^3 organisms/ml.) and 42% of prepared specimens lower counts than unprepared (average difference= 10^2 organisms/ml.). This is a significant difference ($P<0.001$).

Thus with bag urines preparation of the type described here before collection resulted in higher bacterial counts, while with M.S.U.s it did not affect or lowered the bacterial count.

Comparisons Between Organisms Isolated from the Anterior Urethra and from Corresponding Specimens of Urine

In 63% of the 30 cases examined similar organisms were cultured from the anterior urethra and from the urine and in 20% of cases different organisms. In 13% of cases the urine was sterile and in 3% no growth was obtained from the anterior

urethral swab. There is thus considerable correlation between bacterial flora found on the anterior urethral area and in the urine.

Organisms Cultured

The frequency with which the various potentially pathogenic organisms occurred was as follows: *E. coli* 60%, *Proteus* 28%, non-lactose fermenting coliforms 9%, *Ps. pyocyanea* and *Strep. faecalis* 1%, *Klebsiella* and *Staphylococcus aureus* less than 1%. Where potentially pathogenic organisms were associated with a bacterial count of 10^5 or more/ml. they were present in pure growth in 42% of cases in the 0-2 year group but in only 12% in the 2+–14 year group.

Correlation Between Cell Counts and Bacterial Counts

In the first 10 days of life the incidence of bacterial counts for potentially pathogenic organisms of 10^5 or over/ml. (42%) was very much higher than the incidence of cell counts of more than 10/cu. mm. (11%) or 50/cu. mm. (6%). For this period Table III shows the combined cell and bacterial counts at various levels. If the upper limit of the normal cell count is set at 50/cu. mm. and of the bacterial count at 10^4 /ml. only one M.S.U. (1%) was outside these limits. Of the bag urines 10 (8%) exceeded these limits, and if the upper accepted limit of the bacterial count is raised to 10^5 /ml. 5 (4%) did so. With the bag urines it was the females in particular (8 out of 10) who showed high combined counts.

In the 11 days to 2-year period (Table IV) none of the male patients gave specimens which exceeded the combined criteria of 10 cells/cu. mm. and 10^4 bacteria/ml. whether the urine was collected by bag or mid-stream. Nor did any of the female specimens collected as M.S.U.s exceed these limits, but eight of the bag urines in females (16%) did so.

In the 2+–14-year period (Table V) where all specimens were M.S.U.s none of the male specimens exceeded the limits of 10 cells/cu. mm. and 10^4 organisms/ml., but eight specimens from females (6%) lay outside these limits and five (3.5%) exceeded the combined criteria of 10 cells/cu. mm. and 10^5 bacteria/ml.

While there is thus a good deal of variability in the normal cell and bacterial counts in children it is possible from the data presented here to recognize upper limits of normal for cell counts alone, for bacterial counts alone, and for combined cell and bacterial counts for different age groups, and also for

different sexes and for different methods of collection. This has been done in Table IX where are represented "diagnostic levels" which generally just exceed these upper normal limits or in a few instances would be reached in less than 6% of normal children.

Discussion

It is important that urinary tract infection in infancy and childhood should be diagnosed early and confidently, yet the symptoms may be far from specific (Burke, 1961; Smellie *et al.*, 1964). Definitive diagnosis depends largely on examination of the urine for its cellular and bacterial content. The conditions under which this examination is made must be strictly defined, otherwise false and highly misleading results may be obtained. It is very likely that false-positive diagnoses are occurring to a considerable extent at present and that many children are given unnecessary and even harmful antibiotic treatment. Even more dangerous, particularly in infancy, is the possibility that wrongly presumed urinary tract infection may delay or mask the diagnosis of other more sinister disease. On the other hand, failure to diagnose urinary tract infection when it is present may have serious short-term and long-term effects.

Apart from bag collections over the first three days of life the cell count in the normal male child aged 0-14 years, whether urine is collected by bag or M.S.U., hardly ever exceeds 10/cu. mm. or in the case of M.S.U.s after the age of 11 days 5/cu. mm. Thus in the male infant the urinary cell count is a valuable diagnostic procedure.

In the female the position is less clear cut. Over the first 10 days of life high cell counts may be obtained normally due to the presence in the urine of small round non-squamous epithelial cells which are difficult to differentiate from pus cells on simple counting. Differentiation can usually be made by staining a film of the urinary sediment, but this is time-consuming. James (1959) suggested 50 cells/cu. mm. as the upper limit of normal at this age, but from our results a slightly higher level (75/cu. mm.) would be more appropriate with M.S.U.s and a count of over 300/cu. mm. for bag urines.

In female children aged 11 days to 2 years 24% of bag urines and 5% of M.S.U.s show cell counts in excess of 10/cu. mm. but few exceed 50 cells/cu. mm. At this age 50 cells/cu. mm. in M.S.U.s or double this number in bag urines represent the upper limits of normal. In the 2+–14 year age group in girls the cell count can commonly be high and counts of up to 150/cu. mm. can occur normally.

Midstream specimens are difficult to collect in young children and this has popularized the use of adhesive plastic

TABLE IX.—Diagnostic Levels in Children Aged 0-14 Years for Cell Counts Alone, Bacterial Counts Alone, and Combined Cell and Bacterial Counts. Urine Collected by Bags and as Midstream Specimens

Type of Collection	Age	Sex	Cell Count Alone		Bacterial Count Alone		Combined Cell and Bacterial Count	
			Diagnostic Level Cells per cu. mm.	Percentage Chance of Occurrence in Normal Child Ave. $\pm 2 \times$ S.E.	Diagnostic Level Bacteria per ml.	Percentage Chance of Occurrence in Normal Child Ave. $\pm 2 \times$ S.E.	Diagnostic Level Cells per cu. mm./Bact. per ml.	Percentage Chance of Occurrence in Normal Child Ave. $\pm 2 \times$ S.E.
Mid-stream urines	0-10 days	M	> 10	0	> 10^5	0	> 10/> 10^4	0
		F	> 75	0	> 10^5	0	> 75/> 10^4	0
	11 days-2 years	M	> 5	0	> 10^5	0	> 5/> 10^4	0
		F	> 50	0	> 10^5	0	> 10/> 10^4	0
	2+ years-14 years	M	> 5	1.5 $\pm$ 2.1	> 10^5	1.5 $\pm$ 2.1	> 5/> 10^4	0.8 $\pm$ 2.1
		F	> 150	2.1 $\pm$ 2.4	> 10^7	2.1 $\pm$ 2.4	> 10/> 10^5 > 150/> 10^4 or > 50/> 10^5	0.7 $\pm$ 1.4 2.8 $\pm$ 2.8
Bag urines	0-10 days	M	1-3 days > 150	0	> 10^7	0	1-3 days > 10/> 10^5 or > 150/ 10^4	0
			4-10 days > 10	0			4-10 days > 10/> 10^4	0
		F	> 300	1.8 $\pm$ 3.6			> 10/> 10^5	0
	11 days-2 years	M	> 10	0	> 10^7	0	> 10/> 10^4	0
		F	> 100	2.0 $\pm$ 3.9	> 10^5	0	> 100/> 10^4	2.0 $\pm$ 3.9

bags. Bag urines, with bacterial counts on them, have been used in determining the incidence of urinary tract infection in childhood (Smellie *et al.*, 1964). Yet in the present study half of the urines collected in this way in normal infants of both sexes aged 0–2 years were found to produce bacterial counts for potentially pathogenic organisms of 10^5 /ml. and approximately 15% counts of 10^6 /ml. Similar results have been obtained by Lam *et al.* (1967) and Newman *et al.* (1967).

The evidence that bacterial counts on urine voided into a bag within half an hour of the bag being applied are as high as those where the bag has been applied for over two hours before voiding suggests that contamination of the urine takes place at the time that it is passed or of the bag at the time that it is applied. The high bacterial counts in the bags containing sterile water suggest that contact with the genitalia and skin of the perineum results in immediate contamination. Previous cleansing of the skin of the perineum and genitalia with sterile distilled water appeared to increase contamination, possibly by creating a "storm" of bacteria which might otherwise have lain dormant. More extensive irrigation, as practised by Lincoln and Winberg (1964), may reduce contamination.

It has been suggested that when urine is contaminated from the urethra or vulva the bacterial count is unlikely to exceed 10^4 /ml., but that where bacteria multiply in the bladder in genuine urinary tract infection they will reach levels of 10^6 or more/ml. (Kass, 1960). This may be true for the adult but is probably not valid for the infant and child, where the volume of urine is very much smaller and the amount of contamination is likely to be relatively very much greater. It is clear that the bacterial count of 10^5 /ml., which has attained such significance in the adult, is not valid as a dividing line between infected and non-infected urine in the child. Variations in age and sex, the effect of antiseptics used in skin cleansing, and the technique of collection all have to be considered in assessing results. Adult criteria are often misleading in the child, and criteria determined by one method of collection cannot be transposed to interpret results from another.

The normal limits for the diagnosis of urinary tract infection based on single cell or bacterial counts are wide but can be much more narrowly defined when cell and bacterial counts are considered in combination (Houston, 1963). Where M.S.U.s are collected as described here the combined limits of 10 cells/cu. mm. and 10^4 organisms/ml. which are so commonly used (Stansfeld, 1966) would hardly ever be exceeded in males and would be exceeded in only 4% of females. With bag urines under 3% of males and 16% of females would be outside the same limits, but if in females the combined limits are taken as 50 cells/cu. mm. and 10^5 bacteria/ml. less than 4% would lie outside these.

Urinary tract infection should, if possible, be diagnosed both by cell counts and by bacterial counts, repeating these observations and finding them constant, and finding, too, the same pathogenic organisms in pure growth on both occasions. Ideally a midstream specimen should be a true "clean catch" even if it takes several hours to obtain this. Unfortunately it may be impracticable to implement optimum diagnostic procedures. Treatment may have to be instituted without waiting for second specimens; it may be impossible to obtain a perfect midstream specimen; the very frequency with which urinary tract infection is suspected in children makes simple rapid methods of urine collection for diagnostic purposes obligatory. Under these circumstances it appears worth while to know the limits of single specimen observations, both when only the result of a cell count or a bacterial count is available and when combined

observations of cell and bacterial counts have been made on the specimen and can be considered together (Table IX).

With some of the criteria shown in Table IX there will be a small overlap between the findings in the normal child and those in the child with a urinary tract infection. Until absolute methods of diagnosis become possible such overlap is likely in any method of collection of urine passed per urethra. Precise definition of the limits of any method employed will increase its value and point to its limitations.

Summary

Normal cell and bacterial counts in urine obtained both by plastic adhesive bags and as midstream urines from male and female children from birth to 14 years have been determined by a study of 710 specimens obtained from 553 normal children.

At all ages cell counts were significantly higher in female than in male children when urine was collected by bag and as midstream specimens.

Until the age of 2 years bacterial counts were similar in male and in female children, but over the age of 2 years bacterial counts were higher in female children. These similarities and differences were seen in both bag and M.S.U.s.

Cell counts and bacterial counts in both males and females were significantly higher in urine obtained in bags as compared with M.S.U.s.

With midstream specimens previous preparation by washing the genital area with sterile distilled water did not affect the bacterial count up to the age of 2 years but reduced it in children over this age. With bags, previous preparation resulted in higher bacterial counts. There was evidence of rapid and significant contamination of urine collected by bag.

Organisms present on the anterior urethra were commonly the same as those isolated from urine specimens.

The pattern of distribution and upper limits of normal cell and bacterial counts in male and female infants at various ages for urine collected by bag and as midstream specimens are defined. On the basis of these definitions standards suggested for individual counts of cells and bacteria combined counts (on the same specimen) by which urinary tract infection in infancy and childhood can be made.

J. W. M. wishes to thank the Royal Society for research expenses and the Medical Research Council for technical assistance.

Requests for reprints should be sent to Dr. J. W. M. Forfar, Department of Child Life, Edinburgh 9.

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* Department of Child Life and Adolescent Psychiatry, Western General Hospital, Edinburgh 9.
† Central Microbiological Laboratory, Edinburgh 9.

Diagnosis of Urinary Tract Infection in Childhood Based on Examination of Paired Non-catheter and Catheter Specimens of Urine

H. BRAUDE,* M.B., CH.B., M.R.C.P.ED., D.C.H.; J. O. FORFAR,* M.C., M.D., B.SC., F.R.C.P., F.R.C.P.ED., D.C.H.
J. C. GOULD,† M.D., B.SC., F.R.C.P.ED., M.C.PATH., F.R.S.ED.; J. W. MCLEOD,† O.B.E., M.B., CH.B., F.R.S.

Brit. med. J., 1967, 4, 702-705

The accurate diagnosis of urinary tract infection in infancy and childhood based on examination of the urine is made difficult by the number of variables involved. These include the age and sex of the patient, method of collection of the urine, time interval between micturition and urine examination, and technique of examination employed. The method of collection of urine is most important and for two common methods—plastic adhesive bags and midstream specimens—we have suggested diagnostic levels for cell and bacterial counts related to the age and sex of the patient and the type of collection (Braude *et al.*, 1967).

To determine the validity of these levels non-catheter and catheter specimens of urine were obtained from 68 patients.

Material

In most of the patients the suspicion had arisen on clinical grounds that urinary tract infection might be present—a suspicion based on suggestive symptoms such as abdominal pain, dysuria, frequency of micturition, enuresis, unexplained vomiting or anorexia, and, in the case of infants, unexplained failure to thrive. Also in a number of symptomless cases routine examination of the urine had suggested that infection might be present. Of the 68 patients 49 were female and 19 male. The ages ranged from 9 days to 11 years (see Table).

Methods

With the methods described by Braude *et al.* (1967) 92 non-catheter specimens—76 (82%) midstream and 16 (18%) bag—were obtained from 68 patients, and thereafter a catheter specimen was obtained from each of them. Catheterization was carried out by a modification of the technique described by Gould *et al.* (1963), which is effective in delaying urinary tract infection in paraplegic patients, often for many weeks, until change of catheter is made. The external genitalia, after being washed with sterile water and while still moist, are covered with Polybactrin (neomycin sulphate 495 mg., polymyxin B sulphate 150,000 units, zinc bacitracin 37,500 units, and cloxacillin 109 g. with a mixture of the inert and highly volatile dichlorotetrafluoroethane and dichlorodifluoroethane at a distance of 12 in. (30 cm.), the labia being retracted in the female and the foreskin retracted in the male. The area is then covered with a sterile towel.

The catheter is irrigated with aqueous Polybactrin Soluble (neomycin sulphate 495 mg., polymyxin B sulphate 150,000 units, zinc bacitracin 37,500 units per 2 ml. With the catheter fine enough to allow a free return of urine a sterile premature infant-feeding tube size 5 is inserted into the anterior urethra, in order to enter the anterior urethra and to be pushed up to $\frac{1}{2}$ in. (1.3 cm.). While the

operator holds the catheter in position an assistant slowly injects 2 ml. of solution. A return flow alongside the catheter should occur. (If it does not the catheter has been inserted too far and the solution is being injected into the bladder. This may modify bacteriological but not cytological results.) The catheter is then withdrawn and the patient left for half an hour. In young boys catheterization often causes discomfort and it is advisable to anaesthetize the posterior urethra before the second or main part of the catheterization procedure by introducing a little anaesthetic jelly (Duncaine) into the urethra immediately after the irrigation procedure.

After half an hour has elapsed the operator again scrubs up, and, holding the labia apart or retracting the foreskin, using sterile swabs, the genitalia are resprayed with Polybactrin as described above and the patient is retowelled. The operator puts on sterile gloves and catheterizes the bladder, using a sterile disposable plastic tube size 9 F.G. (feeding or umbilical tube) and a non-touch technique. The assistant, controlling the other end of the catheter with forceps, directs the urine into a sterile container. Normally a few drops are collected into a first bottle, which is discarded, and the remainder of the urine into a second. In small babies there may be little urine in the bladder, and under these circumstances the first bottle has to be used for bacteriological examinations.

Effect of Polybactrin Catheterization on Bacterial Growth in the Urine

In most cases the antibacterial activity of the urine obtained after catheterization was determined by means of indicator plates sown with an antibiotic-sensitive staphylococcus and filter-paper discs saturated with urine (Gould, 1965). Such activity was shown in 69% of specimens, and the average zone of elimination was 5–6 mm. This is a very limited antibacterial effect. Experience with this method shows that it is unusual to find bacterial counts in the lower range of 10^3 or 10^4 /ml. If a growth is obtained it is usually of the order of 10^5 or greater/ml. This clear differentiation is probably due to the mild antibacterial effect of the Polybactrin in the urine inhibiting growth of contaminants. With this technique a bacterial count of 10^4 or higher/ml. was considered to indicate infection.

As regards cell counts in catheterized patients infection was reckoned to be present if the count exceeded 10/cu. mm.

Results

Cell counts, bacterial counts, organisms cultured, and urinary pH are shown in the Table. The criteria for infection in catheter specimens were either or both of the cell and bacterial counts given above and, for non-catheterized specimens, one or more of the cell counts, bacterial counts, and combined cell and bacterial counts ("combined counts") given by Braude *et al.* (1967) as indicative of infection. In columns 7, 8, and 9 of the Table positive or negative signs indicate whether or not these criteria were met.

* Royal Infirmary, University of Edinburgh and
† Royal Infirmary, Edinburgh.

Summary of Results

Case No.	Age	Sex	Type of Collection	Cell count/cu. mm.	Bact. count/ml.	Diagnostic Criteria			Culture	pH
						Cells	Bact. count	Cells and Bact. count		
I.—Cases in which non-catheter and catheter specimens corresponded and in which infection was thought to be present										
1	9 dy.	M	MSU C	2,000 2,000	10 ⁵ 10 ⁵	+	+	+	Coliforms Coliforms	6 6
2	1 mo.	M	MSU C	1,000 1,000	10 ⁷ 10 ⁷	+	+	+	E. coli E. coli	6 6
3	1 mo.	M	MSU C	1,000 1,000	10 ⁷ 10 ⁶	+	+	+	E. coli E. coli	6 6
4	1 mo.	M	MSU C	15 15	10 ³ NG	+	+	—	Staph. albus	6 6
5	6 wk.	M	MSU C	8 50	10 ⁵ 10 ⁵	+	+	+	E. coli E. coli	6 6
6	7 wk.	M	MSU C	1,000 1,000	10 ⁶ 10 ⁷	+	+	+	Coliforms Coliforms	6 6
7	5 mo.	M	MSU C	2,000 2,000	10 ⁷ 10 ⁶	+	+	+	E. coli E. coli	6 6
8	5 mo.	F	MSU C	100 100	10 ⁶ 10 ⁷	+	+	+	E. coli E. coli	7 7
9	6 mo.	M	MSU C	45 12	10 ⁷ 10 ⁵	+	+	+	E. coli E. coli	7 7
10	11 mo.	M	MSU C	1,000 70	10 ⁸ 10 ⁵	+	+	+	Proteus Proteus	8 6
11	1 yr.	F	MSU C	2,000 2,000	10 ⁷ 10 ⁷	+	+	+	E. coli E. coli	6 6
12	1 yr.	M	Bag C	400 200	10 ⁶ 10 ⁶	+	+	+	Staph. pyog. Staph. pyog.	6 6
13	2 yr.	F	MSU C	140 200	10 ⁷ 10 ⁷	+	+	+	E. coli E. coli	6 6
14	3 yr.	F	MSU C	500 100	10 ⁷ 10 ⁵	+	+	+	Proteus Proteus	8 8
15	4 yr.	F	MSU C	1,000 1,000	10 ⁷ 10 ⁷	+	+	+	E. coli E. coli	7 7
16	5 yr.	F	MSU C	100 45	10 ⁸ 10 ⁵	+	+	+	E. coli E. coli	6 6
17	5 yr.	F	MSU C	1,000 500	10 ⁶ 10 ⁶	+	+	+	Proteus Coliforms	8 6
18	6 yr.	F	MSU C	200 125	10 ⁵ 10 ⁵	+	+	+	E. coli E. coli	6 6
19	8 yr.	M	MSU C	0 0	10 ⁷ 10 ⁴	+	+	+	E. coli E. coli	6 6
20	8 yr.	F	MSU C	120 100	10 ⁷ 10 ⁷	+	+	+	E. coli E. coli	6 6
21	9 yr.	F	MSU C	200 50	10 ⁷ 10 ⁷	+	+	+	E. coli E. coli	7 7
22	9 yr.	F	MSU C	40 150	10 ⁸ 10 ⁶	+	+	+	E. coli E. coli	6 6
23	9 yr.	F	MSU C	25 1,000	NG 10 ⁵	+	+	+	E. coli E. coli	7 6

II.—Cases in which non-catheter and catheter specimens corresponded and in which no infection was thought to be present

24	10 dy.	F	Bag C	125 1	10 ⁵ NG	—	—	—	<i>E. coli</i> ; <i>Proteus</i>	6 6
25	11 dy.	M	MSU C	2 0	10 ⁴ 10 ⁵	—	—	—	<i>E. coli</i> <i>E. coli</i>	6 6
26	13 dy.	F	Bag C	27 0	10 ⁵ NG	—	—	—	<i>E. coli</i> ; <i>Proteus</i>	6 6
27	2 wk.	F	Bag C	0 0	10 ⁶ NG	—	—	—	<i>E. coli</i> <i>E. coli</i>	6 6
28	2 wk.	F	MSU C	0 0	10 ⁶ NG	—	—	—	<i>Str. faec.</i> ; <i>Staph. pyog.</i>	6 6
29	1 mo.	F	MSU C	0 0	10 ⁴ —	—	—	—	<i>Proteus</i> ; <i>Proteus</i> ; <i>Str. faec.</i> ; <i>E. coli</i>	6 6
30	4 mo.	F	Bag C	0 0	10 ³ NG	—	—	—	<i>E. coli</i>	6 6
31	5 mo.	M	MSU C	0 0	10 ⁵ —	—	—	—	<i>Proteus</i> ; <i>Str. faec.</i> ; <i>Proteus</i> ; <i>Str. faec.</i>	6 6
32	5 mo.	F	MSU C	2 0	10 ⁵ NG	—	—	—	<i>E. coli</i>	6 6
33	5 mo.	F	Bag C	16 0	10 ⁵ NG	—	—	—	<i>Proteus</i>	6 6
34	5 mo.	F	Bag C	20 10	10 ⁶ 10 ⁶	—	—	—	<i>E. coli</i> <i>Staph. albus</i>	6 6
35	6 mo.	F	MSU C	0 0	10 ⁶ NG	—	—	—	<i>Staph. pyog.</i>	6 6

Summary of Results—Continued

Case No.	Age	Sex	Type of Collection	Cell count/cu. mm.	Bact. count/ml.	Diagnostic Criteria			Culture	pH
						Cells	Bact. Count	Cells and Bact. Count		
36	7 mo.	M	Bag MSU	0 0	10 ³ 10 ⁴	—	—	—	<i>Proteus</i> <i>Proteus</i> ; <i>Str. faec.</i>	6 6
37	7 mo.	F	MSU C	0 0	NG 10 ⁶	—	—	—	<i>Proteus</i> ; <i>Str. faec.</i>	6 6
38	8 mo.	F	MSU C	1 0	10 ⁶ NG	—	—	—	<i>Proteus</i> <i>Str. faec.</i>	6 6
39	10 mo.	M	Bag MSU	0 0	10 ⁶ 10 ⁶	—	—	—	Coliforms; <i>Proteus</i>	6 6
40	10 mo.	F	MSU C	0 0	10 ⁶ NG	—	—	—	<i>E. coli</i>	6 6
41	1 yr.	F	MSU C	30 0	10 ⁶ 10 ⁵	—	—	—	<i>Proteus</i> <i>Proteus</i> <i>Proteus</i>	6 6
42	2 yr.	F	MSU C	0 0	10 ⁵ 10 ⁵	—	—	—	<i>E. coli</i> <i>E. coli</i> ; <i>Str. faec.</i> ; <i>Staph. albus</i>	6 6
43	2 yr.	F	Bag MSU	3 3	10 ⁵ 10 ⁴	—	—	—	<i>Proteus</i> <i>Proteus</i> ; <i>Str. faec.</i>	6 6
44	2 yr.	F	MSU C	30 0	<10 ³ NG	—	—	—	<i>E. coli</i> ; <i>Staph. albus</i>	6 6
45	3 yr.	F	MSU C	0 0	10 ⁴ NG	—	—	—	<i>Micrococcus</i>	6 6
46	5 yr.	F	MSU C	0 0	10 ⁷ 10 ⁷	—	—	—	<i>Str. faec.</i> <i>Str. faec.</i>	6 6
47	5 yr.	F	MSU C	0 0	10 ⁵ NG	—	—	—	<i>E. coli</i>	7 7
48	5 yr.	F	MSU C	30 10	10 ⁶ NG	—	—	—	<i>E. coli</i>	6 6
49	5 yr.	M	MSU C	0 0	10 ⁴ NG	—	—	—	Coliforms	6 6
50	7 yr.	M	MSU C	0 0	10 ⁴ NG	—	—	—	<i>E. coli</i>	6 6
51	8 yr.	M	MSU C	3 0	10 ⁴ NG	—	—	—	<i>E. coli</i> ; <i>Str. faec.</i>	7 7
52	9 yr.	F	MSU C	0 0	10 ⁵ NG	—	—	—	<i>E. coli</i>	7 7
53	9 yr.	F	MSU C	5 7	10 ⁵ NG	—	—	—	<i>E. coli</i> <i>E. coli</i>	7 7
54	11 yr.	F	MSU C	0 0	10 ⁴ NG	—	—	—	Coliforms	6 6
III.—Non-catheter specimens showing infection: catheter specimens negative										
55	1 wk.	F	Bag C	2,000 0	10 ⁴ 10 ⁵	+	—	—	<i>E. coli</i> ; <i>Staph. albus</i>	6 6
56	3 mo.	F	MSU C	1,000 0	10 ⁴ NG	+	—	—	<i>E. coli</i> ; <i>Str. faec.</i>	6 6
57	4 mo.	F	Bag C	160 0	10 ⁴ NG	+	—	—	<i>Klebsiella</i>	6 6
58	5 yr.	F	MSU C	0 0	10 ⁸ NG	—	+	—	<i>E. coli</i>	6 6
59	7 yr.	M	MSU C	350 0	10 ⁷ NG	+	—	+	<i>E. coli</i>	6 6
60	8 yr.	F	MSU C	200 25	10 ⁵ 10 ⁵	+	—	+	<i>E. coli</i> <i>E. coli</i>	8 8
61	9 yr.	F	MSU C	50 9	10 ¹⁰ 10 ¹⁰	+	+	+	<i>E. coli</i> <i>E. coli</i>	6 6
IV.—Non-catheter specimens negative: catheter specimens showing infection										
62	1 yr.	F	MSU C	0 50	10 ⁵ 10 ⁶	—	+	—	<i>E. coli</i> <i>E. coli</i>	6 6
63	1 yr.	F	MSU C	0 500	10 ⁵ 10 ⁹	—	+	—	<i>Proteus</i> <i>Proteus</i>	8 8
64	4 yr.	F	MSU C	0 0	10 ⁶ 10 ⁷	—	+	—	<i>E. coli</i> <i>E. coli</i>	8 8
65	5 yr.	F	MSU C	0 0	10 ⁵ 10 ⁵	—	+	—	<i>E. coli</i> <i>E. coli</i>	6 6
66	6 yr.	F	MSU C	50 30	10 ⁴ <10 ³	—	+	—	<i>E. coli</i> <i>E. coli</i>	6 6
67	7 yr.	F	MSU C	0 0	10 ⁷ 10 ⁷	—	+	—	<i>E. coli</i> <i>E. coli</i>	7 7
68	9 yr.	F	MSU C	60 5	10 ⁵ 10 ⁵	—	+	—	<i>E. coli</i> <i>E. coli</i>	7 7

MSU = Midstream urine. C = Catheter urine.

In making comparison between catheter and non-catheter urines evidence of infection in the catheter urine was considered to indicate genuine infection (with the exception of two cases mentioned later).

Correlation between Non-catheter and Catheter Specimens

The technique of catheterization should reduce to a minimum contamination with cells and bacteria and growth of any contaminant. The Polybactrin may even have caused some reduction in the bacterial count in infected cases. Thirty-nine (57%) of the catheter urines showed no growth on culture. Twenty-nine (43%) showed a growth—two with counts of less than 10^3 /ml., one with a count of 10^4 /ml., and the remainder with counts of 10^5 or more/ml. In contrast only 3 of the 76 (4%) midstream urines showed no growth and none of the 16 bag urines did so. The bacterial count in these urines ranged much more widely.

The Table is divided into four groups. The first of these contains 23 cases in which the urine was thought to show evidence of infection in both catheter and non-catheter specimens. In all but three of the catheter specimens (87%) both cell count and bacterial count were "positive." In the non-catheter specimens all of the three possible criteria (cell count, bacterial count, and combined count) were positive in 9 cases (39%), two in 10 cases (44%), and one in 4 cases (17%). Combined counts alone were positive in 21 of the 23 cases (92%), cell counts in 19 cases (83%), and bacterial counts in 11 cases (48%). Thus combined counts were most effective and single bacterial counts least effective in diagnosis.

In all 23 infected cases a single species of pathogens was isolated in pure culture, and, apart from one case in which the organisms were different and two in which in the catheter specimen there was no growth, the same organism was found in the catheter and non-catheter specimens.

The second group in the Table consists of 31 cases in which there was no evidence of infection, according to the criteria indicated above, in either catheter or non-catheter specimens. In these cases, in contradistinction to the infected cases, there were 12 in which a mixed flora was isolated or different species were obtained from catheter and non-catheter urines.

In the third group in the Table are seven cases in which the non-catheter specimen showed evidence of infection but the catheter specimen was negative. In five of these (Cases 55, 56, 57, 58, and 60) it seemed likely that the non-catheter specimens had given false-positive results. The symptomatology was unconvincing, the criteria were only minimally positive, a subsequent specimen in two of them was negative or there was a mixed growth. In two (Cases 59 and 61) the findings in the non-catheter urine were probably correct. Both had symptoms very suggestive of urinary tract infection, and pure growths of *Escherichia coli* were obtained. One of them produced two positive non-catheter specimens, each with bacterial counts of 10^{10} /ml. Imperfections in the catheterization technique with the escape of Polybactrin into the bladder might account for the occurrence of occasional false bacteriological negatives in catheter specimens.

The fourth section of the Table comprises seven cases in which a non-catheter specimen was negative but the catheter specimen positive. In three of these (Cases 63, 64, and 67) the urinary pH was 8, 8, and 7 respectively and there was an absence of cells. Thus the alkaline pH may have created false negativity in the non-catheter urines by reducing the cell count. In Case 66 the symptoms were very suggestive of urinary tract infection, and in Case 68 the criteria in the non-catheter specimen of urine just missed being positive. In the remaining cases (Nos. 62 and 65) there was no additional supportive evidence in either direction and the catheter urine is thought to be the valid one.

Thus there was correspondence between catheter and non-catheter specimens in 54 of the 68 cases (80%). Excluding

Cases 59 and 61, five (7%) of the non-catheter specimens gave false-positive results and seven (10%) false-negative results.

As a check on the cases which were catheterized and thought to be non-infected three successive non-catheter specimens of urine were obtained from each six weeks later. These showed no evidence of infection.

Discussion

In the collection of urine from young children, particularly females, the use of adhesive plastic bags is the simplest procedure, but even when the bags are removed as soon as urine is passed into them a considerable amount of contamination has already occurred (Braude *et al.*, 1967). Ideal "clean-catch" midstream specimens from girls can at times be obtained only after many attempts and many hours of patience. Where such specimens are very carefully collected by specially trained nursing staff, after preparation of perineum and vulva with antiseptic solution, bacterial counts approximate to those found in specimens obtained by catheter and suprapubic aspiration (Pryles and Steg, 1959; Pryles *et al.*, 1959, 1961), but there are many circumstances where it is difficult or impossible to obtain such specimens—in the home, the busy outpatient department or ward, with refractory children. Criteria applicable to specimens obtained from adults and to "ideal" specimens from children are often widely applied to routine specimens, so that a false-positive diagnosis of urinary tract infection is a very frequent occurrence in paediatric practice. There does, therefore, appear to be a case for setting standards by which bag urines and midstream urines which may not be entirely ideal can be used in making the diagnosis of urinary tract infection.

Cell counts and pH must be on fresh specimens, and bacterial counts be carried out within half an hour of micturition, or if a longer time is to elapse the urine must be refrigerated at 4° C. This can be simply achieved during transmission to a laboratory by placing the specimen in its container in a vacuum flask containing an ice pack.

With these methods it seems likely that the diagnosis of urinary tract infection can be made in a high proportion of cases from examination of a single routine specimen of urine. If it is accepted that 32 of our cases were in fact suffering from urinary tract infection 25 (78%) were effectively diagnosed in this way. As regards the five false-positives, two showed a mixed growth in the urine, which should always raise diagnostic doubts, and in two a second non-catheter specimen was negative.

Of more importance are the seven (10%) false-negatives. Clearly if a certain amount of contamination is accepted in a large majority of specimens and standards for cell and bacterial counts are adjusted accordingly a specimen which, by accident as it were, is collected ideally may show lower cell and bacterial counts in the presence of infection, corresponding more to the standards in specimens obtained by catheter. A high urinary pH may also predispose to false negativity.

Recognizing that in a small number of infected cases cell and bacterial counts from single non-catheter specimens will not reach the diagnostic standards which have been set, there would need to be a safeguard in the use of these standards. We suggest a "re-examination" standard which, though it would not indicate infection, would indicate the need to obtain a further specimen of urine before a diagnosis could be made. A suitable standard for this would be a cell count of 10 or higher/cu. mm. combined with a bacterial count in males of 10^5 or more/ml. and in females of 10^6 or more/ml. That these standards are not suitable for making a diagnosis of urinary tract infection is shown by the fact that over 60% of the non-infected cases reached them.

The opinion is widely held that catheterization of the bladder is an important cause of urinary tract infection (Ansell, 1962). The risk of infection in children has probably been overstated

(Pryles *et al.*, 1959), though it was thought to be 7% in one series (Virtanen *et al.*, 1962). The method of catheterization which we have used has been widely and successfully employed in the catheterization of paraplegic patients, in whom the risk of infection is very high (McLeod *et al.*, 1963). Though catheterization of the urinary bladder is undesirable for other reasons as well as the possible risk of infection, there are instances where it is indicated. One of these would be continuing doubt about the diagnosis of urinary tract infection in children after the examination of non-catheter specimens. The method described here seems to be a safe and practical one.

Summary

Non-catheter (bag or midstream specimen) and catheter specimens of urine from 68 children suspected to be suffering from infection of the renal tract have been compared. Accepting the catheter specimen predominantly as the indicator of urinary tract infection, it was concluded that 32 children (47%) were suffering from pyelonephritis.

With the use of certain specified diagnostic criteria on single non-catheter specimens of urine 25 (78%) of the infected cases were diagnosed positively. In the 68 cases there were only five (7%) false-positives among the non-catheter specimens, suggest-

ing that the criteria used reduce significantly the high incidence of false-positive results which tends to occur with random non-catheter specimens.

Means by which false-negative results can be avoided include a "re-examination" standard and consideration of urinary pH.

A method of bladder catheterization in children with the use of a Polybactrin technique appears to be safe and can be used in cases where diagnoses cannot be readily established from non-catheter specimens.

J. W. M. wishes to thank the Royal Society for a grant for expenses, the M.R.C. for the provision of technical assistance, and Messrs. Calmic for supplies of Polybactrin G.U.

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"Clean Catch" Urines in the Newborn—Bacteriology and Cell Excretion Patterns in First Week of Life

GILLIAN CRUICKSHANK,* M.B., B.CH., D.C.H.; ELIZABETH EDMOND,† M.B., CH.B.

Brit. med. J., 1967, **4**, 705-707

Urinary tract infection in the newborn may not be uncommon (Stansfeld, 1954, 1966; Lincoln and Winberg, 1964a; Smellie *et al.*, 1964). Clinical signs may be variable or absent, and diagnosis depends on the demonstration of a significant bacteriuria. However, in the absence of a reliable and simple method of collection of specimens diagnosis is difficult. Catheterization and suprapubic puncture are probably not acceptable as routine procedures (Pryles, 1965). The reliability of three supervised "clean catch" specimens of urine in the newborn has been assessed by bacteriological techniques, with particular reference to the problem of contamination. At the same time the urinary cell-excretion pattern in the first week of life was studied by means of a differential staining technique (Prescott and Brodie, 1964).

Method

Forty babies (21 male and 19 female) who were free from recognized infection and not receiving antibiotics were included in the study. Details of delivery and drug therapy in the mother were noted. A clean-catch specimen, personally supervised by one of us, was collected from each baby on the second, fourth, and sixth day of life. The buttocks and perineum were well cleansed with soap and water only, the labia were separated, but the foreskin was not retracted. The skin was dried with a sterile swab. The baby was supported with the

thighs abducted, and any urine passed was collected directly into a sterile container, which was not allowed to come into contact with the baby's skin at any time. If no urine was passed within 20 minutes the baby was rewashed or the collection postponed until a more opportune moment. Urine specimens were discarded if there was a simultaneous bowel movement and further specimens collected only after rewashing.

The collected specimen was divided into two portions. One was refrigerated and transported to the bacteriological laboratory in a cooled vacuum flask. A maximum of four hours occurred between collection and plating. Quantitative bacteriological culture was carried out as described by Urquhart and Gould (1965). Blood agar and MacConkey plates were inoculated and incubated aerobically for 24 hours. The second portion was examined microscopically within two hours of collection. For staining, 2:7-diaminofluorene phloxine-B was used as described by Prescott and Brodie (1964), thereby allowing differentiation of leucocytes and renal tubular cells. Examination of the uncentrifuged, well-shaken, and stained urine was carried out on an improved Neubauer counting-chamber, counting five squares and multiplying by two (Lawson and Hewstone, 1964).

Results

One hundred and twenty "clean catch" specimens were collected from the 40 babies. A total of 103 specimens (86%) produced on culture a colony count of 10^4 organisms per ml. or less, and 71 of these specimens (59%) produced no growth on culture (Table I). If a level of 10^5 organisms per ml. is

* Paediatric Registrar, Elsie Inglis Maternity Hospital, Edinburgh.
 Present appointment: Scientific Staff, Medical Research Council, Western General Hospital, Edinburgh.
 † Registrar in Bacteriology, Central Microbiological Laboratory, Western General Hospital, Edinburgh.

taken as significant of infection 86% of these specimens could be regarded as showing no evidence of infection.

Table II indicates how the 71 specimens producing no growth on culture were distributed. There were only five babies from whom all three specimens produced growth.

Bacteria were isolated from a total of 49 specimens (41%). The distribution of species and viable count from these 49 was as shown in Table III. For the purpose of this Table, *Staphylococcus albus*, corynebacteria, and *Streptococcus viridans* are regarded as skin commensals, while *Escherichia coli*, non-lactose-fermenting coliforms, *Proteus* species, and enterococci are classed as potential pathogens.

Seventeen specimens produced counts greater than 10^4 organisms per ml. In seven of these skin commensal bacteria were present, suggesting an "unclean" specimen and indicating the necessity for repeating the examination. Ten specimens collected from seven babies produced a high count of potential pathogens in either pure or mixed culture.

TABLE I.—Distribution of Bacterial Counts in 120 Clean-catch Specimens

Colony Count	Specimens	
	No.	%
No growth	71	59
Less than 10^3 organisms per ml. .. .	14	12
10^3 – 10^4 organisms per ml. (inclusive) .. .	18	15
10^5 organisms per ml. .. .	12	10
10^6 organisms per ml. .. .	5	4
	120	100

TABLE II.—Incidence of "No Growth" Cultures Among 40 Babies

	No. of Babies	No. of Specimens
"No growth" on 3 occasions .. .	14	42
"No growth" on 2 occasions .. .	8	16
"No growth" on 1 occasion only .. .	13	13
	35 (87.5%)	71 (59%)

TABLE III.—Analysis of Organisms Obtained from Clean-catch Urines

Count (orgs./ml.)	Total Specimens	Character of Isolate			
		Pathogens in Pure Culture	Pathogens in Mixed Culture	Mixed Pathogens and Commensals	Commensals in Pure Culture
Less than 10^3	14	2	1	8	3
10^3 – 10^4	18	7	5	3	3
10^5	12	4	3	4	1
10^6	5	2	1	2	0

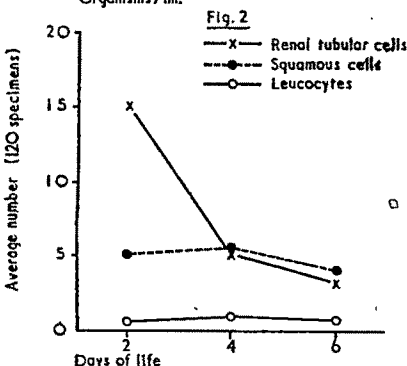
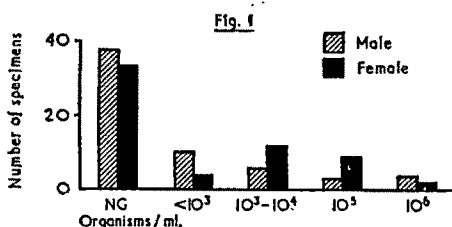
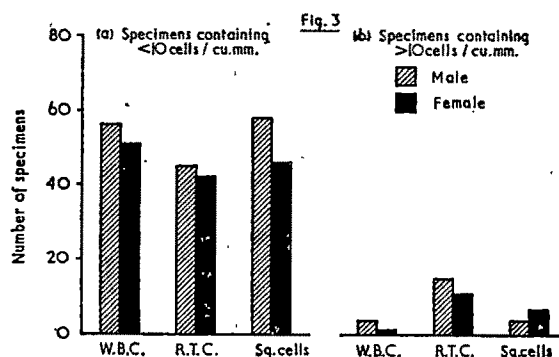


FIG. 1.—Sex ratio in bacterial counts. FIG. 2.—Cell excretion patterns in first week of life. FIG. 3.—Sex ratio in cell counts.



In one baby two specimens producing no growth on culture were followed by a growth of mixed pathogens to a count of 10^5 organisms per ml. Four babies each produced two specimens with high mixed counts, but the third specimen in each case yielded no growth. In two babies there was growth from all three specimens and a high count of pathogens in one specimen from each. The other specimens from both babies produced smaller counts of pathogens, and in neither baby was the species isolated identical in all three specimens. Progress during the first week of life was normal in both babies, and follow-up was uneventful. Later specimens from these babies repeatedly produced no growth.

As shown in Fig. 1, there was no marked difference in the sex distribution of the colony counts, though there was a tendency for female infants to predominate in the 10^3 to 10^4 and 10^5 organisms per ml. groups.

The pattern of urinary cell excretion in the first week of life is shown in Table IV and Fig. 2. The excretion of squamous cells and leucocytes remained at a low level throughout the first week, average counts of squamous cells ranging from 4.1 to 5.4 /cu. mm., and average counts of leucocytes varying from

TABLE IV.—Differential Urinary Cell Counts in First Week of Life

	Cellular Excretion per cu. mm. in First Week of Life					
	2nd Day		4th Day		6th Day	
	Average	Range	Average	Range	Average	Range
Renal tubular cells ..	14.9	0–40	5.1	0–16	3.0	0–16
Squamous cells ..	5.0	0–36	5.4	0–32	4.1	0–32
Leucocytes ..	0.5	0–46	1.2	0–27	0.8	0–21
Total cells ..	19.5		11.7		7.9	

0.5 to 1.2/cu. mm. The excretion of renal tubular cells shows a very different pattern, falling rapidly from a high average excretion rate of 14.9/cu. mm. on the second day to a low average value of 3 cells/cu. mm. on the sixth day. These cells were easily distinguished from leucocytes by the peroxidase-positive stain.

Ninety-six per cent. of specimens contained fewer than 10 leucocytes per cu. mm. These were collected from 57 males and 51 females. Of the four specimens containing more than 10 leucocytes per cu. mm. two were associated with a high count of mixed organisms suggestive of contamination, and subsequent specimens contained a smaller number of cells. One specimen was associated with dehydration of the newborn, and the fourth specimen, with a high white cell excretion, produced no growth on culture.

There was no correlation of bacterial counts and cell counts in this series. This is shown in Table V, where the apparently high leucocyte count associated with bacterial counts greater than 10^5 /ml. cannot be taken as significant in view of the small number involved (four), including one isolated count of 48 leucocytes per cu. mm. apparently associated with dehydration of the newborn.

The birth history and immediate postnatal progress of the babies were studied in relation to the renal tubular cell count. There were 19 babies showing one or more

counts of more than 10 renal tubular cells per cu. mm. (range 12–40). In 15 of these labour and the postnatal period were uneventful, and in four there was some complication. In the other 21 babies, none of whom produced specimens with high counts of renal tubular cells, there was a history of difficulty in delivery in four and a premature delivery in one.

Only nine (8%) specimens contained more than 10 squamous cells per cu. mm. These were collected from nine babies (six females and three males). While this suggests some sex difference, total numbers are small. No significant sex difference was found in the excretion of renal tubular cells or leucocytes (Fig. 3).

TABLE V.—Relation of Cell Counts to Bacterial Counts

		< 10 ⁵ /ml.	> 10 ⁵ /ml.
Renal tubular cells ..	Average	8	3.1
	Range	0–40	0–16
Squamous cells ..	Average	5	3.8
	Range	0–32	0–12
Leucocytes	Average	0.8	4.7
	Range	0–22	0–48

Discussion

The possibility of contamination in normally voided urine in the neonate has led to the use of catheterization (Pryles *et al.*, 1961; McCarthy and Pryles, 1963) and suprapubic bladder aspiration (Pryles *et al.*, 1959; Pryles, 1965; Nelson and Peters, 1965; Newman *et al.*, 1967) for the collection of urine specimens for diagnostic purposes. The inherent dangers of both techniques indicated the necessity for the reassessment of the value of clean-catch specimens in this age group. The presence or absence of infection in the urinary tract has been assessed by consideration not only of the viable count but also of the species isolated in three consecutive clean-catch specimens. A viable count of 10⁵ organisms per ml. in a carefully collected midstream specimen is suggestive in the adult of infection in the urinary tract (Kass, 1957). There has been doubt about whether this criterion can apply in the neonate (Nelson and Peters, 1965). Houston (1963) suggested that 10⁶ organisms per ml. or more is abnormal in neonates, but that with counts between 10⁵ and 10⁶ organisms per ml. confirmation of infection is required. In the present series 86% of specimens contained fewer than 10⁵ viable organisms per ml. and 59% produced no growth. This compares favourably with the 31% of specimens producing no growth in the series of McCarthy and Pryles (1963), and is a considerable improvement on series collected by the bag method (Newman *et al.*, 1967).

Urinary cell excretion in the neonate has been the subject of considerable study (Thomson, 1944; Houghton and Pears, 1957; James, 1959; Aas, 1961; Stansfeld, 1962; Lincoln and Winberg, 1964b; Lawson and Hewstone, 1964). In spite of this the number of leucocytes which may be accepted as normal remains in doubt. Lawson and Hewstone (1964) concluded that the finding of more than 10 white blood cells per cu. mm. on two or more occasions is abnormal. Lincoln and Winberg (1964b) fixed the highest acceptable normal number at 25/cu. mm. in males and 50/cu. mm. in females. In this series, with the use of a differential staining technique, 96% of specimens contained fewer than 10 leucocytes per cu. mm.

The high number of renal tubular cells excreted in the first few days of life has been noted by earlier workers (Craig, 1935; Thomson, 1944; Lawson and Hewstone, 1964). The similarity in size and shape of unstained renal tubular cells and leucocytes has in the past made differentiation difficult, but with the peroxidase-positive stain the particular pattern of renal tubular cell excretion emerges.

The high numbers present during the first few days of life have been ascribed to a period of rapid growth and shedding

of cells from the renal tract epithelium at this time of life (Aas, 1961). Hypoxia and renal shut-down have also been suggested as causative factors (Jonsson, 1951; Halvorsen and Aas, 1962). This series produced no evidence to support the latter view.

Conclusions

Normally voided urine can be collected from the newborn without gross contamination by a careful clean-catch technique. When three specimens are collected from one patient contamination rather than infection is suggested by variation in the number and species of organisms isolated from specimen to specimen. Viable counts of less than 10⁵ organisms per ml. are usually due to contamination. Higher counts may also be due to contamination, and the presence of infection should be suspected only when counts of 10⁵ organisms per ml. or more of the same species are isolated in at least two consecutive specimens. This procedure is time-consuming, and personal supervision is essential, but it is without hazard to the infant. Only when every effort has been made to reach a conclusive diagnosis on the results of specimens collected in this way should other methods of urine collection be contemplated.

The newborn infant excretes a large number of renal tubular cells which may be confused with leucocytes if a differential stain is not used. The number of renal tubular cells excreted falls rapidly during the first week of life, while the excretion of leucocytes and squamous cells remains relatively constant. Leucocyte counts up to 10/cu. mm. can be accepted as normal in both sexes.

The value of using a simple differential stain, as described above, when carrying out microscopical examination of the urine is emphasized.

Summary

Three specimens of urine were collected from each of 40 babies on the second, fourth, and sixth day of life. A clean-catch technique was employed and shown to be a reliable method of urine sampling.

The cell excretion pattern during the first week of life was studied. Ninety-six per cent. of specimens contained fewer than 10 leucocytes per cu. mm. A high rate of excretion of renal tubular cells was observed during the first few days of life.

We would like to thank Professor J. O. Forfar and Dr. J. C. Gould for their helpful criticism and encouragement. Also we would like to acknowledge the co-operation of the nursery nursing staff at the Elsie Inglis Maternity Hospital, Edinburgh.

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Haemoglobin Concentration and Other Values in Women Using an Intrauterine Device or Taking Corticosteroid Contraceptive Pills

J. ALAGHBAND ZADEH,* L.M.S.S.A.; C. D. KARABUS,† M.B., M.MED.(PAED.), M.R.C.P.
J. FIELDING,‡ M.R.C.P., F.C.PATH.

Brit. med. J., 1967, 4, 708-711

Surveys have shown that 20-25% of women in this country have iron-deficiency anaemia with haemoglobin concentrations less than 12 g./100 ml. (Davidson *et al.*, 1943; Kilpatrick and Hardisty, 1961). In addition, about 30% of apparently normal women with haemoglobin above 12 g./100 ml. have been shown to be sideropenic (Fielding *et al.*, 1965; de Leeuw *et al.*, 1966.)

Two of the newer methods of contraception now being widely adopted—the intrauterine device and oral corticosteroid contraceptive pills—are both said from subjective observation to alter menstrual blood loss: the intrauterine device to increase it, the oral corticosteroids to diminish it. In neither case have these changes been quantitated. However, iron balance in adult women is so precarious that changes in blood loss are likely to lead to changes in the incidence and severity of iron deficiency.

The present paper reports a pilot survey of 219 women attending a Family Planning Association clinic. We find that the continued use of an intrauterine device leads to a significant fall in the mean haemoglobin concentration and to an increase in the incidence of anaemia. The steroid contraceptive pill of "combined" formulation leads to an increase in the concentration of haemoglobin, but the results suggest that the effect may be a complex one.

Methods and Clinical Material

A total of 294 women attending a Family Planning Association clinic were investigated. Seventy-five have been excluded from the analysis. These consisted of blood donors, women who had been pregnant or who had received iron therapy within the previous six months, those who attended for gynaecological abnormalities, a small number who were using other mechanical methods of contraception, and those who had previously used an intrauterine device and who were now taking oral contraceptives or vice versa. Also among those excluded were 13 women who were taking oral contraceptive pills with a sequential formulation, since they were too few for statistical analysis.

The remaining 219 women are divided into three groups: (1) a control group of 53 women who were attending the clinic for the first time; (2) 72 who had been fitted with an intrauterine contraceptive device, almost all of the Lippes loop type; and (3) 94 who had been taking oral contraceptive pills with a combined formulation of various types, which included Anovlar, Gynovlar, Lyndiol, Ortho-Novin, Ovulen, and Ovrin.

A venous sample was taken from each patient by a standard technique to ensure minimal venous stasis. Haemoglobin was estimated in duplicate by the cyanmethaemoglobin method, the packed cell volume (P.C.V.) in duplicate by a microhaematocrit method, and the mean corpuscular haemoglobin concentration (M.C.H.C.) was calculated from these observations.

The validity of considering women who were attending the clinic for the first time as a control group was ascertained, after

the investigation had been completed, by dividing these into two groups according to the method of contraception subsequently advised by the medical staff of the clinic. Since the type of contraceptive advice depended on clinical observations, differences in age group and parity were expected between the groups assigned to contraceptive pills or to intrauterine device. Table I shows that the intrauterine device is advised for women of higher age group and greater parity than those given the contraceptive pill. Nevertheless, there are no haematological differences between the two subgroups, and therefore the use of the combined group of 53 women appears to be a valid control for the haematological values investigated.

TABLE I.—53 Women Attending Clinic for the First Time. Means $\pm$ Standard Error

	No.	Age (Years)	Parity	Haemoglobin (g./100 ml.)	P.C.V. (%)	M.C.H.C. (%)
Control group	53	27.8 $\pm$ 0.81	1.7 $\pm$ 0.21	13.4 $\pm$ 0.11	40.2 $\pm$ 0.26	33.4 $\pm$ 0.17
Assigned to I.U.D. ..	32	30.3 $\pm$ 0.97	2.2 $\pm$ 0.20	13.4 $\pm$ 0.15	39.9 $\pm$ 0.47	33.5 $\pm$ 0.20
Assigned to C.P. ..	21	23.9 $\pm$ 0.90	0.8 $\pm$ 0.35	13.5 $\pm$ 0.15	40.5 $\pm$ 0.33	33.3 $\pm$ 0.32
Student's <i>t</i> ..		<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> > 0.5	<i>P</i> > 0.9	<i>P</i> > 0.9

I.U.D. = Intrauterine device. C.P. = Contraceptive pill.

It should be stressed here that in this survey only one investigation was made in each subject. The control group and the groups on contraceptives for varying periods of time consisted of different women. Mean values are given in the results with their standard errors.

Effect of Intrauterine Contraceptive Device

Age and parity in this group were similar to those of the control subgroup subsequently assigned to the intrauterine device. Their mean haemoglobin concentration was 12.8 $\pm$ 0.12 g./100 ml. compared with 13.4 $\pm$ 0.11 g. in the controls (*P* < 0.01). The packed cell volume also showed a significant decrease (*P* < 0.001); the M.C.H.C. in the group as a whole was less than that in the control women but failed to reach significant levels of difference. Table II summarizes these results.

The three values decreased progressively up to 12 months of use. The fall in M.C.H.C. followed later than that in the haemoglobin and was significantly reduced after 7 to 12 months' use. Later the trend appears to reverse, with a general increase

TABLE II.—Haemoglobin, P.C.V., and M.C.H.C. in Women Using an Intrauterine Device. Means $\pm$ Standard Error

	No.	Haemoglobin (g./100 ml.)	P.C.V. (%)	M.C.H.C. (%)
Control group	53	13.4 $\pm$ 0.11	40.2 $\pm$ 0.26	33.4 $\pm$ 0.17
I.U.D.				
After 1-6 months	38	12.8 $\pm$ 0.14*	38.3 $\pm$ 0.38†	33.4 $\pm$ 0.24
" 7-12 "	20	12.3 $\pm$ 0.29*	37.7 $\pm$ 0.66†	32.5 $\pm$ 0.34‡
" 13-24 "	14	13.0 $\pm$ 0.24	39.6 $\pm$ 0.65	32.8 $\pm$ 0.38
Total	72	12.8 $\pm$ 0.12*	38.3 $\pm$ 0.33†	33.1 $\pm$ 0.18

Student's *t* compared with control group: * *P* < 0.01; † *P* < 0.001; ‡ *P* < 0.02.

* Registrar in Pathology, Paddington General Hospital, London W.9.

† Research Registrar in Haematology, Paddington General Hospital, London W.9.

‡ Consultant Haematologist, Paddington General Hospital, London W.9.

in values after 12 to 24 months. The changes in these measurements are emphasized by noting that after 7 to 12 months no women had haemoglobin levels above 14 g./100 ml., while 60%

TABLE III.—Haemoglobin Concentration

	No.	More than 14 g./100 ml.		Less than 13 g./100 ml.	
		No.	%	No.	%
Controls	53	10	18.9	11	20.8
I.U.D.	72	4	5.6	35	48.6
Student's <i>t</i>		$P < 0.05$		$P < 0.01$	

of them were below 13 g./100 ml. (Fig. 1). The proportion of women with haemoglobin concentration 'outside these limits is significantly different in the intrauterine device group than among the controls (Table III). The deterioration in haematological status is also apparent in the distribution of M.C.H.C.; it is bimodal in the control group, but changes to a single distribution around the lower mode after 7 to 24 months' use (Fig. 2).

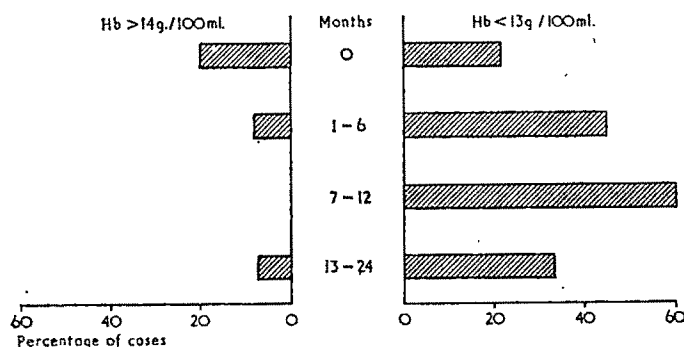


FIG. 1.—Intrauterine device. Proportion of women with haemoglobin concentration above 14 g. and below 13 g./100 ml. after varying periods of time. 0=Control group.

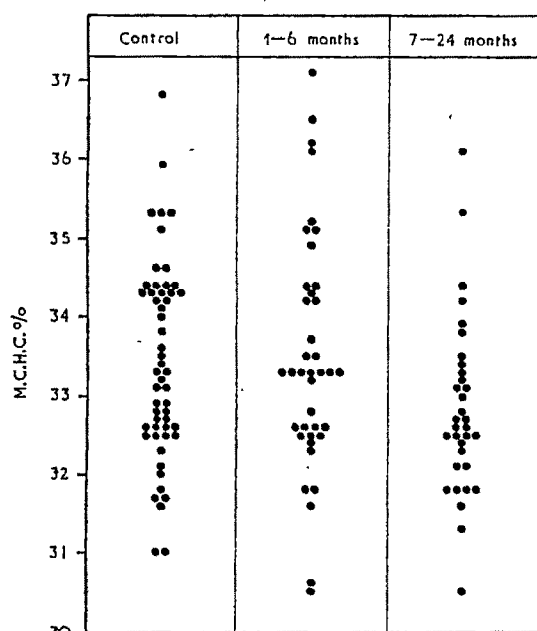


FIG. 2.—Intrauterine device. Scattergram of M.C.H.C. in controls and in women using an intrauterine device.

Effect of Contraceptive Pills

The age and parity of women taking contraceptive pills are similar to those of the subgroup of the controls subsequently advised to take the pill as their method of contraception. Table IV summarizes the findings. Haemoglobin values increase from a mean of 13.4 ± 0.11 g./100 ml. in the controls to 13.7 ± 0.10 g., but this increase fails to reach accepted levels of significance

($0.05 < P < 0.1$). The increase in P.C.V., however, is significant at the 1/50 level. There were no significant changes in the M.C.H.C.

TABLE IV.—Haemoglobin, P.C.V., and M.C.H.C. in Women Taking Contraceptive Corticosteroids. Means $\pm$ Standard Error

	No.	Haemoglobin (g./100 ml.)	P.C.V. %	M.C.H.C. (%)
Control group	53	13.4 ± 0.11	40.2 ± 0.26	33.4 ± 0.17
Contraceptive pill:				
After 1-6 months	31	13.7 ± 0.19	41.1 ± 0.68	33.3 ± 0.27
" 7-12 "	22	13.8 ± 0.19	41.1 ± 0.39	33.7 ± 0.35
" 13-24 "	19	13.5 ± 0.20	41.3 ± 0.48	32.8 ± 0.43
" > 24 "	22	13.7 ± 0.20	41.0 ± 0.41	33.4 ± 0.27
Total	94	$13.7 \pm 0.10^*$	$41.1 \pm 0.21^\dagger$	33.3 ± 0.16

Student's *t* compared with control: * $0.5 < P < 0.1$; $^\dagger P < 0.02$.

The rise in haemoglobin and P.C.V. occurs mainly in the first six months, with little change thereafter. These trends are emphasized by considering the proportion of women with haemoglobin concentration above 14 g. and below 13 g./100 ml. (Fig. 3). After taking contraceptive pills for one to six months and also after 7 to 12 months the proportion of women with haemoglobin above 14 g./100 ml. is increased compared with the control group ($P < 0.01$). Thereafter the differences are not significant.

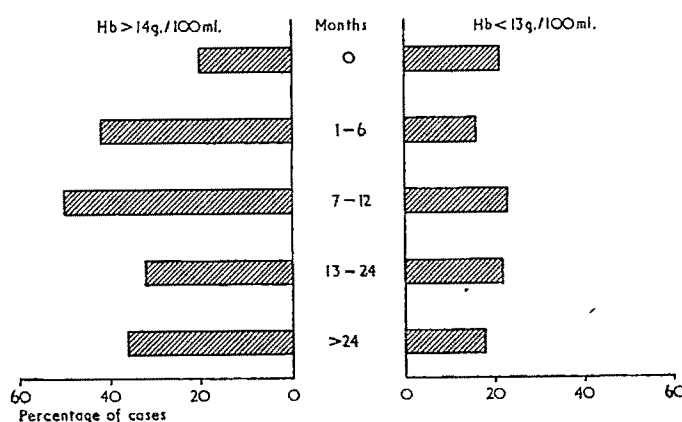


FIG. 3.—Contraceptive pills. Proportion of women with haemoglobin above 14 g. and below 13 g./100 ml. after varying periods of time.

However, though the increase in the proportion of women in the higher haemoglobin ranges is well marked, no changes were found in the proportion with haemoglobin levels below 13 g./100 ml. (Table V). This anomalous finding is discussed below.

TABLE V.—Haemoglobin Concentration

	No.	More than 14 g./100 ml.		Less than 13 g./100 ml.	
		No.	%	No.	%
Controls	53	10	18.9	11	20.8
Pill	94	38	40.4	18	19.1
Student's <i>t</i>		$P < 0.01$		$P > 0.8$	

Discussion

Intrauterine Device

It is evident from this survey that the intrauterine contraceptive device increases menstrual loss markedly, and affects the haematological status of women using it. Our results show a fall in haemoglobin values from a mean of 13.4 g./100 ml. to 12.8 g./100 ml. after 7 to 12 months' use. Perhaps more striking is the observation that after 7 to 12 months none of these women had haemoglobin concentrations above 14 g./100 ml., compared with about 19% in the control group; whereas 60%

had haemoglobin levels below 13 g./100 ml. compared with about 20% in the control group.

The fall in haemoglobin values is in general paralleled by a lesser fall in the haematocrit, as is usual in iron-deficiency anaemia, resulting in a decreasing M.C.H.C. It is interesting to note that the distribution of M.C.H.C. in the control group is bimodal, whereas this is replaced by a single mode at the lower level in women using the intrauterine device. It may be permissible to conclude that after 7 to 12 months' use the majority of women are suffering from varying degrees of iron-deficiency anaemia.

There appears to be a trend towards improvement after the intrauterine device has been used for more than a year. This may indicate that blood loss gradually returns to more normal values. However, it is more likely to mean a selection of cases during this time, since a study of the clinic records showed that about 25% of women fitted with an intrauterine device were no longer using it after two years.

The effect of such an increase in menstrual loss would not be experienced uniformly among all women. Those who began without anaemia would probably augment the intestinal absorption of iron and thus compensate in part for the effect of the increased loss; those who were already iron-depleted are also likely to be at the limit of their iron-absorption capability and would suffer a greater fall in haemoglobin for a given increase in loss. Thus the effect of the intrauterine device is relatively more severe in those who are already anaemic or iron-depleted.

This marked effect in inducing iron deficiency should be considered when giving contraceptive advice, and certainly in a programme of population control in less-developed countries.

Contraceptive Pill

Clinical observations on the reduction of menstrual loss in women taking oral contraceptives of combined formulation had prompted a search for possible changes in haematological status. Burton (1967) found a significant increase in haematocrit, and an increase in haemoglobin concentration which failed to reach 1/20 significant level. In our larger series we, too, have found a significant increase in haematocrit and an increase in mean haemoglobin concentration which we have analysed in greater detail. We observed no differences in the M.C.H.C.

The changes are more clearly demonstrated by considering the proportion of women with haemoglobin above 14 g./100 ml. and those below 13 g./100 ml. Of those taking contraceptive pills 40% had haemoglobin concentrations above 14 g./100 ml. compared with 19% in the control group ($0.001 < P < 0.01$). This increase in the proportion of haemoglobin concentration in the higher range seems to occur quite soon: after 1 to 6 months it was 42%, and at 7 to 12 months it was 50%.

It might be expected that an increase in haemoglobin concentration which resulted from diminished blood loss would be more readily detected in the range below 13 g./100 ml., which presumably includes minor degrees of anaemia, than in the higher range. We found, however, that the proportion of women with haemoglobin below 13 g./100 ml. did not appear to change significantly at any time up to two years compared with the control group. This anomalous finding suggests that the observed increase in haemoglobin concentration and in haematocrit is not due to a single factor, such as a diminution in blood loss, operating uniformly in all women.

The group taking pills were heterogeneous from several points of view. They varied, for instance, by age and parity. It is possible that, though haematologically similar before starting the pill, these differences might be correlated with differing responses to corticosteroids. We found, however, that there were no differences based on age or parity.

In all, six types of combined formulation of pill were used. We compared the effect of pills containing the progestogen norethisterone acetate with others and found a significant differ-

ence between the groups (Fig. 4). Furthermore, the difference between the mean haemoglobin concentration of women taking this progestogen was 13.8 g./100 ml. and reached significant levels of difference from the control group ($0.025 < P < 0.05$). Nevertheless, in this subgroup of pills containing norethisterone acetate, as in the pill group as a whole, the effect on haemoglobin concentration is more pronounced in the higher than in the lower ranges.

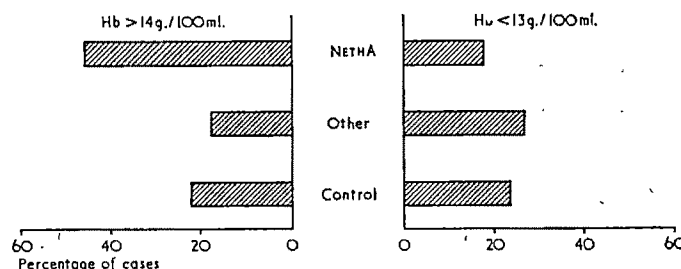


FIG. 4.—Contraceptive pills. Proportion of women with haemoglobin above 14 g. and below 13 g./100 ml. NethA=Pills containing norethisterone acetate.

We may only speculate at this stage on the significance of this finding. Haemoglobin mass may vary at differing rates from plasma volume. In pregnancy, to which the hormone status of "taking the pill" is most often compared, plasma volume increases relatively more than red cell mass and contributes to the fall in haemoglobin concentration seen in pregnancy. However, steroid status in pregnancy differs considerably from the use of the contraceptive pill, and there is no reason to expect similar haemodynamic changes. For instance, Burton (1967) shows that serum iron increases with the pill, whereas it falls in pregnancy; furthermore, some anabolic corticosteroids have been shown to produce haemoconcentration (Verwilghen *et al.*, 1966). A relative reduction in plasma volume occurring in some women, but not in others, might account for the uneven increase in haemoglobin concentration. Should haemoconcentration indeed be one of the effects of some combined formulations, the resulting increase in blood viscosity may have a bearing on the problem of thrombotic phenomena. Lastly, it is possible that hyperplasia of the marrow may occur as a result of corticosteroid stimulation, similar to the well-known hyperplasia seen in pregnancy.

Though we show an increase in haemoglobin concentration and in haematocrit in women taking oral contraceptives, the effect is irregularly distributed and we cannot be certain that the increase is due solely to diminished blood loss.

Summary

Haemoglobin concentration, P.C.V., and M.C.H.C. were estimated in 219 women attending a Family Planning Association clinic. In the control group of 53 women attending the clinic for the first time there was no difference in haematological status between those subsequently fitted with an intrauterine device and those advised to take the contraceptive pill.

Among 72 women who had been using an intrauterine device there was a progressive fall in mean haemoglobin concentration up to one year of use ($P < 0.001$). After 7 to 12 months' use none of these women had haemoglobin concentrations above 14 g./100 ml., while in 60% it was less than 13 g./100 ml. The changes in M.C.H.C. indicated that virtually all were iron-deficient after seven months' use.

In 94 women taking oral contraceptive pills of combined formulation the mean haemoglobin concentration was 13.7 ± 0.10 g./100 ml. compared with 13.4 ± 0.11 g. in the controls. The mean P.C.V. increased from 40.2 to 41.1 ($P < 0.02$). There were no changes in the M.C.H.C.

Forty per cent. of women taking the pills had haemoglobin concentrations greater than 14 g./100 ml. compared with 19%

in the control group. The increase in haemoglobin in the higher ranges occurred mainly in the first six months of use. In the range below 13 g./100 ml. there were no differences from the control group. Some formulations, especially those containing norethisterone acetate as progestogen have greater effect than others in raising haemoglobin concentrations.

Diminished blood loss alone does not account for all the changes observed. Haemoconcentration may occur in some subjects; if this is so the resulting increased viscosity may have some bearing on thrombotic phenomena. A further possible explanation is corticosteroid stimulation of bone-marrow activity.

We wish to thank the Managing Committee of the Family Planning Association, Dr. Hilary Hill, and Dr. Mary Pollock for

their helpful co-operation. The work was supported by grants from the Medical Research Council and the North-west Metropolitan Regional Hospital Board. Requests for reprints should be made to J. Fielding.

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Psychiatric Study of a Consecutive Series of 19 Patients with Regional Ileitis*

FRED FELDMAN, M.D.; DAVID CANTOR, M.D.; SIDNEY SOLL, M.D.; WILLIAM BACHRACH, M.D.

Brit. med. J., 1967, **4**, 711-714

This paper reports a study of psychiatric factors in regional ileitis. The study parallels a similar survey (Feldman *et al.*, 1967) in which we reported a series of 34 unselected cases of ulcerative colitis. In the latter inquiry a disease regarded by many psychiatrists as an unimpeachably psychosomatic illness was found to have probably no essential emotional causation.

Regional ileitis, a disease of obscure origin, has not attained the same almost classical reputation of ulcerative colitis as a psychosomatic illness. Nevertheless, since 1935 a number of authors have expressed the opinion that regional ileitis is a psychosomatic disease. A leading American textbook (Beeson and McDermott, 1967) stated: "It is thought that the repeated impact of emotional stress may give rise to dysfunction of the small intestine, with subsequent structural changes. This is supported by the clinical observation that recurrent symptoms are, at times, chronologically related to disturbing psychologic events."

Relation between Regional Ileitis and Ulcerative Colitis

The question is still open whether regional ileitis is actually a separate pathological entity from ulcerative colitis. Many physicians—for example, Eisenstadt (1965a), Ross (1965), and Crohn (1965)—say they are but different manifestations of the same disease. If this is true, then why has there been such prominence given to the notion of ulcerative colitis as a psychosomatic disease compared with the lesser emphasis on regional ileitis? The question is still very controversial. However, evidence for suspecting that there is a strong relation between the two diseases is found in: (1) their beyond-chance genetic coincidence (Crohn and Yarnis, 1958; Sherlock *et al.*, 1963; Edwards and Truelove, 1964; McConnell, 1965); (2) the association of both diseases with ankylosing spondylitis (McBride *et al.*, 1963; McConnell, 1965; Acheson, 1965); (3) immunological studies (Phear, 1958; Taylor, 1965; Acheson, 1965); (4) the higher risk in Jews, of approximately the same order of magnitude for both diseases (Acheson, 1960; Acheson and Nefzger, 1963); (5) a number of cases where the condition of the colon suggested

that both diseases were present (Lumb, 1951; Porritt and Hunt, 1960); (6) the occurrence of the same complications, including erythema nodosum, pyoderma gangrenosum, arthritis, uveitis, and conjunctivitis; and (7) the many overlapping clinical features of the diseases, so that one is sometimes misdiagnosed for the other (Cooke and Brooke, 1955; Yarnis, 1955; Hendrix, 1964).

In our small series of 19 cases a number of the foregoing features were present. (1) Genetic coincidence: a 47-year-old man with onset of regional ileitis at 19 had a brother who had ulcerative colitis at 16 and a sister who had ulcerative colitis at 40. (2) Ankylosing spondylitis: one of our patients had ankylosing spondylitis preceding the onset of regional ileitis. (3) Higher risk in Jews: 10 of the 19 patients were Jews, a higher proportion than would have been expected from the wide referral area. (4) Complications: a 19-year-old girl had erythema nodosum. (5) Overlapping clinical features: three cases were first diagnosed as ulcerative colitis, and several months of careful study were required to confirm the correct diagnosis of regional ileitis.

Validation of Psychosomatic Disease

The term "psychosomatic disease" has gone somewhat out of vogue during the past few years. It is now more fashionable to speak of "multifactorially-caused diseases" in referring to illness of undetermined origin. Nevertheless, if one of the components of an illness is psychosomatic, then an emotional cause of some type must be presumed to exist, or the disease cannot occur. In our study of ulcerative colitis we set up a catalogue of criteria for validating whether one essential component of a disease's cause was psychogenic. The same criteria have been examined for evidence of a psychogenic factor in regional ileitis. The seven criteria are: (1) a characteristic personality disorder or other serious psychiatric illness; (2) a clear emotional precipitating factor chronologically related to the illness; (3) general, conscious stress; (4) basic emotional problems of long duration (unconscious stress); (5) alternation of symptoms, or syndrome shift; (6) characteristic patterns of illness in the life history; and (7) efficacy of psychotherapy.

* From the Department of Psychiatry and Department of Medicine, Cedars-Sinai Medical Center, Mount Sinai Division, Los Angeles, California.

Material and Method

Nineteen patients with regional ileitis were studied, constituting every known patient with regional ileitis admitted to the Mount Sinai Hospital between August 1964 and June 1967. Tables I and II list age, sex, severity of disease, length of illness, area of involvement, patients requiring surgery, and complications. Two types of control groups were used. The first was a control group only in the loosest sense, since it consisted of the general population, divided into normal and abnormal according to arbitrary criteria. The second control group comprised the first 74 consecutive patients admitted to the gastroenterology service while the study on regional ileitis was in process. No patients with disease of the large intestine were included.

TABLE I.—Age Groups and Sex Distribution of 19 Regional Ileitis Patients

Age Group (At Time of Onset)	Males	Females	Total
10-20	8	2	10
21-30	1	3	4
31-40	1	1	2
41-50	—	1	1
51-60	—	1	1
61-70	—	1	1

TABLE II.—Other Clinical Data on 19 Regional Ileitis Patients

Severity of disease	Mild	0
	Moderate	4
	Severe	15
Average length of illness in years	Moderate disease	3
	Severe disease	9
Area of involvement	Ileum alone	10
	Ileum and colon	9
Patients requiring surgery		9
Complications	Rheumatoid spondylitis	1
	Erythema nodosum	1

The team members were essentially those who conducted the concurrent study on ulcerative colitis, and consisted of a psychiatrist, physician, and two gastroenterologists. Each patient had two standard psychiatric interviews by the team, of the free-association type, but eventually including a discussion of sufficient current and past material to yield data for scoring 65 variables regarded as salient for personality evaluation (Table III). Subsequently the team saw the patient as often as possible during his hospital stay. Each patient was designated as "normal" or "abnormal" in each of the 65 categories of the protocol. Normal was scored as 3, 4, or 5; abnormal as 1 or 2. A normal distribution curve was used (Fig. 1). The curve

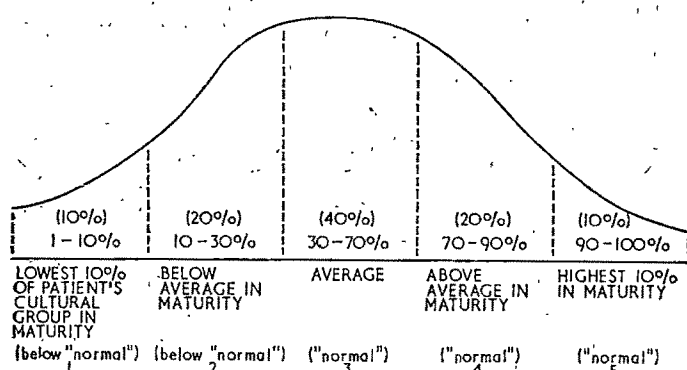


FIG. 1.—Normal distribution curve.

refers to the general population—that is, an arbitrary assumption was made that approximately 70% of the general population was "normal" and 30% definitely "abnormal." It may be noted that four recent large epidemiological studies of psychiatric illness in general populations have confirmed the approximate correctness of this original guess at the distribution of "normality" (Essen-Möller, 1956; Srole *et al.*, 1962; Leighton *et al.*, 1963; Bahn *et al.*, 1967).

Results

Personality Types and Psychiatric Illness.—Seventeen of the 19 patients were regarded as essentially "normal" within the limits we have described, and two were "abnormal." The two abnormal patients were a compulsive and somewhat impulsive man of 30 and an impulsive, somewhat eccentric, adventurous woman of 32. Both, however, had many ego strengths. Neither was psychotic. The other 17 patients were eight diagnosed as normal passive personality types and nine as normal aggressive types. There were no other significant psychiatric diagnoses, except in the 68-year-old woman who had moderate phobias 10 years before the onset of the regional ileitis.

Precipitating Factors and Chronological Relations.—There were no cases where a significant precipitating factor was

TABLE III.—List of Variables for Personality Evaluation

	1 10%	2 20%	3 40%	4 20%	5 10%
	Abnormal (30%)		Normal (70%)		
Ego strengths:					
1. Work					
2. Love, friendship					
3. Sex					
4. Parental					
5. Self-awareness					
6. Frustration toler.					
7. Humour					
8. Wide interests					
9. Reality testing					
10. Energy level					
11. Creativity					
12. Ethical standards					
13. Identity					
14. Appearance					
Defensiveness: general:					
1. Projection					
2. Denial					
3. Intellectualizing					
Acting out					
Dependence					
External problems					
Attitude to illness					
Cognition					
Symptoms:					
A. Thought content:					
1. Self-doubt					
2. Compulsions					
3. Obsessions					
4. Phobias					
5. Unreality					
6. Delusions					
7. Hallucinations					
B. Anxiety:					
1. (Subjective) anxiety					
2. (Objective) tension					
C. Depression:					
1. Withdrawal					
2. Apathy					
3. Crying spells					
4. Inappropriate guilt					
5. Manic behaviour					
Background:					
A. Patient:					
1. Severe illnesses					
2. Severe discipline					
3. Indulgence					
4. Adoption					
5. Institutional placem.					
6. Parent dependence					
B. Parents:					
1. Death/abandonment					
2. Sev. illness (physical)					
3. Mental illness (psychosis)					
4. Marital conflicts					
5. Unusual culture					
C. Role reversal:					
1. Occupation/father					
2. Pt. responsibility					
3. Reversal M/F roles					
D. Siblings:					
1. Rivalry					
2. Severe illness					
3. Death; guilt; loss					
4. Disparity					
Psychosomatic relations:					
1. Symbolism					
2. Separation anxiety					
3. Dependence					
4. Syndrome shift					
5. Forward steps					
6. Relation to past					
7. System preoccupation					

thought to have occurred close in time to the onset of regional ileitis. In two instances there appeared to be significant stress at the time of relapses. However, the total number of "attacks," "relapses," or "exacerbations" was quite high (probably numbering 40 or more for the 19 patients), and the figure of two, associated with stress, would therefore appear small. There were no instances of extreme separation anxiety at the time of either onset or relapse, and no instances where a fear of taking forward steps in career, education, or marriage seemed crucial.

General Conscious Stress, Perhaps Cumulative.—In one case there was the possibility of long stress, associated with work, before relapses. Onset of the illness, however, had occurred 10 years previously, when the patient was in college. Moreover, he enjoyed his work, and ranked very high in professional capacity and conscientiousness. There were four other cases in which moderate stress was present before a relapse.

Basic or Nuclear Emotional Problems, with Significant Background Features, Symbolically Related to the Illness (Unconscious Stress).—There were six cases in which the total background or dynamic factors were of some significance, but none was extreme. It was felt that none of the patients had had nuclear conflicts in his earlier years that were definitely expressing themselves symbolically in the form of the somatic illness.

Alternation of Symptoms, or Syndrome Shift.—No true alternation of either psychiatric or physical symptoms with the regional ileitis was encountered in the history or hospital course of the patients. There was one instance of rheumatoid spondylitis, which had begun before the ileitis but did not alternate with it. Moderate depression was present in four cases but was linked to the severity of the illness.

Characteristic Patterns of Illness in the Life History.—There was no significant hypochondriasis, even in the two "abnormal" patients. There was no history of preoccupation with bowel habits.

Efficacy of Psychotherapy.—Five patients had had psychotherapy ranging from one month to one and one half years. It had effected no improvement in the regional ileitis itself in any case.

Results in Control Group

The results in the 74 control patients are not described in detail here, but are compared with the regional patients in Fig. 2. In general, the control patients showed as much psychopathology as, or more than, the regional ileitis cases.

Discussion

Regional ileitis has been arraigned as a psychosomatic disease by a number of psychiatric investigators and denied as one by

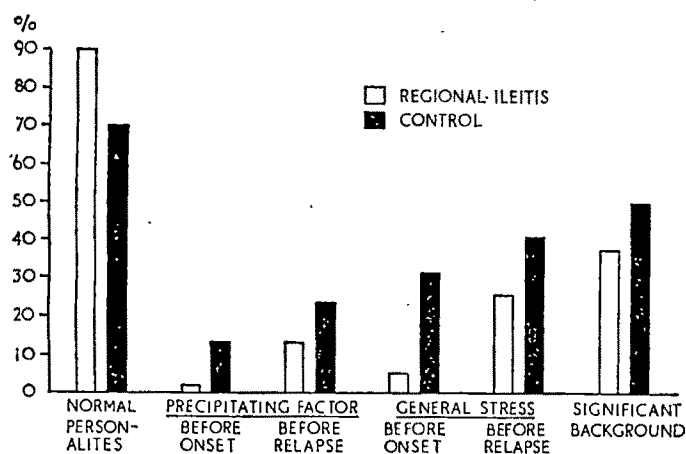


FIG. 2.—Comparison of frequency of occurrence of the mentioned psychiatric factors between 19 regional ileitis and 74 control patients.

a few. Gastroenterologists generally have avoided a definite statement about the role of emotions. Some, including Crohn himself (Crohn and Yarnis, 1958), have stated that there is no support for the psychosomatic concept. No studies and no statements have been sufficiently definitive to give physicians a firm foundation for their thinking. We found that many of our patients had been told by one or more physicians that emotional tension might be the cause of their illness. One of the patients, a busy surgeon, had been advised by several physicians to change his specialty to some field of medicine where there would be "little tension."

The psychiatric literature is remarkably scanty—approximately 13 studies in 30 years. So limited and contradictory a literature, to make even the impact it has on medical education, must have derived from other sources. The unavoidable association with ulcerative colitis has prevailed to some extent, and the unconscious need to divine magical answers for diseases of unknown cause has played a part. Arieti (1959) states that "regional ileitis and ulcerative colitis are conditions involving tissue breakdown that are, at least in part, determined by emotional problems." Kaelbling and Patterson (1966) assert that "importance is attached to the significance of emotional factors in regional ileitis."

The studies by psychiatrists are subject to the following criticisms: (1) they sometimes dealt with very few patients, studied at great length; (2) there were no unselected consecutive series; (3) some were retrospective studies; (4) patients were often only those selected by other physicians for referral to psychiatrists because of concurrent but not necessarily associated emotional problems; and (5) the criteria for emotional evaluation were usually not given in detail.

The studies by psychiatrists who favoured the psychosomatic explanation included series of seven patients (Stewart, 1949), 11 patients (Paulley, 1948), four patients (Grace, 1953), one patient (Sperling, 1960), and two patients (Mersereau, 1963). Two psychiatric studies objecting to the psychosomatic hypothesis were those involving eight patients (Kraft and Ardali, 1964) and 16 patients (Crocket, 1952). The latter was the only series approaching ours in size, and was carefully done, but the material was not consecutive or unselected.

The reports by gastroenterologists referring to psychiatric causation were impressionistic, and no rigorous psychiatric evaluations were carried out. Reports favouring the psychosomatic hypothesis somewhat vaguely were those of 40 cases (Dashiell *et al.*, 1951), 20 cases (Richman, 1955), 34 cases (Armitage and Wilson, 1950), 33 cases (Hunt, 1965), and no definite number of cases (Schepers, 1945; Eisenstadt, 1965b).

In contrast to the papers noted above there are many hundreds by gastroenterologists, who reported much longer series of cases, including collections of 700 patients (Crohn and Yarnis, 1958), 600 patients (Van Patter *et al.*, 1954), 500 patients (Turner, 1953), and other large series (Strömbeck, 1937; Warren and Miller, 1942; Tallroth, 1943; Janowitz, 1955). In these studies, and in many others reviewed, either no reference was made to psychiatric factors or they were thought to be minimal or insignificant. The impression gained is that gastroenterologists regard their patients as no different from any other seriously ill patients.

Summary and Conclusions

Nineteen consecutive unselected cases of regional ileitis were studied psychiatrically. No evidence was found that an emotional factor was a significant aetiological component. Seventeen of the 19 patients were regarded as "normal." The results of a study such as this are qualified by questions concerning the concept of normality; our recognition that the assumption of 70% normality in the general population is open to criticism; the reliability of diagnostic criteria in psychiatry; the difficulty of assessing deeper problems with brief interviews;

and the central problem of whether primary psychosomatic disease exists. Nevertheless the significant emotional factors relating to psychosomatic illness noted in the literature were investigated and found not to apply to any important degree. We do, therefore, raise the question whether the disease should be regarded as psychosomatic in any way.

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Evaluation of a Screening Survey for Anaemia in Adult Non-pregnant Women

P. C. ELWOOD,* M.D., D.P.H., D.C.H.; W. E. WATERS,* M.B., B.S., D.I.H.; W. J. GREENE,* M.B., CH.B.

M. M. WOOD,† B.S.C.

WITH THE ASSISTANCE OF E. H. EVANS,‡ M.D., M.R.C.P., J. DE SWIET,‡ M.D., M.R.C.P., AND J. V. WILLIAMS,‡ M.D., M.R.C.P.

Brit. med. J., 1967, 4, 714-717

Considerable interest has been shown recently in community health screening (Backett, 1960; Wilson, 1963; Acheson, 1963; Horne, Clark, and Patterson, 1967). The value of any health-screening procedure depends both on the proportion of persons detected with the disease (or diseases) being sought, or with treatable associated conditions, and on the importance to life or health of these conditions. The number of affected persons detected is dependent both on the prevalence of the disease, or the conditions associated with it, in the community to which screening is offered, and on the nature and extent of selection, if any, of those members of that community who co-operate. In fact very little is known about the selection of persons who readily co-operate in health-screening procedures except in a very few situations, such as mass miniature radiography (Brad-

bury, 1948) and cervical cytology (Wakefield and Barić, 1965), in both of which it seems that affected individuals are, on average, less likely to co-operate than those who are unaffected, though in coal-workers' pneumoconiosis (Cochrane, 1951) and possibly in other compensatable industrial diseases the reverse is probably true. Other than in a few such cases very little is known about how persons who spontaneously attend community screening clinics differ from other members of the community.

Assessment of the importance of the conditions detected during a screening survey necessitates value judgements which are not easily made and which ideally should be based on data relating to changes in the subsequent mortality or morbidity in the community screened. In the haematological community study described here the initial survey was evaluated as an ad hoc health-screening procedure. This evaluation was based on the following: (1) the proportion of subjects seen who were thought to be "anaemic," (2) the symptomatic benefit which resulted from iron therapy in these subjects, and (3) the pre-

*From the Epidemiological Research Unit of the Medical Research Council, Cardiff.

†External Staff, Medical Research Council, Llandough Hospital, Penarth.

‡Physicians, Llwynypia Hospital, Rhondda.

valence of serious underlying conditions detected in subjects believed to be anaemic.

In addition, the opportunity was taken to study some aspects of the selection of subjects who spontaneously attend a community health-screening survey. This was based on comparisons of the distributions of certain haematological and other variates, including symptomatology, in almost all the adult women in the geographically defined area selected for the survey with the same data in a large group of women of the same age who lived in immediately adjacent areas and who, without being contacted by the survey team, spontaneously attended the survey clinic.

The screening survey on which this report is based was confined to adult women. It was conducted as one of a series of studies of epidemiological aspects of iron deficiency. These studies included an examination of the symptoms associated with low haemoglobin levels and the effect of iron therapy on symptoms; an examination of the symptomatic benefit of iron therapy in women with "normal" haemoglobin levels who complained of excessive fatigue; an evaluation of the part played in iron deficiency by dietary intake and menstrual loss of iron; and studies relevant to the prevention of iron deficiency in the community.

Method

An area in the Rhondda Fawr, an industrial valley in South Wales, was defined, and all female residents aged 20 to 64 years (inclusive) were visited and invited to attend a clinic. At the clinic a questionnaire was administered which covered certain aspects of symptomatology and general health, and the number of visits paid to a general practitioner during several intervals before the survey. Measurements were made of height, weight, triceps skin-fold thickness, and one simple aspect of lung function (the peak expiratory flow rate, as recorded on a Wright Peak Flow Meter). A sample of venous blood was taken for estimations of haemoglobin level and packed cell volume, and, in those found to have a haemoglobin level below 12 G., a blood film was examined. Haemoglobin level was estimated as cyanmethaemoglobin, and is expressed here as G. (grammes of haemoglobin per 100 ml. of blood). Packed cell volume (P.C.V.) was estimated by a microhaematocrit method.

On leaving the clinic a self-administered questionnaire was given to each woman, together with a stamped addressed envelope for its return. This was a modified version of the one described by Wood and Elwood (1966), and enabled six of the symptoms commonly attributed to iron-deficiency anaemia to be graded on seven point scales. In addition, this questionnaire contained two series of 10 questions in random order. One series related to symptoms or signs commonly believed to occur in iron-deficiency anaemia; the other 10 were similar to questions in the Cornell Medical Index which have been used in community studies of psychoneurosis by Rawnsley (1966), Abramson, Terespolsky, Brook, and Kark (1965), and others. These latter questions were used here to give a measure of psychoneurosis in each subject.

The general practitioners in the area were visited, and with their permission all women with haemoglobin levels below 10 G. who were not already on treatment were offered referral to a local hospital outpatient clinic for examination and investigation by a consultant physician. The women with haemoglobin levels between 10 and 12 G. who were not already on treatment were questioned in a conventional clinical interview about symptoms which might indicate serious underlying disease, and then, together with those with levels below 10 G., were screened for occult blood in three faecal specimens by Hematest. In an attempt to evaluate the relevance of these results to anaemia a representative sample of an almost equal number of women with haemoglobin level of 12 G. and above were also screened in the same way for occult blood.

Women with haemoglobin levels between 8 and 12 G. who were not already on treatment were admitted to a clinical trial of the effects on symptoms of iron therapy (200 mg. of elemental iron as ferrous carbonate in Ferrodic per person per day for eight weeks). This study was very similar to the one described by Elwood and Wood (1966), and detailed results will be published elsewhere. Only data from this trial which are relevant to the evaluation of the basic screening survey are referred to here.

In an attempt to ascertain factors which might be relevant to the selection of persons who spontaneously attend a community health survey clinic comparisons were made between the distributions in the basic population and the spontaneous attenders (these groups are defined below) of a large number of attributes and variates, including age, parity, haemoglobin level and P.C.V., height, weight, skin-fold thickness, symptoms (including the neurotic grade described above), and estimates of the number of visits paid to a general practitioner during one week, one month, and one year immediately before the survey.

Results

During the survey 1,138 women were seen. Nine hundred and twenty were residents in the defined area and were aged 20–64 years; 19 of these were pregnant and are omitted from all subsequent discussion. The others are subsequently referred to here as "the basic population." The remaining 218 women seen were either outside the age limits of the study or were residents in surrounding areas who were not visited or contacted in any way by the survey team but heard about the survey and attended the survey clinic spontaneously. The 180 of these who were aged 20–64 years are subsequently referred to here as "the spontaneous attenders." Those who were outside 20–64 years of age have been excluded from all that follows. Table I summarizes all these data and incidentally shows some evidence of a relative deficiency of women in the younger age groups, probably due to migration out of the area.

TABLE I.—Distributions by Age of Basic Population and Spontaneous Attenders

Age	Basic Population			Spontaneous Attenders
	Total	Seen	Refused	
15–	—	—	—	18
20–	66	64 (11)	2 (3.0%)	13
	81	77 (1)	4 (4.9%)	11
30–	110	102 (4)	8 (7.3%)	26
	140	128 (1)	12 (8.6%)	24
40–	143	132 (2)	11 (7.7%)	30
	114	107	7 (6.1%)	24
50–	105	96	9 (8.6%)	20
	118	105	13 (11.0%)	25
60–	128	109	19 (14.8%)	7
65+	—	—	—	20
Total	1,005	920 (19)	85 (8.5%)	218

Women outside age limits of study (20–64 years) together with those who were pregnant (shown in parentheses) omitted from χ^2 tests and all subsequent discussion. Basic population seen and spontaneous attenders: $\chi^2 = 13.28$. D.F. = 8: $0.2 > P > 0.1$.

Basic population seen and refusals: $\chi^2 = 12.46$, D.F. = 7: $0.1 > P > 0.05$.

The distributions of the basic population and the spontaneous attenders by haemoglobin level and P.C.V. are shown in Table II. There is no evidence of a significant difference (at $P < 0.05$, the criterion of significance used throughout) in the distributions of these variates in the two populations. No case of megaloblastic anaemia was detected.

There were 31 (3.4%) women in the basic population and 13 (7.2%) in the spontaneous attenders who had haemoglobin levels below 10 G. These proportions do not differ significantly. Thirty-seven of these were not already under treatment for anaemia, and agreed to referral to hospital outpatient departments for further examination and investigation. In nine cases (0.8% of all the women) further action relevant to the iron-deficiency anaemia was taken. One woman had haemorrhoids injected, six had uterine dilatation and curettage, one who could

not tolerate oral iron was admitted to hospital for blood transfusion, and one was found on routine x-ray examination to have an opacity in her chest, which was removed and found to be a carcinoid adenoma.

TABLE II.—Distribution of Basic Population and Spontaneous Attenders by Haemoglobin Level and Packed Cell Volumes

Haemoglobin Level			Packed Cell Volume		
G.	Basic Population	Spontaneous Attenders	%	Basic Population	Spontaneous Attenders
6.5	—	1	26	2	—
7.0	3	—	27	1	—
7.5	4	—	28	3	1
8.0	7	1	29	6	1
8.5	4	—	30	4	1
9.0	5	1	31	1	2
9.5	8	10	32	6	2
10.0	9	2	33	7	10
10.5	18	2	34	14	6
11.0	14	4	35	22	4
11.5	22	5	36	18	7
12.0	50	9	37	40	5
12.5	67	12	38	71	19
13.0	144	21	39	107	15
13.5	194	36	40	121	31
14.0	143	35	41	116	13
14.5	116	26	42	123	22
15.0	44	8	43	94	18
15.5	28	3	44	52	8
16.0	10	2	45	37	5
16.5	7	—	46	12	3
17.0	3	—	47	14	1
17.5	—	—	48	5	1
18.0	1	—	49	5	—
18.5	—	1	50+	5	—
Total	901	179	Total	886*	175*
Mean	13.32	13.45	Mean	40.49	40.00
S.E.	0.05	0.12	S.E.	0.12	0.28

* Several estimations inadvertently omitted.

The 63 women in the basic population and the 13 of the spontaneous attenders who had haemoglobin levels between 10 and 12 G. were visited in their homes and questioned in a conventional clinical interview. In a very few cases symptoms were elicited that were suggestive of underlying conditions (such as haemorrhoids, etc.), but in no case in which these symptoms might have been relevant to the iron-deficiency anaemia were they thought to be severe enough to warrant the initiation of further investigations.

There were 120 women with haemoglobin levels below 12 G. These were all asked to supply three specimens of faeces for testing for occult blood, except 10 women whom it was thought injudicious to include in this part of the study, as they were already receiving iron therapy from their general practitioners. Of the other women 19 refused and 91 (83%) each supplied three specimens. These data, together with the results of Hematest examinations by two independent observers, are shown in Table III. One or more samples from 15 subjects (16% of those tested) gave a definite positive result, though only in four (4%) was there agreement between the two observers. There is no evidence of any association between the proportion of positive results with haemoglobin level. Indeed, none of the seven with levels below 8 G. who were tested had evidence of faecal occult blood. A representative sample of 69 women with haemoglobin levels above 12 G. were contacted, and the 64 (93%) who co-operated were tested in the same way. Of these, five (8%) gave a positive result, and, though this is lower than

TABLE III.—Details of Samples Tested by Hematest for Faecal Occult Blood on Three Occasions by Two Independent Observers

Hb Level (G.)	No. Identified During Screening	On Iron Therapy from G.P. (etc.)	Refused	Total Tested	Results of Hematest			
					Negative		Doubtful	Positive
					No.	%		
<8	8	—	1	7	7	100	—	—
8-10	36	3	4	29	22	76	—	7 (1)
10-12	76	7	14	55	45	82	2 (-)	8 (3)
Total	120	10	19	91	74	81	2 (-)	15 (4)
12+	Representative sample of 69 women			64	58	91	1 (-)	5 (3)

No. of tests in which there was agreement between the two observers shown in parentheses.

the proportion in women with haemoglobin levels below 12 G. found to be positive, it does not differ from it significantly. Each of the 20 women with a positive result was visited again, asked about rectal bleeding, and asked to supply a further three faecal specimens. Eight said they had haemorrhoids which bled occasionally, and faecal specimens from four of these gave a second positive Hematest. Other than these none of the women had a second positive test.

Almost all the women with haemoglobin levels between 8 and 12 G. were admitted to the clinical trial of the effect of iron therapy on symptoms. Detailed results will be presented elsewhere; suffice to say here that there was no evidence of a beneficial effect of eight weeks of conventional iron therapy on the symptoms of irritability, palpitations, dizziness, breathlessness, fatigue, or headache which was greater than that of identical placebo tablets which contain no iron.

There were no significant differences between the basic population and the spontaneous attenders in any attribute or variate measured, other than in weight. The spontaneous attenders were 6.8 ± 2.1 lb. (3.1 ± 0.95 kg.) heavier on average than the basic population. Apart from this difference the two groups were homogeneous with respect to age, parity, height,

TABLE IV.—Summary of Comparisons Between Spontaneous Attenders and the Basic Population

Variate	Basic Population	Spontaneous Attenders
Age	43.8 $\pm$ 0.40	42.7 $\pm$ 0.82
Parity	2.0 $\pm$ 0.07	2.1 $\pm$ 0.13
Height	61.0 $\pm$ 0.08	61.3 $\pm$ 0.18
Weight	140.2 $\pm$ 0.97	147.1 $\pm$ 1.81
Triceps skin-fold thickness	18.0 $\pm$ 0.26	18.8 $\pm$ 0.60
Haemoglobin level	13.3 $\pm$ 0.05	13.5 $\pm$ 0.12
P.C.V.	40.5 $\pm$ 0.12	40.0 $\pm$ 0.28
Symptom grades:		
Irritability	2.8 $\pm$ 0.07	2.9 $\pm$ 0.16
Palpitations	2.4 $\pm$ 0.07	2.6 $\pm$ 0.09
Dizziness	0.8 $\pm$ 0.05	0.7 $\pm$ 0.13
Breathlessness	1.9 $\pm$ 0.06	2.0 $\pm$ 0.14
Fatigue	2.2 $\pm$ 0.06	2.5 $\pm$ 0.15
Headache	2.7 $\pm$ 0.08	2.9 $\pm$ 0.19
Neurosis	25.9 $\pm$ 0.79	26.4 $\pm$ 1.73
Visits to G.P.:		
During past week	0.6 $\pm$ 0.04	0.8 $\pm$ 0.2
During past month	1.5 $\pm$ 0.08	1.8 $\pm$ 0.2
During past year	2.9 $\pm$ 0.23	3.0 $\pm$ 0.5

triceps skin-fold thickness, haemoglobin level, P.C.V., symptom grades, and their own estimates of the number of visits to a general practitioner during one week, one month, and one year immediately before the survey (Table IV).

Discussion

Screening for disease should be regarded as one step in the diagnostic process and not as an end in itself. Thus a general practitioner seeing his surgery attenders, or a consultant physician his outpatients, are simply forms of screening and fundamentally differ little from community screening procedures. However, a realistic evaluation of any screening procedure cannot be made without consideration of the benefit, if any, which results from the screening, and this aspect often seems to be ignored—for example, by Horne *et al.* (1967) in their report of a local health authority screening survey. Acheson (1963) lists five criteria which ideally should be fulfilled before any health-screening procedure is instituted, and similar criteria are incorporated in the discussion by Wilson (1963). These criteria include matters relating to the prevalence of the condition being sought, its importance, the sensitivity and specificity of the tests required for its diagnosis, the acceptability of this test by the subjects screened, and the acceptability and effectiveness of treatment available for those found to have the condition sought. Few diseases, if any, fully meet all the criteria outlined, but Acheson (1963) specifically mentions anaemia as probably fulfilling all the criteria except perhaps those relating to its importance in terms of morbidity and mortality.

Our study, however, appears to us to give very little encouragement for community health screening for anaemia. Though a fairly high proportion of women were detected with haemoglobin levels below commonly accepted lower limits of normal, thus being consistent with data obtained in the community surveys of Kilpatrick (1961), Elwood (1964), and others, yet the importance of "anaemia," so defined, appears to be relatively small. This assessment of importance is based both on the apparent absence of serious treatable underlying conditions in the subjects with the lowest haemoglobin levels and on the absence of unequivocal benefit in the symptoms of those treated with iron. Even in those in whom further action was taken, in only one was there evidence of serious disease, and this was almost certainly a chance finding, unrelated to the anaemia. Furthermore, the relevance to anaemia of the other conditions treated—haemorrhoids and menorrhagia—and the success of the treatment given, can strictly only be assumed, as we made no quantitative measurements of blood loss.

It might be argued that our subjects were not investigated with sufficient thoroughness to detect all serious underlying disease. In particular it could be pointed out that all the subjects whose faecal specimens were positive to Hematest were not exhaustively investigated. This criticism is valid, but one of the main aims of this survey was to evaluate the existing facilities for further investigation and not to create an unrealistic situation. So far as possible, therefore, subjects were treated at the local hospital as if they had been normally referred by local general practitioners. In any case, further detailed investigation of subjects identified in this way, most of whom had no definite gastrointestinal symptoms, is not easily justified, and can be easily misunderstood and possibly resented. However, almost all the women found in this survey to have haemoglobin levels below 12 G. are involved in further epidemiological studies and will be followed for a considerable time.

With regard to the data relating to positive Hematests, it appears that much further work would need to be done to enable a "positive" result to be defined more clearly and to evaluate positive results, in particular with regard to their relevance to low haemoglobin levels in the community. Illingworth (1965) showed that the diet must be carefully controlled to a considerable degree before a positive Hematest is accepted as firm evidence of gastrointestinal bleeding, but even with careful dietary control Ross and Gray (1964) feel that "no value can be attached to the results of any of the chemical tests" for occult blood, and they feel it is questionable whether these tests should be retained in modern medicine. It is not felt justified in the present study to attempt to control the diets of the subjects in any way, but in spite of this and the view expressed by Ross and Gray (1964) the difference in the prevalence of positive tests in the subjects with haemoglobin levels below 12 G. and in those with haemoglobin levels of 12 G. or more, all of whom were tested in exactly the same way by "blind" observers, is of interest in an epidemiological context.

It was possible to examine aspirin-taking in these women, as questions relating to this had been asked routinely in the initial survey, and there was no evidence that the women with positive Hematests took aspirin more often than the other women. In fact the difference, though not significant, suggested the reverse. Interpretation of these data as they stand is therefore difficult, though it is of interest that our estimate of 16% positive tests in the women with lower haemoglobin levels is not very different from that obtained by Illingworth (1965) in 126 "normal people eating an unrestricted diet" (21% quoted in text, 31% shown in Table). The results of this part of the study are therefore equivocal, but make it seem unlikely that serious underlying disorder is a causative factor of any magnitude in iron-deficiency anaemia in the community. The present data therefore give no support to the view that "in the adult (the

basic disease process) is all too frequently a malignant tumour of the gastrointestinal tract" (Harris, 1963).

Backett (1960) has stressed that high-risk groups should be identified for screening procedures. In an approach to the community as a whole this would be achieved to some extent if the less healthy persons more readily attended surveys such as the one described here than the rest of the community. The data presented here show that this is most unlikely to be the case in a survey for anaemia, as the persons who spontaneously attended the clinic differed from the basic population in none of the ways examined, other than in weight. It is difficult to interpret this difference in weight, but in the absence of any other significant difference it is unlikely to be of clinical importance.

Further data which bear indirectly on this aspect of health screening can be obtained by examining the trend in mean haemoglobin during the survey. If the women who attend a survey such as ours least readily are those with, on average, higher or lower haemoglobin levels, then the mean levels of successive groups of subjects, examined in the order in which they attended, should show a rise or a fall. In fact the mean level of the last 67 women, most of whom required considerable persuasion to attend the survey, was 13.9 ± 0.20 G., and though this is higher than the mean of the whole basic population (13.3 ± 0.05 G.) the difference is not significant. It appears likely, therefore, that neither the women who attend a survey most willingly nor those who attend most reluctantly differ with regard to their haemoglobin level from the population from which they come. In fact the absence of a real difference in the distributions by haemoglobin level had been predicted in view of the lack of evidence in an earlier community survey of a significant association between haemoglobin level and symptomatology (Wood and Elwood, 1966). In view of the fact that the symptoms examined in our study are not specific for iron deficiency, our data suggest that in any screening survey of the type we conducted high-risk groups are unlikely to attend selectively to any important extent.

Summary

An evaluation of a community screening survey for anaemia has been made. This is based on the proportion of women found to have a low haemoglobin level in a large survey, the proportion of these found to have a serious underlying disorder, and the symptomatic benefit in them after iron therapy. In addition, the selection of women who voluntarily attend a screening survey is examined by comparing the distributions of a wide variety of variates in a large group of women who spontaneously attended the survey with these distributions in the whole community. These studies give very little encouragement for ad hoc community screening.

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Fibrin Degradation Products in Sera of Normal Subjects

P. C. DAS,* M.B., B.S.; A. G. E. ALLAN,† F.I.M.L.T.; D. G. WOODFIELD,‡ M.B., CH.B., M.R.C.P.E.D.
J. D. CASH,§ M.B., CH.B., B.SC., PH.D., M.R.C.P.E.D.

Brit. med. J., 1967, 4, 718-720

During the proteolysis of fibrinogen and fibrin by the fibrinolytic enzyme plasmin several large fragments are released which are incapable of undergoing further digestion (Nussenzweig and Seligmann, 1960; Alkjaersig *et al.*, 1962). Some of these fragments, with a molecular weight of approximately 88,000, contain an antigenic determinant which is identical to the parent fibrinogen (Nussenzweig *et al.*, 1961). An accurate quantitative estimation of circulating fibrin/fibrinogen degradation products (F.D.P.) would be of considerable importance in investigations of physiological and pathological states of coagulation and fibrinolysis, for circulating F.D.P. represent a certain criterion that fibrinolysis is taking place. They play a significant part in the pathogenesis of certain bleeding disorders (Niewiarowski *et al.*, 1959; Fletcher, 1966; Jerushalmy and Zucker, 1966; Kopic *et al.*, 1966); they may be of importance in the physiological control of the microcirculation (Buluk *et al.*, 1966) and could provide valuable information in further studies on the hypothesis of a continuous dynamic equilibrium between fibrin deposition and fibrinolysis postulated to be an important aetiological factor in thrombosis and atherosclerosis (Astrup, 1956).

While prolongation of the thrombin time has been advocated as a useful screening procedure for estimating high levels of F.D.P. in pathological fibrinolysis (Sherry, 1965), the method is devoid of specificity, has poor sensitivity, and is therefore of limited value. The application of immunological techniques such as immunodiffusion and immunoelectrophoresis has greatly extended the specificity and sensitivity of F.D.P. assays. Further progress has been made with the use of a tanned red cell haemagglutination inhibition immunoassay (Murakami, 1965a; Merskey *et al.*, 1966) which has been claimed to be more sensitive and more easily adapted to accurate quantitative estimation of circulating F.D.P. than either immunodiffusion or immunoelectrophoresis. This investigation was designed to establish the normal range of serum F.D.P. values before the study of those pathological conditions believed to be associated with excessive focal or disseminated intravascular coagulation and to extend our studies of the Astrup hypothesis. This communication describes our experiences with the tanned red cell haemagglutination inhibition immunoassay in a group of apparently healthy subjects.

Methods

A total of 106 healthy volunteers (62 male and 44 female) aged 21-64 years (mean 40 ± 15) were studied. Cubital venous blood samples were obtained by clean venepuncture with the minimum venous occlusion, a plastic disposable syringe being used, after a period of 20 to 30 minutes' rest.

Five millilitres of blood was added to a non-siliconized glass test-tube containing 0.1 ml. of Trasylol (5,000 units/ml.) and placed in a water-bath at 37° C. for four hours. The serum was removed after centrifugation at 2,000 r.p.m. for 10 minutes, and one-tenth of its volume of thrombin (100 units/ml.) was

added and incubated for 30 minutes at 37° C. to remove any residual fibrinogen. F.D.P. assays were performed by the method of Merskey *et al.* (1966) on serum samples which had previously been absorbed for two hours at 4° C. with one volume of saline-washed normal sheep red cells to two volumes of serum. Rabbit anti-human fibrinogen serum supplied by Hoechst Pharmaceuticals Ltd. was used in the immunoassay. Daily controls were run with standard solutions of human

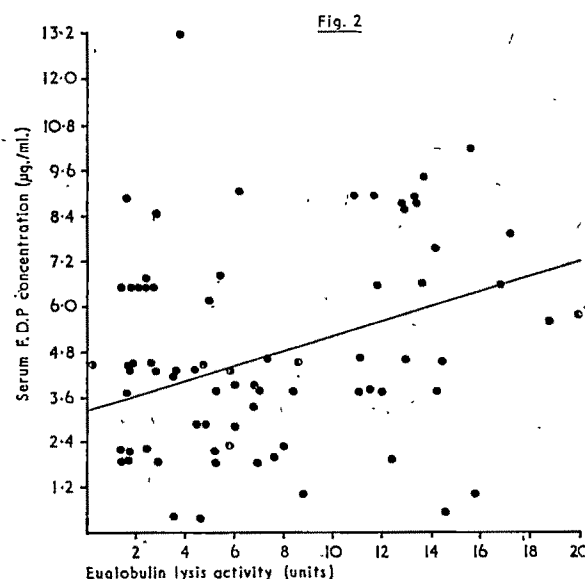
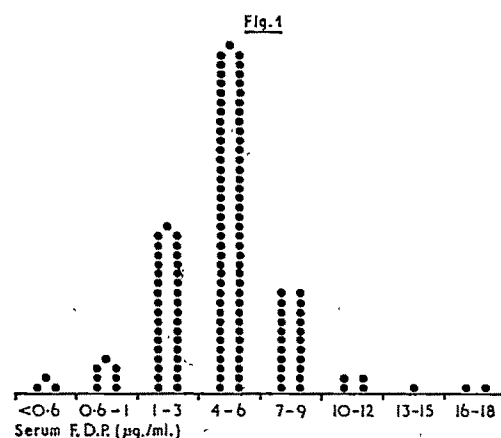


Fig. 1.—Frequency distribution of serum F.D.P. of 147 samples from 106 normal subjects. Fig. 2.—Correlation between serum F.D.P. and plasma euglobulin lysis activity in 75 normal subjects. $r=0.226$; $0.05 < P < 0.02$; $y=6.82+0.20x$.

fibrinogen prepared by the Blombäck and Blombäck method and supplied by Kabi Pharmaceuticals Ltd. The quantity of clottable protein in these solutions was checked periodically by the method of Ratnoff and Menzie (1951) as modified by Alkjaersig (1960). The immunoassay was sufficiently sensitive to demonstrate fibrinogen levels of 0.6 µg./ml.

A further 9 ml. of blood was added to 1 ml. of 3.8% sodium citrate, in a previously cooled siliconized glass centrifuge tube,

* Honorary Registrar

† Senior Technician.

‡ Registrar.

§ Senior Registrar.

South-east Scotland Regional Blood Transfusion Research Laboratories, Royal Infirmary, Edinburgh 3.

and centrifuged at 4° C. for 20 minutes at 3,400 r.p.m. Euglobulin lysis time assays were performed by the method described previously (Cash, 1966), but the clot lysis end-point was recorded objectively by means of an automatic clot lysis recorder (Cash and Leask, 1967). The euglobulin lysis activity was expressed in arbitrary units derived from the formula 1300/T of Janusko and Dubinska (1964), where T was the euglobulin lysis time in minutes.

Results

Normal Resting Level of Serum F.D.P.—The mean serum F.D.P. level of 147 samples from 106 subjects was 4.9 ± 2.8 $\mu\text{g./ml.}$ The distribution of these values is shown in Fig. 1, and it can be seen that the immunoassay was able to detect F.D.P. in all but 2% of the serum samples. No significant sex difference was shown, nor was there a consistent change in serum F.D.P. throughout a menstrual cycle in the four women studied. Table I gives the individual variation in serum F.D.P. of 12 subjects from whom blood was withdrawn at weekly intervals, whereas Table II shows the variability of the assay system on aliquots of eight serum samples which were stored at -40°C. and assayed at weekly intervals.

Exercise and Adrenaline Studies.—Table III shows the serum F.D.P. levels in 26 subjects before and after an eight-minute exercise procedure on a treadmill moving at 3.4 m.p.h. (5.5 k.p.h.) at 5 degrees elevation, and in five subjects before

TABLE I.—Serum F.D.P. Levels ($\mu\text{g./ml.}$) of Blood Samples Withdrawn at Weekly Intervals from 12 Normal Resting Subjects

Subject No.											
1	2	3	4	5	6	7	8	9	10	11	12
6.1	2.0	8.2	4.5	3.7	1.9	6.5	2.2	6.5	4.5	8.8	2.3
2.9	2.2	7.8	4.5	1.9	<0.6	8.6	2.2	6.5	4.5	8.9	2.3
2.9	4.6	10.1	3.7	4.6	4.6	6.5	4.3	6.5	8.9	8.9	6.8
—	—	—	3.7	—	4.5	—	—	—	11.7	—	—

TABLE II.—F.D.P. Level ($\mu\text{g./ml.}$) of Eight Serum Samples, Aliquots of Which Were Kept at -40° C. and Assayed at Weekly Intervals

Sample No.							
1	2	3	4	5	6	7	8
3.0	9.0	4.8	6.6	4.8	7.8	7.8	15.6
3.0	9.0	4.8	9.0	4.8	8.4	7.8	19.0
3.0	9.0	4.8	6.6	5.4	7.8	7.8	15.6

TABLE III.—Serum F.D.P. Levels Before and After a Moderate Exercise and Intravenous Adrenaline Procedure

Exercise			Adrenaline		
Subject No.	Serum F.D.P. ($\mu\text{g./ml.}$)		Subject No.	Serum F.D.P. ($\mu\text{g./ml.}$)	
	Before	After		Before	After
1	3.2	12.5	1	6.2	18.7
2	1.8	6.2	2	10.9	24.9
3	1.8	12.4	3	3.1	12.5
4	1.0	6.2	4	1.6	6.2
5	3.7	14.0	5	4.9	14.0
6	3.7	18.7			
7	1.9	6.2			
8	3.7	18.7			
9	1.9	6.2			
10	1.5	14.4			
11	3.4	16.8			
12	3.6	8.0			
13	2.4	9.8			
14	5.2	11.4			
15	3.0	10.5			
16	2.2	8.6			
17	3.0	8.6			
18	4.3	12.2			
19	3.2	8.2			
20	4.5	13.6			
21	4.1	11.3			
22	5.7	12.2			
23	6.7	10.4			
24	8.8	13.4			
25	10.2	13.6			
26	6.8	10.2			
Mean	3.3	6.7	Mean	3.3	9.1

and two minutes after a two-minute intravenous infusion of 10 $\mu\text{g.}$ of adrenaline per minute (Parke-Davis and Co.). Statistical analysis of these results by Student's *t* test showed the resultant increases of serum F.D.P. to be significant (exercise, $t=5.922$, $P<0.001$; adrenaline, $t=3.03$, $0.005<P<0.01$).

Correlation Between Serum F.D.P. and Euglobulin Lysis Activity.—A plot of the resting serum F.D.P. values and plasma euglobulin lysis activity in 75 samples (Fig. 2) shows a significant correlation between these two criteria ($r=0.226$; $0.02<P<0.05$; $y=6.82+0.20x$).

Discussion

There are few studies on the detection of F.D.P. in the serum of normal subjects: Ferreira and Murat (1963) and Ferri and Ferreira (1963), using a "fibrin degradation flocculation test" and immunoelectrophoresis, found no evidence of circulating F.D.P. in normal subjects; Niléhn and Nilsson (1964), using comparative immunoelectrophoresis in agar gel, demonstrated F.D.P. in the serum in 5 of their 28 normal subjects; and Murakami (1965b), employing the tanned red cell haemagglutination inhibition immunoassay, observed lysis products without exception in 69 cases, including normal controls, whereas Merskey *et al.* (1966), using the same basic method, demonstrated the presence of F.D.P. in only 3 out of 33 controls.

The present investigation indicates that the tanned red cell haemagglutination inhibition immunoassay can show a serum F.D.P. content in about 95% of normal serum samples. This high incidence of detection in normal sera does not accord with the findings of Merskey *et al.* (1966) but is similar to the observations of Murakami (1965b). At the present time it is not possible to explain these different results, but the greater sensitivity of our immunoassay and small differences in technique, reagents, and sheep red cells may be relevant factors. It is also possible that there was a difference in the age and sex ratio of the normal populations studied in the three different centres.

In view of the pathophysiological significance of these findings it is important to be certain that the assay system is in fact detecting products of degradation of in-vivo fibrin by the fibrinolytic enzyme system. It is possible that the fibrinopeptides (Blombäck *et al.*, 1966) released during the clotting of the plasma fibrinogen were reacting positively in the immunoassay. However, we have shown that the supernatant, obtained after the incubation at 37° C. for 30 minutes of purified fibrinogen with thrombin in the presence of Trasylol, does not produce haemagglutination inhibition. It is also possible that residual traces of fibrinogen remained in the sera despite the addition of thrombin. We have no evidence to substantiate this view and have found no correlation between the plasma fibrinogen and level of serum F.D.P. in 20 subjects.

Previous studies have indicated that exercise and adrenaline will bring about an increase in activity of both the coagulation and fibrinolytic enzyme systems (Biggs *et al.*, 1947; Forwell and Ingram, 1957; Genton *et al.*, 1961; Iatridis and Ferguson, 1963; Burt *et al.*, 1964). The demonstration of a highly significant increase in circulating F.D.P. after these fibrinolytic stimulants would suggest that previous assumptions related to an increase in coagulation and fibrinolysis are valid and that the haemagglutination inhibition immunoassay is detecting levels of F.D.P. Further collateral evidence in favour of latter point was obtained by the observation of high level F.D.P. in a patient with severe haemorrhagic diathesis by a primary fibrinolysis associated with a hypernephroma; this patient the F.D.P. level fell precipitously and stopped after the administration of aminocaproic acid. Subsequent efforts to withdraw the aminocaproic acid resulted in a rapid rise of serum F.D.P., associated with a return of the bleeding which was again controlled by resumption of the administration of aminocaproic acid.

Though we showed a positive correlation between the resting levels of circulating F.D.P. and the plasminogen activator in normal subjects the relation was not highly significant. This indicates that the concentration of circulating F.D.P. is probably the end-result of a complex dynamic system which will include fibrin deposition and active fibrinolysis associated with fibrinolytic inhibition.

It cannot be assumed that the results of our study necessarily represent definite proof of continuous in-vivo intravascular coagulation and fibrinolysis as envisaged by Astrup, though the exercise and adrenaline studies are very suggestive. More information is required on the rate of excretion of circulating F.D.P. in physiological circumstances, for if the present concept of a half-life of approximately nine hours is substantiated (Sherry, 1965), then the resting values obtained in this study could merely represent the end-product of transient episodes of exercise or anxiety which occurred several hours before the blood was withdrawn. Furthermore, we have no proof that these F.D.P. are derived from intravascular deposits of fibrin, for it is possible that they may represent a by-product of minute damage and repair within the tissues. Further work on these problems is in progress.

Summary

From 106 apparently healthy subjects 147 serum samples were assayed for their fibrin degradation product (F.D.P.) content by the tanned red cell haemagglutination inhibition immunoassay technique. In 98% of these samples it was possible to detect a measurable quantity of F.D.P., the mean value being 4.9 ± 2.8 $\mu\text{g./ml.}$ There was no significant sex difference or a consistent change during the menstrual cycle. Further studies with the use of exercise and intravenous adrenaline were carried out in order to evaluate the significance of these findings in relation to the concept of an in-vivo dynamic equilibrium between coagulation and fibrinolysis.

We wish to thank Dr. R. A. Cumming, Director of the South-East Scotland Regional Blood Transfusion Centre, who has been responsible for the provision of our excellent laboratory facilities and has given us much encouragement and helpful advice, and Dr.

A. E. Robertson, who kindly assisted in obtaining the co-operation of many of our subjects. Finally we wish to express our sincere appreciation to Dr. Clarence Merskey, of the Albert Einstein College of Medicine, New York, U.S.A., whose helpful correspondence maintained our interest and played a significant part in the successful development of this assay. This research programme was supported by a grant from the Scottish Hospital Endowments Research Trust. One of us (P. C. D.) was in receipt of a postgraduate scholarship from the Government of East Pakistan.

Requests for reprints should be addressed to Dr. J. D. Cash, South-East Scotland Regional Blood Transfusion Research Laboratories, Royal Infirmary, Edinburgh 3.

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Medical Memoranda

Malignant Tumour of Brown Fat in Patient with Turner's Syndrome

Brit. med. J., 1967, **4**, 720-721

CASE REPORT

A 24-year-old typist was first seen in January 1966, when she complained of a slowly enlarging painless swelling in the right scapular region that had been present for one year. She had no other complaints, but on systematic questioning it was noted that she had primary amenorrhoea.

On examination there was a non-tender subcutaneous swelling measuring 5 by 5 cm. below the right scapula. The tumour was not attached to skin but was attached to deep structures. There were no signs of inflammation, but there were some dilated veins over the tumour. The patient had a short stature with a total height of 54 in. (137 cm.) and an arm span of 60 in. (142 cm.). She had unusual facies with a small mandible, prominent inner canthal folds, and large low-set ears. There was no webbing of the neck or cubitus valgus, but she had a low hair-line with

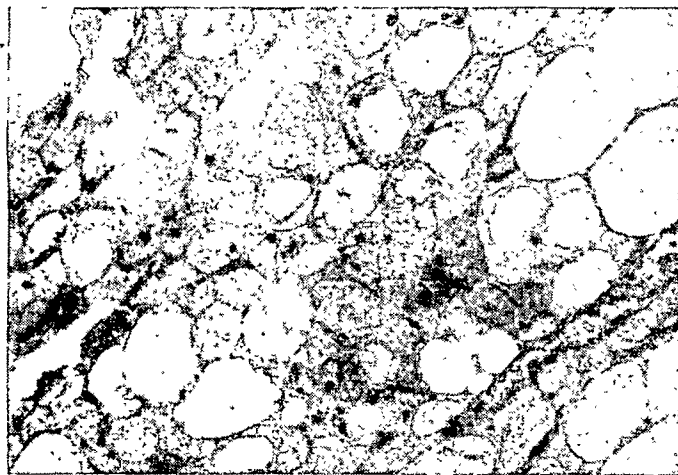
syndactyly of the fingers and toes. The chest had a shield-like configuration. Breast development was present but slight. Pubic and axillary hair were scanty. Blood pressure was 135/90 mm. Hg. Hypoplastic genitalia were noted on pelvic examination, and the ovaries could not be palpated.

Investigations.—X-ray examination showed a normal sella turcica and small facial bones; the radial and ulnar epiphyses had not united, but fusion had occurred at all the epiphyses of the elbow. 17-Ketosteroids 4.3 and 5.5 mg./24 hours. 17-Hydroxycorticosteroids 12.4 and 4.4 mg./24 hours. After four days' A.C.T.H. stimulation 17-KS was 27.8 and 17-OHCS was 26 mg./24 hours. Gonadotrophins 1.8-3.6 $\mu\text{g./24 hours}$. Buccal smears showed a chromatin-negative pattern.

Five hundred neutrophils were examined and only one type A and three type B appendages were seen (normal for female is six or more). There was a predominance of type C nuclear appendages that are seen more often in the male. Blood culture gave a good growth of cells for chromosome studies. The modal number was 45. Karyotypes from several cells showed the chromosome pattern of Turner's syndrome 45/XO. However, a few cells with 46 chromosomes showed the normal number of chromosomes (16) in group C. The probable diagnosis seemed to be a mosaic with some cells containing 45/XO chromosomes and others 46/XX.

At operation a lobulated flabby vascular tumour was partially removed deep to the latissimus dorsi. Though the tumour was mainly encapsulated a radical excision was not possible, since part of it was attached to the spinous process and lamina deep to the surface of the erector spinae muscle.

The specimen consisted mainly of lobulated tumour tissue infiltrating between muscle bundles. It was more reddish brown than fat. Histologically the tumour consisted of fat cells that varied considerably. Some approached the adult type but others had a rounded outline and contained cytoplasm of fine foaming granules of fat (see Fig.). The tumour was not well encapsulated, and there was an intimate relation between the tumour elements and the muscle bundles. The tumour resembled a hibernoma, but in view of the intimate infiltration between muscle bundles it was treated as a form of liposarcoma.



Photomicrograph of tumour.

As a result the residual tumour bed was irradiated with megavoltage x rays to a dose of 4,500 rads in five weeks. The geometry of the treatment fields had to be carefully arranged to avoid irradiating the spinal cord. This hampered a radical approach.

The patient was finally discharged from hospital on a regimen of cyclical oestrogens. At follow-up clinic she remained well, and there was no evidence of tumour recurrence. In addition she had her first episode of breakthrough menstrual bleeding after four and a half months on a priming dose of ethinyloestradiol.

Case of Mumps Nephritis

Brit. med. J., 1967, 4, 721-722

An association between mumps and renal involvement has been infrequently reported. In a series of 20 cases of mumps in Servicemen, Utz *et al.* (1964) reported demonstrable transient renal impairment in all cases. There were no symptoms. In all previously reported cases of mumps in which symptoms of renal damage have been present, death has occurred.

CASE REPORT

The patient, a girl of 15 years, weighing 7 st. 3 lb. (45.8 kg.), was admitted to hospital on 15 January 1967. She gave a history of bilateral parotid mumps two weeks previously. She had been a contact. Her presenting symptoms were enlarged cervical glands, intermittent vomiting, fever, and a petechial rash on the right forearm accompanied by periorbital oedema of four to five days' duration. The latter two features developed some 24 hours after a dose of Metatone (a proprietary preparation containing vitamin-B complex, glycerophosphate, and strychnine), prescribed by her general practitioner for listlessness. No other drug history was elicited.

C

COMMENT

Since the description by Turner (1938) of seven examples of sexual infantilism, congenital web neck, and cubitus valgus in females of short stature many additional abnormalities have been described (Lemli and Smith, 1963).

Hibernoma, or brown fat lipoma, is a rare variant of simple lipoma. Only a small number of cases have been reported in the literature (Sandison and Graham, 1959). The tumour arises in brown "hibernating" fat usually found only in human embryos and hibernating animals. The brown fat lipoma has always been described as a simple tumour. So far as we know this is the first report of malignant degeneration in this tumour.

The infrascapular site of the tumour is of interest, since it is mainly in this site that brown fat is found in mammals (Dawkins and Hull, 1964). Moreover, at one time the hibernoma was called the interscapular tumour.

The unusual occurrence of a rare tumour in a patient with Turner's syndrome is of added interest, since it is recognized that chromosomal damage can lead to malignant disease. In addition, recent studies suggest that certain cancers and congenital defects occur together more often than can be attributed to chance (Miller, 1966).

We are indebted to Dr. J. E. Morison and Dr. W. R. M. Morton for the histological and chromosome investigations. We should also like to thank Dr. A. R. Lyons, Dr. D. A. D. Montgomery, and Dr. D. R. Hadden for their friendly interest and advice.

W. S. B. LOWRY, M.B., M.Sc., D.M.R.T.

Royal Victoria Hospital,
Belfast, N. Ireland.

P. B. HALMOS, M.D., M.R.C.P.I.

University Hospital of West Virginia, U.S.A.

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Flitting knee arthralgia was present for a period of 24 hours after admission. There was no recent cough or sore throat.

She had been admitted to hospital with abdominal pain seven months previously. Spontaneous remission occurred 24 hours later. She was allergic to sticking plaster, but no other history of allergy was obtained.

On clinical examination she was flushed, with an oral temperature of 103° F. (39.4° C.). The tongue was dry and furred. Also evident was bilateral non-tender cervical adenitis and parotid fullness. Petechial haemorrhages were present on the roof of the hard palate and right antecubital fossa—the Hess test was positive on two successive days. On admission her pulse was 110/minute and her blood pressure 110/70 (see Fig.). Clinically, there was no evidence of tonsillitis or pharyngitis. At no stage did she have pretibial oedema. Her temperature was raised for the first 24 hours only.

In spite of a poor fluid output in the first 36 hours, her fluid balance throughout remained reasonable apart from impairment of urine concentration initially. Daily ward urine analysis showed varying amounts of blood and albumin. Early morning midstream specimens produced from a few to numerous red blood cells on microscopical examination. Protein content of urine varied from 0.5 to 2 g./24 hours. Two specimens were productive of occasional granular casts. No pathogen was isolated from the urine. Blood urea and erythrocyte sedimentation rate (E.S.R.) were raised for the

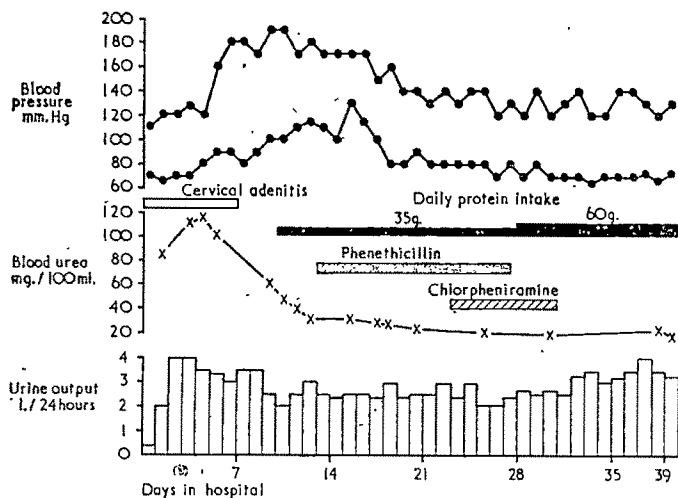
first two weeks; the highest values were a blood urea of 114 mg./100 ml. and an E.S.R. of 50 mm./hour. Antistreptolysin titre (A.S.O.) estimation was 100 international units on the seventh hospital day, and 200 international units 61 days later. Mumps virus serology performed on the first and fourteenth hospital day showed a fourfold increase in titre (+1/20 to +1/80) compatible with a recent mumps infection. Hypertension developed in the first week. The highest diastolic pressure recorded was 130 mm. Hg. There was spontaneous regression without treatment. Total white blood count ranged from 10,000 to 7,000/cu. mm., with normal differentials throughout. Platelet counts on the second and seventh days of illness were 200,000 and 210,000/cu. mm. respectively. Four throat swabs and blood cultures were negative. Serum amylase was 4 units. Serum electrolytes were normal throughout. Paul-Bunnell agglutination was negative. Her management was along symptomatic lines.

Dietary protein was restricted to 35 g. daily, on a fluid load of 2.5 litres/24 hours, until improvement became evident. A course of phenethicillin and chlorpheniramine had no obvious therapeutic effect. Improvement occurred during her stay in hospital, as evidenced by the return of the blood urea and E.S.R. to normal values, the disappearance of haematuria, and the marked diminution of proteinuria.

COMMENT

Epidemiological data from Norway in the pre-insulin era suggested a connexion between waves of mumps and increased incidence of diabetes mellitus some years later (Gundersen, 1927).

It is recognized that in some children the swelling of the salivary glands in mumps is replaced by a lymphadenitis in the



Treatment and progress in case of mumps nephritis.

neck (*Lancet*, 1961). The 1961 mumps epidemic in the United Kingdom differed from previously recognized forms of the disease because of the frequency of gastrointestinal upsets. These observations suggest that medical interest in this condition should no longer be focused exclusively on the salivary glands, pancreas, and nervous system. More recently it has been pointed out that a connexion may exist between gestational

mumps and primary endocardial fibroelastosis (St. Geme *et al.*, 1966; Gersony *et al.*, 1966).

A review of the literature produced four cases of nephritis complicating mumps. They were all fatal. In none of these cases was hypertension reported as being a prominent feature (see Table).

Contrasting Features of Mumps Nephritis and Post-streptococcal Glomerulonephritis

	Mumps Nephritis (5 cases)	Post-streptococcal Glomerulonephritis
Throat infection	Nil	90%
"Latent period"	1-3 weeks	3-5 weeks
Cervical adenitis	1/5 in some children	Nil
Throat culture	Nil	Positive in 80-90%
Pyrexia of more than 101° F. (38.3° C.)		+ 90%
W.B.C. more than 10,000 cells/ cu. mm.		100%
E.S.R. more than 30 mm./hr. ..	1/5	100%
A.S.O. more than 250 i.u. ..	Nil	+ 90%

In the present case the possibility of a Metatone-induced nephritis can be excluded on clinical grounds. Previous administration had been without ill effect. The significance of a transient hypertension and its late sequelae are difficult to assess. In view of the patient's rapid improvement and subsequent complete clinical recovery, we did not consider it justifiable to submit her to the added trauma and possible complications of a renal biopsy.

"Viral infection" has been suggested as a cause of some nine cases of acute glomerulonephritis not associated with group A streptococcal infection (Bates *et al.*, 1957). More specifically, three cases (in children) of fatal nephritis developing after mumps infection in the absence of serological or cultural evidence of streptococcal infection have been reported (Hughes *et al.*, 1966).

We suggest that the present case may not be unique and that such cases may not be unusual in adults.

If this possibility of a mumps infection as a cause of acute nephritis can be accepted on the evidence presented, then the mumps virus must be added to the lengthening list of nephropathic "agents."

G. E. MONTEIRO, M.B., B.S.,
Medical Senior House Officer.

C. A. LILLICRAP, M.D., F.R.C.P.,
Senior Consultant Physician.

Lincoln County Hospital, Lincoln.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Bleeding from the Upper Gastrointestinal Tract

G. N. CHANDLER,* D.M., M.R.C.P.

Haematemesis and melaena are symptomatic of haemorrhage into the upper gastrointestinal tract. When such bleeding has occurred the patient will almost always volunteer the information that the blood, if it has been vomited, has come from the stomach. Occasionally the origin of the blood may not be immediately obvious—as when haematemesis occurs as an isolated symptom in a previously healthy person—and there may also be difficulty when the supposed blood vomit has not been kept to be seen by the doctor. Examination of the stools will resolve any such doubts. Haematemesis never occurs without some blood appearing in the stools, and even in the absence of melaena chemical examination of the faeces will show the presence of much more blood than could be accounted for by other means.

Incidence and Mortality

Haematemesis is one of the commonest medical emergencies that may threaten life, and of the complications of peptic ulcer it is the most frequently encountered. Estimates of the clinical incidence of haematemesis vary from a quarter to approximately a third of all patients with peptic ulcer. The tendency to bleed is about the same during the whole course of the disease, with the exception of the first year, in which it is somewhat greater. Most published series show a mortality rate of between 5% and 10% under conservative medical treatment. However, if only examples of massive haemorrhage are considered the death rate is higher. Massive bleeding is defined as haemorrhage that is accompanied by shock, a lowering of the red cell count to 3,000,000/cu. mm. or less, and a haemoglobin level below 50%. With these criteria of selection the mean mortality rate is about 15%, with a range of 4% to 66%.

Though the mortality from haemorrhage in chronic ulcer is considerably higher than in bleeding from acute lesions, the most important correlation is with age. Below 45 years the death rate is small, but it increases sharply after the age of 60; in most western countries haematemesis is steadily increasing both in frequency and severity as the age structure of communities alters with increasing numbers of older people.

Cause of Bleeding

Peptic ulcer is easily the most important cause of haematemesis and melaena, accounting for about 9 out of every 10 admissions, but rather more than a quarter of these patients have no demonstrable radiological abnormality when examined after bleeding has ceased. Nevertheless, gastroscopy or gastro-camera inspection performed in the early stages of illness will reveal the presence of an acute ulcer in over half of this group with negative x-ray findings. These lesions heal quickly, and

it is in this group that aspirin consumption makes its appreciable contribution to the number of hospital admissions for upper gastrointestinal bleeding.

Haematemesis and melaena are not uncommon complications of carcinoma of the stomach, but the diagnosis has usually been made before the onset of bleeding. In these cases the loss of blood is generally small, though exceptionally, as in the ulcerating type of cancer, it may be profuse. As the blood remains in the stomach for some time before it is vomited, it is generally coffee coloured and mixed with food and mucus.

Haemorrhage from oesophageal varices is not uncommon in cirrhosis of the liver, but confusion in diagnosis may occur since there is often a dyspeptic history and sometimes an associated ulcer. Bleeding from an oesophageal growth is rarely an early symptom and a diagnosis is likely to have been made already on account of dysphagia. Likewise an aortic aneurysm leaking into the oesophagus will almost certainly have given rise to other symptoms and signs to betray its presence. Oesophageal hiatus hernia, sliding or fixed in character, is a common gastro-enterological lesion, and bleeding may occur either from an associated oesophagitis or from a gastric ulcer straddling the region of constriction at the level of the diaphragm.

Certain blood dyscrasias may be associated with haematemesis and melaena, but they are infrequent causes of these symptoms. Nevertheless, when the source of bleeding is not obvious nor the history typical the possibility of an underlying haemorrhagic diathesis should always be investigated. Usually a history of bleeding elsewhere will be obtained. Anticoagulants should not be given to patients with known gastroduodenal ulceration, but nevertheless patients on anticoagulant treatment can develop acute ulceration.

Symptoms and Signs

The clinical picture in massive haemorrhage is dominated by the development of shock. The patient is pale both from blood loss and compensatory vasoconstriction. The pulse is rapid and small; there may be marked sweating. One of the first changes to be recorded is a fall in blood pressure, and repeated measurements are essential in estimating cessation of recurrence of bleeding. Restlessness may be extreme, and rapid shallow respirations are of grave import. It is usual for any ulcer pain preceding the bleeding to disappear with the onset of haemorrhage, and the persistence of pain of any severity should always suggest the possibility of concomitant perforation, a particularly lethal combination.

The management of patients with haematemesis and melaena depends to a large extent on the diagnostic probabilities, and an adequate history should be obtained either from the patient or, if he is too ill, from an informed relative. Inquiry should be made for any antecedent history suggestive of peptic ulceration, and any record of perforation or previous radiological confirmation of the existence of an ulcer is extremely valuable.

* Consultant Physician, Chapel Allerton Hospital, Leeds.

The physical examination of these patients should be undertaken with care so as not to exhaust them. The severity of the bleeding will be immediately apparent and should be confirmed by measurement of pulse rate and blood pressure. Abdominal examination must include palpation for an enlarged spleen and an epigastric mass. The existence of a collateral circulation in hepatic cirrhosis is diagnostic of this condition. Malignant disease of the stomach may suggest its presence by a palpable tumour and enlarged glands in the supraclavicular fossa. An assessment of the extent of arteriosclerotic change in older patients is important and demands examination of the superficial arteries and the fundi. Where thrombocytopenic purpura is suspected, a tourniquet test with a sphygmomanometer cuff should be carried out.

Principles of Treatment

There is no longer any controversy about the advisability of liberal feeding. Most patients tolerate bland diet extremely well, given two-hourly with sufficient fluid to correct dehydration and maintain an adequate urinary output. Confinement to bed is essential if bleeding continues and morphine 15 mg. or sodium phenobarbitone 200 mg. may be given to allay restlessness or anxiety. Pulse rate and blood pressure should be measured hourly and the details recorded, together with any further episode of bleeding, on a chart available at the bedside.

There can be no hard-and-fast rules on when blood transfusion is required. While determinations of blood volume would enable the clinician to assess the amount of blood lost accurately, such techniques are as yet unsuitable for routine use and reasonable indications for transfusion are a pulse rate of 110 or more or a systolic blood pressure of 110 mm. Hg or less. Such patients need transfusion urgently, and prompt action is particularly important in the elderly to prevent the irreversible cerebral damage that may complicate prolonged shock. If severe anaemia is allowed to develop a compensatory increase in venous pressure leads to greater cardiac filling and improved cardiac output. This hyperkinetic phase is shown by the presence of a full, bounding pulse, raised pulse pressure, and jugular venous distension. The venous pressure also rises during the initial stages of transfusion, and though it falls again as the arterial pressure rises overtransfusion carries the risk of precipitating heart failure. Ideally part of the replacement after massive bleeding should consist of packed red cells to minimize the possibility of overloading the circulation and to reduce the risk of pulmonary oedema. Usually gastroduodenal bleeding stops within 12 or 24 hours of admission, most often permanently, and during this time 1,500–3,000 ml. of blood may be given by slow drip transfusion (40 drops per minute). Occasionally there is a continuous slow loss of blood requiring intermittent transfusion, and this seems to happen most commonly in patients bleeding from acute lesions; the vessels from which an acute ulcer bleeds are mostly small and submucosal, and such bleeding lacks the dramatic quality of arterial haemorrhage from the base of a chronic ulcer. Exceptionally, chronic ulcers bleed so severely that the only hope for the patient lies in intra-arterial transfusion and immediate operation.

Transfusions of 500 ml. are unnecessary and wasteful. Large volumes of blood given rapidly carry risks of citrate intoxication and hyperkalaemia. The former may lead to defective clotting and myocardial failure and it is wise to give 10 ml. of 10% calcium gluconate intravenously after every fourth bottle of blood. Potassium intoxication carries the very real threat of cardiac arrest—particularly if bank-blood near the limit of its expiry is used—when serum potassium levels may reach 25 mEq. Warming the blood before use will encourage the return of potassium to the cells and the danger can be further diminished by the infusion of dextrose solutions. However, when such massive transfusions are in question the need for surgical arrest of haemorrhage should be urgently reviewed.

Medication other than vitamin concentrates is best avoided, though iron may be given by mouth from the start. Constipation is the rule after haematemesis and is usually well tolerated by the patient. Purgatives should not be administered, but there is no contraindication to the giving of an enema or the use of a glycerin or Dulcolax (bisacodyl) suppository.

Time in Bed

There is no reason why the patient whose course is uncomplicated should not be allowed up by the second or third day in hospital. There is no evidence that recovery after haematemesis is hastened by confinement to bed, the dangers of which are obvious, especially in older people with associated degenerative disease.

The management of bleeding from oesophageal varices consequent on cirrhosis will be considered in a separate article. Some of these patients die from haemorrhage long before the reduction of hepatic function has become a threat to life.

Though brisk continued bleeding from peptic ulcer is an indication for surgical treatment, there are a few patients in whom operation is out of the question because of severe associated disease or overwhelming senility. Nevertheless, however unpromising the prognosis may appear, neither hope nor treatment should be abandoned. Distension of the stomach with blood clot may be an important factor preventing the atonic stomach of a shocked patient from arresting the bleeding by contraction. Emptying the stomach with a Senoran's evacuator followed by lavage with ice-cold water may help to stop bleeding. The use of a topical haemostatic such as thrombin after lavage with 1:1000 adrenaline has been advocated in the treatment of bleeding acute peptic ulcer. In such cases the stomach should first be emptied through a large bore tube and then washed with 1:1000 adrenaline; finally, thrombin in a suitably viscous vehicle as methylcellulose is instilled into the stomach. Gastric cooling has not won any wide acceptance either for the treatment of bleeding peptic ulcer or for haemorrhage from oesophageal varices using an oesophageal extension of the gastric balloon.

Early Diagnosis in Haematemesis

The difficulty of treating bleeding peptic ulcer largely concerns the detection of those patients in whom the prognosis with medical measures must be considered poor and who will bleed to death unless surgery is employed. The problem, however, is not always easily solved. Acute ulceration or erosion of the stomach or duodenum is a common lesion which usually responds well to medical treatment. Unfortunately this diagnosis is not always obvious, being largely based on negative evidence and frequently confirmed only in retrospect by a negative x-ray. The vessels from which an acute ulcer bleeds are mostly small and submucosal, and operation should be undertaken only as a life-saving measure or because a chronic ulcer is suspected.

Extragastric sources of bleeding must also be excluded before patients are submitted to surgery. The history is most valuable in achieving a correct diagnosis; thus where chronic peptic ulceration is responsible for the bleeding it will be unusual to find such a patient denying previous periodic dyspepsia with relief of his pain by food and alkalis. The shorter the history of preceding dyspepsia, the more likely is the lesion to be acute and therefore susceptible to cure by medical means alone. Unfortunately the diagnosis is not always obvious and the history often misleading.

An attempt to obtain diagnostic information in the acute stages of illness can be helpful in subsequent management, for if chronic peptic ulcer can be diagnosed with confidence surgical treatment is to be recommended for patients over the age of 50 in whom bleeding continues or recurs. The success of such

a selective surgical policy has been shown by its favourable influence on overall mortality (which can be reduced to about 4%), and the prompt submission of suitable patients to operation is almost certainly an important factor in achieving the best results.

Early barium-meal examination has been adopted in some centres as a means of obtaining useful information. The procedure can be undertaken on the ward using a portable x-ray set and without manipulation or the need to move the patient from his bed. Combined with gastroscopy or the use of the fibroscope or gastro-camera it has proved possible to achieve a correct diagnosis of the cause of bleeding in about 80% of patients admitted with haemorrhage from peptic ulcer, usually within 24 or 36 hours from admission. The introduction of the fibroscope or the blind use of the gastro-camera has further

minimized the interference and discomfort suffered by the patient, for, unlike gastroscopy, the procedures can be undertaken on the ward and are far less disturbing.

The importance of reaching an early decision as to the surgical treatment of haematemesis cannot be overemphasized; nevertheless, if it is decided to operate, a little time may be allowed to improve the patient's condition by blood transfusion unless bleeding is so profuse as to permit no delay. Chronic gastric ulcer is a particularly strong indication for surgery; bleeding from this source carries a high mortality under medical treatment and its operative arrest by gastrectomy is generally easier than is the surgery of bleeding duodenal ulcer. The indications for surgical intervention in haematemesis and the treatment of bleeding oesophageal varices will be discussed in further contributions to this series.

TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Epsilon Aminocaproic Acid

Epsilon aminocaproic acid (E.A.C.A.), marketed by Kabi Pharmaceuticals Ltd. under the name of Epsikapron, is a potent synthetic inhibitor of fibrinolysis. It is used in the treatment of haemorrhagic states.

Chemistry and Pharmacology

E.A.C.A. is a monoamino carboxylic acid structurally related to lysine; its full inhibitory action is dependent on the epsilon position of the amino group. It does not occur naturally but is synthesized as a white crystalline substance, freely soluble in water, with a molecular weight of 131.

E.A.C.A. inhibits the activators which convert the inactive globulin plasminogen into plasmin, the enzyme which normally digests fibrin. At concentrations greater than 10^{-4} M. E.A.C.A. competes with the activators for the enzyme-binding sites of the plasminogen molecule.¹ Weak non-competitive inhibition of plasmin occurs only after a hundredfold increase of concentration, and even then no effect is apparent on blood coagulation or platelet aggregation.

Clinically significant effects are seen with a plasma E.A.C.A. concentration of 10^{-3} M.; this can be produced by a dosage of 0.1 g./kg. body weight given either orally or intravenously every four hours.²

E.A.C.A. is absorbed rapidly from the gut with peak plasma levels two hours after a single oral dose. The drug is distributed throughout the body water, freely entering the intracellular compartment. The half-life in plasma after a single intravenous injection is of the order of one to three hours; continuous infusion is therefore necessary to maintain adequate blood levels by the intravenous route. Excretion is almost entirely via the kidney, and within 12 hours of a single oral dose 60% to 90% appears unchanged in the urine.²

Clinical Indications

The use of E.A.C.A. should be considered when bleeding cannot be controlled by conventional procedures.

Coagulation Disorders, including Haemophilia.—Whenever fibrin formation is deficient, inhibition of even the normal

fibrinolytic process may preserve sufficient fibrin to permit adequate haemostasis. The use of E.A.C.A. need not therefore be confined to those cases in which an increase in fibrinolysis can be demonstrated.

In haemophilia treatment with E.A.C.A. has been shown to reduce bleeding after tooth extraction.³ Patients under treatment with anticoagulants, and patients with von Willebrand's disease, have also been successfully treated, both for tooth extractions and for menorrhagia.

These examples are concerned with bleeding to the exterior. E.A.C.A. may be just as effective in the control of internal bleeding, but great care in the evacuation of blood clot from the body cavities is necessary if residual damage due to formation of fibrous tissue is to be avoided. In cases of haematuria successful results have been claimed, but urinary obstruction is known to be a possibility, and the incidence of this complication has yet to be defined.

E.A.C.A. has also been used in double-blind trials to test its efficacy in reducing the incidence of spontaneous bleeding episodes in haemophilia.⁴ Early results are promising but not yet conclusive.

Menorrhagia.—The concentration of plasminogen activators in the endometrium is high and increases as menstruation approaches to reach a maximum on the first day of the period. Double-blind trials have shown that inhibition of fibrinolysis reduces the volume of menstrual flow.⁵ If curettage has excluded organic lesions of the uterus and endometrium treatment with E.A.C.A. may be useful for those patients who wish to preserve fertility, especially if hormone therapy has failed or is contraindicated. The drug need be started only when bleeding becomes heavy and need be continued only so long as the flow lasts.

Prostatectomy.—Several trials have shown that the blood loss after prostatectomy can be reduced by giving low doses of E.A.C.A.⁶ The incidence of thrombotic complications in the postoperative period is not affected by E.A.C.A. alone. However, a considerable reduction in pulmonary embolic complications has been achieved by the routine prophylactic administration of heparin, made possible by the simultaneous use of E.A.C.A.⁷

Hyperfibrinolysis.—Excessive amounts of plasminogen activators in the blood may provoke bleeding by the release of plasmin in amounts which overwhelm the natural antiplasmins and attack essential clotting factors, reducing their concentration and blocking fibrin formation still further by the anticoagulant effects of the split products of fibrinogen. In these

circumstances E.A.C.A. is one of the ideal treatments, but primary hyperfibrinolysis is difficult to distinguish from other causes of the defibrination syndrome. It is probably rare unless activators such as streptokinase or urokinase are being deliberately administered as a part of thrombolytic therapy.

Defibrination Syndrome.—In complicated obstetrics, major surgical operations, and disseminated cancer massive bleeding may occur suddenly after widespread intravascular clotting has depleted the available clotting factors.⁸ A common secondary phenomenon in these cases is an increase in fibrinolysis, which is likely to have a protective effect. For this reason when a low level of circulating fibrinogen is demonstrated E.A.C.A. is probably best held in reserve.

Treatment should begin with controlled replacement of fibrinogen and other missing factors, including platelets. If the stimulus to defibrination persists and bleeding continues heparin may be used as an anticoagulant; once the stimulus to clot formation has been controlled in this way E.A.C.A. may assist haemostasis by preventing the removal of fibrin.⁹

Other Uses.—The list of examples in which E.A.C.A. may be used to assist haemostasis is not exclusive. Other suggested uses include epistaxis, ulcerative colitis, and haematemesis; precise indications have yet to be defined.

An anti-allergic action has been attributed to the drug, which has been said to provide improvement in progressive systemic sclerosis and in eczema.¹⁰ Experimental results are conflicting, and the clinical impressions do not stem from organized trials.

Toxicity and Side-effects

Non-thrombotic.—One large carefully investigated series reports the administration of the drug to 774 patients without serious toxicity.¹¹ Minor side-effects include nasal congestion, conjunctival suffusion, nausea, vomiting, diarrhoea, maculopapular rashes, and transient hypotension.

Daily injection into pregnant rats has been reported to cause teratogenic effects in the embryos.¹² Although more recent work failed to confirm this finding,¹³ E.A.C.A. should not be given in the early stages of pregnancy until further studies are available. E.A.C.A. also inhibits the incorporation of lysine into the proteins of a rat diaphragm preparation,² and may slow the growth rate of rats given 100 mg. daily.¹⁴ For these reasons prolonged administration should be avoided during the active growth period of childhood.

High doses have been reported to cause subendocardial haemorrhages in dogs,¹⁰ but no such lesion has been described in man. The intravenous administration of 5 g. of E.A.C.A. per hour, a fivefold increase of the usual dose, causes a small (about 5%) decrease in systolic and diastolic blood pressure, together with a bradycardia, but without any significant change in renal blood flow or glomerular filtration rate.¹⁵ No electrocardiographic changes have been noted. One patient has been reported,¹⁶ who died 32 days after being given E.A.C.A. to control a haemorrhagic state associated with prostatic carcinoma. At necropsy scattered areas of necrosis were found in heart and liver, but their cause was not clear.

Thrombotic.—Fibrin is necessary to promote haemostasis or repair, but once its immediate purpose has been accomplished it must be removed by the fibrinolytic system, normally in dynamic equilibrium with the coagulation system. Undesirable effects may occur if the balance is disturbed by the administration of E.A.C.A., so that removal of fibrin is prevented.

Fibrin formed from blood within a body cavity may remain to become organized into fibrous tissue. In the pleural space this may form a rigid coating surrounding the lung.¹⁰ Similar persistence of clot within a joint cavity may potentiate residual damage to the joint. If clotting occurs in the urinary passages during treatment of haematuria with E.A.C.A. the indestructible

clots may cause permanent obstruction to the urinary outflow tract.⁶

Widespread intravascular fibrin formation is a feature of the defibrination syndrome and also of the later phases of shock. In most of these cases plasminogen activators are released which stimulate endogenous fibrinolysis. If this protective effect is blocked by E.A.C.A. widespread persistence of intravascular thrombi may have fatal results. Examples of such a condition have been found in experimental animals and in man.¹⁷

Presentation and Dose

For oral use there are sachets of effervescent powder, each containing 3 g. of E.A.C.A. There is also a 30% w/v syrup.

For intravenous use, or local application, a 40% w/v solution may be given diluted at least fourfold in physiological saline or glucose solution.

The usual dose, oral or intravenous, is 0.1 g./kg. body weight repeated every four hours. Intravenous administration is started by giving the calculated dose in 30 minutes, followed by a sustaining infusion. Dosage should be reduced if renal function is impaired. As the drug is concentrated in the urine, 3 g. of E.A.C.A. by mouth every eight hours is sufficient to maintain urinary activity in the adult.

There is no contraindication to the simultaneous administration of heparin or oral anticoagulants.

E.A.C.A. is available as Epsikapron. The basic N.H.S. price of 30 sachets of 3 g. is 39s. 10d., and of 250 ml. of 30% syrup is 35s.

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<i>Charles Hastings and Worcester</i>	Price 3s. 6d.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Transmission of Rays through Glass

Q.—*Is there any form of window glass which permits the passage of a large proportion of ultra-violet rays?*

A.—Almost all of the biological actions of ultra-violet radiation occur at wavelengths below 3,100 Å. Ordinary window glass transmits very little below this limit. Special glasses with better transmitting properties were developed during the 1920s. The heavy absorption of ultra-violet rays by glass is associated with the presence of small amounts of ferric oxide. Vita glass differs from common window glass mainly by the addition of a small proportion of boric oxide and the careful exclusion of iron oxide.

The manufacture of Vita glass ceased in Britain some 30 years ago, though the material is still available in the United States. No other window glass with enhanced transmission in the ultra-violet region is currently being made in Britain. The daily amount of ultra-violet rays received at most points in a normal building, even if its windows are glazed with Vita glass, is very small—seldom more than would be obtained by spending a few minutes out of doors in the middle of the day.

Transmission of Abnormalities by Homozygotes

Q.—*A marriage of first cousins produced a healthy boy and a healthy girl. Each of these has married, and the boy has two girls, one of whom has a mitral murmur and the other has syndactylia, webbing of the second and third toes of each foot, and band amputation of the terminal phalanges of all fingers. The girl has a daughter who has been diagnosed as suffering from Turner's syndrome, and has abnormal feet and hands, wide chest, and webbed neck. To what extent is the first-cousin relationship of the grandparents responsible for these congenital abnormalities?*

A.—It is unlikely that the grandparental-cousin marriage is in any way responsible for the varied congenital malformations in the grandchildren. There is at present no evidence that increased homozygosity in a parent leads to an increased risk of chromosomal or other congenital abnormalities in the children.

Effectiveness of A.T.S.

Q.—*Is the effectiveness of antitetanus serum in preventing tetanus lessened in proportion to the length of time after the injury when it is first given?*

A.—To be effective, antitetanus serum must be given in sufficient quantities to ensure that the subject at risk has a protective level of circulating antitoxin at the time tetanus spores start germinating and producing toxin. After administration of 1,500 I.U. A.T.S. the blood antitoxin titre rises to a maximum within one to three days but

then steadily falls to below protective levels within two to three weeks. A longer period of passive immunity is obtained with human tetanus immunoglobulin.

The incubation period of tetanus in man is usually 5 to 14 days but can vary from 3 days to 5 weeks. A.T.S. given within 24 hours of injury should therefore protect against all tetanus infections except those with a long incubation period. If its administration is delayed toxin may have already been formed in cases with a short incubation period. Once formed it is rapidly fixed by the tissues and cannot be neutralized by subsequent injections of antitoxin. It is for these reasons that the effectiveness of tetanus prophylaxis is related to the interval between injury and administration of serum.

Oral Poliomyelitis Vaccine

Q.—*Should a dose of oral poliomyelitis vaccine be repeated when vomiting occurs after its administration? What sort of interval from administration to vomit must elapse for it to be unnecessary to repeat the dose?*

A.—Oral poliomyelitis vaccine (O.P.V.) consists of attenuated strains of the three types of poliovirus. When taken by mouth they can infect and multiply in the alimentary canal, producing antibodies and intestinal resistance to reinfection with the same type poliovirus. A dose between 100,000 and 1 million particles of the different types is the least amount of virus required to immunize consistently, allowing for wastage and individual resistance. Since infection with one type may interfere with another, the vaccine is fed three times at intervals of at least four weeks, thus giving each type three separate opportunities to infect the intestines.

If vomiting occurs immediately after O.P.V. is given the retained amount of each type of poliovirus may be insufficient to give rise to infection and multiplication in the intestines. A supplementary dose should therefore be given at the time to compensate for the amount lost, but if a few minutes elapse before vomiting occurs there is no need to repeat the dose.

Baldness in Women

Q.—*Is punch-grafting of hair-bearing skin a feasible treatment for baldness in women? What other treatment might there be for severely thinned, greasy hair in a middle-aged woman?*

A.—Punch-grafting has been developed essentially for male-type patterned baldness, in which there is a vigorous growth of hair on the back and sides of the scalp and more or less complete baldness in the vertex and frontal region. Punch grafts are taken from the hair-bearing area and arranged along the frontal margin of the scalp so as to blend with a wig. Occasionally it may be possible for sufficient hair to be produced in this way for a wig to be unnecessary. Punch-grafting is not often likely to be satisfactory treatment

in women because the loss of hair is likely to be only partial and probably more diffuse.

Severely thin, greasy hair in a middle-aged woman may result from a wide variety of causes. First it is necessary to ascertain that the thinning of hair is not due to brittleness. When it is broken hairs can easily be seen over the scalp, and the condition may be traced to injudicious hairdressing treatments such as waving, bleaching, etc. More diffuse falling of hair may result from inflammatory conditions of the scalp, particularly seborrhoeic dermatitis. Thinning of the hair of the scalp at the time of the menopause and soon after is so common as to be virtually physiological. Treatment is ineffective.

A diffuse falling of hair may also result from iron deficiency, even in cases where there is no anaemia. It may be dietary in origin or may be the result of deficient absorption of iron. Because of this, a complaint of diffuse falling out of hair without ascertainable cause is often taken as an indication for oral iron therapy for at least a period of a few months. Various types of endocrine disorder may result in diffuse thinning of the hair, and sometimes it is the first sign of an insidious endocrine disorder. In recent years attention has particularly been directed to thyroid diseases, and even when there are no other clinical signs of hypothyroidism or hyperthyroidism laboratory tests should be carried out.

The results of various investigations will indicate treatment. At all times, however, the patient should be cautioned against over-vigorous local treatment. It is suspected that shampooing two or three times a week may in itself promote greasiness and possibly falling of hair. Energetic massage may also do more harm than good. Unless there is a clearly recognized underlying local condition any local treatment is likely to be ineffective.

Inhalation of Iron Dust

Q.—*Is there a medical indication for exhaust-extraction of dust when large cast-iron castings are being turned on a lathe? Some lathes doing this work seem to be fitted with means of extraction and others not.*

A.—It is assumed that the cast-iron castings referred to have been cleaned and that the dust which may arise during lathe-turning will be iron dust free from silica and other dusts which are known to cause fibrosis of the lungs. Though iron dust does not cause fibrosis, it is radio-opaque and will produce changes in a chest x-ray. It is desirable to prevent inhalation of any dust by applying suitable local exhaust ventilation.

Arctic Spray

Q.—*What safety precautions should plumbers take when using Arctic Spray, which consists of dichlorodifluoromethane, for freezing small-bore water pipes, bearing in mind that the majority of plumbing repairs are carried out with the operator working in a restricted space, about 2 ft. (61 cm.) below ground level?*

A.—The freons, of which dichlorodifluoromethane is an example, are chemically inert and non-toxic. Their accepted threshold limit value is 1,000 p.p.m.

NEW APPLIANCES

Peritoneal Dialysis with In-line Sterilization of Dialysate by Filtration

Dr. P. SHARPSTONE, lecturer in medicine, King's College Hospital Medical School, London S.E.5, and Dr. F. S. GOLDBY, medical registrar, King's College Hospital, London S.E.5, write: Peritoneal dialysis by means of commercially prepared solutions and disposable giving sets (Maxwell *et al.*, 1959) is a simple and effective technique, and is in general use in the management of renal failure and sometimes for the correction of overhydration. Disadvantages inherent in this system, however, include the high cost of the dialysate and the risk of introducing infection during the repeated interruption of the fluid pathway in order to change and to make additions to individual 1-litre containers of dialysate. McDonald (1965) has overcome these problems by preparation of dialysate in bulk at the time of use by diluting a concentrated solution with water and sterilizing the final solution by filtration through a 0.22-micron filter during its passage to the patient. He used an automatic peritoneal dialysis machine, but as manual methods of dialysis are more widely used at present we describe here a manually controlled system in which in-line filtration sterilization of the dialysate is used.

METHODS

Five hundred millilitres of a $\times 40$ peritoneal dialysis concentrate (Romford Laboratories Ltd.), 500 to 1,500 ml. of 50% dextrose solution, and potassium, heparin, etc., as required are placed in a 20-litre stainless steel pressure vessel (Millipore (U.K.) Ltd.), which is then filled to a 20-litre internal calibration mark with distilled water. The water is pyrogen-free but unsterilized, and is obtained from the hospital pharmacy in 25-litre polyethylene aspirator bottles. The dialysate is mixed by stirring and its concentration checked by osmometry. The vessel is pressurized by air at 15 lb./sq. in. (1.05 kg./sq. cm.) from a cylinder fitted with 0-30 lb./sq. in. (0-2.1 kg./sq. cm.) regulating valve (British Oxygen Co. Ltd.). Opening the outlet tap of the pressure vessel allows the required exchange volume of dialysate to flow through a 0.22-micron 142-mm. Millipore filter (Millipore (U.K.) Ltd.) into a modified 2-litre polypropylene measuring cylinder (Xlon Products Ltd.) suspended from a transfusion pole 5 ft. (1.5 m.) above the patient (see Diagram). Release of a tubing clamp then allows the dialysate to flow by gravity into the peritoneal cavity through a disposable warming coil (R66 blood warmer, Baxter Laboratories Ltd.) in a thermostatically controlled water bath (JB 1, Grant Instruments (Cambridge) Ltd.). With a bath temperature of 42° C. and a flow rate of 200 ml./min., the dialysate reaches the patient at a temperature of about 33° C.

Disposable vinyl tubing (Portland Plastics Ltd.) is used throughout. After use the pressure vessel and measuring cylinder are thoroughly cleaned and sterilized by autoclaving. The filter holder, after cleaning, is reassembled with a new filter membrane and pre-filter and sterilized in ethylene oxide. Before each dialysis the integrity of the filter

the hospital from a concentrate and distilled water. Sterilization of fluid in large containers is, however, difficult (Bosch *et al.*, 1966) and has led to the adoption of the present technique, which also eliminates the risk, inherent in the conventional method, of introducing infection during the conduct of the dialysis itself. The 0.22-micron filter

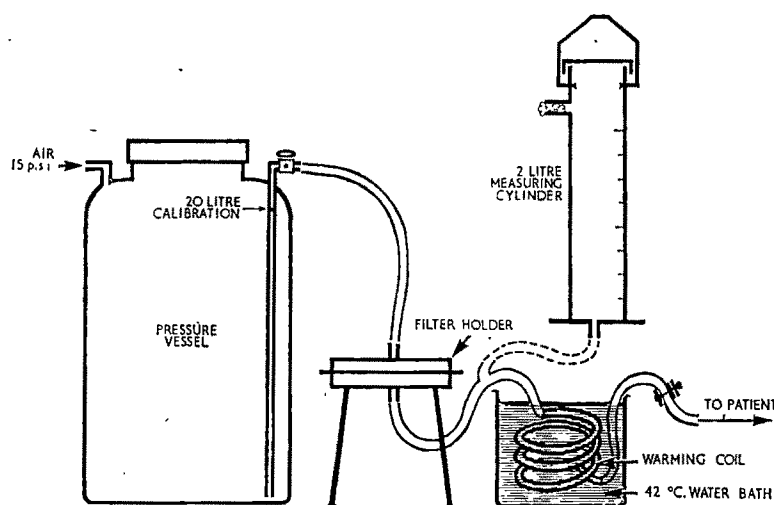


Diagram of apparatus for sterilization of dialysate by filtration, and the delivery of measured volumes to the patient via a heating coil.

is confirmed by demonstrating its inability, when wet, to pass air at 25 lb./sq. in. (1.76 kg./sq. cm.).

Animal tests for pyrogens were carried out on samples of dialysate taken from the patient's side of the filter at the end of every third dialysis. Each was given intravenously, in a dose of 3 ml./kg., to three rabbits whose temperatures were monitored for three hours by rectal thermocouples.

RESULTS

Thirty 20- to 40-litre dialyses have been performed with this system. After preparation of the dialysate and apparatus (by medical or specially trained nursing staff) the dialyses were conducted by nurses who required only brief instruction in the technique. Up to 40 litres of dialysate could be exchanged before blockage of the filter membrane necessitated its replacement.

The patients' oral temperatures were recorded two-hourly during dialyses and no pyrexial reactions occurred. All 10 samples of dialysate tested in rabbits were completely free of pyrogenicity.

DISCUSSION

A very considerable saving in dialysis fluid costs is achieved by its bulk preparation in

does not remove pyrogens, but with attention to the cleanliness of the apparatus and the use of pyrogen-free water the dialysate has proved free of pyrogenicity.

Additional advantages of the in-line sterilization system are that the dextrose content and exchange volume of dialysate can be adjusted to the requirements of individual patients; and that as no adjustment of potassium or dextrose content of the dialysate is made during the conduct of the dialysis this may safely be left in the hands of relatively untrained and unsupervised personnel.

We are grateful to Professor J. Anderson and Dr. V. Parsons for permission to treat patients under their care; to Professor A. C. Cunliffe and Dr. A. Dasgupta for help with the bacteriology; and to Dr. D. Gall, of the Wellcome Research Laboratories, for advice and for performing the pyrogen tests. We thank also Mr. J. G. Mulvany, of Millipore (U.K.) Ltd., and Mr. C. H. Chapman, of Grant Instruments (Cambridge) Ltd., for the loan of equipment.

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Metabolic Balance Cot for the Newborn Infant

Dr. COLIN H. M. WALKER, consultant paediatrician, Dundee Royal Infirmary and the Department of Child Health, University of Dundee, writes: Techniques for the performance of metabolic balance studies in infants can be divided into two main categories—those in which diaper collection is used (Slater, 1961; Widdowson, 1965) and those in which a special cot with a catchment area is employed (Forfar and Prain, 1950; Barness *et al.*, 1957). A disadvantage of the first method is the risk of loss from a loose diaper or leakage of soft stool past a displaced plastic liner. Balances which require the application of cups (Thomson, 1944) or adhesive bags (Baldwin *et al.*, 1962) have the disadvantages of skin trauma, and constant observation by nursing staff is required to ensure adequate application of the collector. In fact it has been said that "success ultimately depends upon the persistent and personal supervision of the collections by members of the team, who must be prepared to devote a considerable part of their time solely to this aspect of the study" (Stevens *et al.*, 1962).

As medical and nursing staff become more and more difficult to obtain there is a reluctance to ask staff to take part in those metabolic balance studies which might be regarded as yielding useful information yet non-essential to immediate patient-care. For the purpose of performing total metabolic balances of fat and calcium in the newborn an alternative method of collection has therefore been designed.

METABOLIC COT

The cot consists of two main parts which can be used in conjunction with a standard folding crib currently in use in many nurseries (Fig. 1). The outer part consists of a V-shaped catchment which declines to the feet and drains into a funnel at the foot end

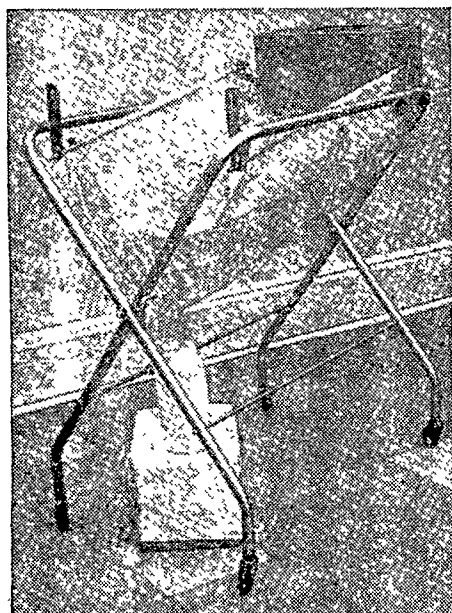


FIG. 1.—Metabolic cot assembled without covers.

of the cot. It is made of 0.01-in. (0.25 mm.) transparent polyvinyl chloride plastic and is electronically welded at the edges in such a way that cleaning is not difficult. The inner layer is suspended on a second pair of rods and is a sling of 0.02-in. (0.5-mm.) opaque polyvinyl chloride in which $\frac{3}{8}$ -in. (1-cm.) holes have been punched $\frac{3}{8}$ -in. (1.6-cm.) apart (Fig. 2). The holes are punched in such a way that there is slight embossing with the sharp edge pointing downwards, and though the skin is marked by the holes no injury or

the infants behave normally while nursed on the sling and are fully observable. The assembly is inexpensive, is easily cleaned, and sustains contact with detergent and chemical antiseptics and cleaners. A standard ward cot can be employed and the catchment and sling can be stored in a small space when not in use.

The disadvantages include the need for a temporary napkin collection during breastfeeding, though the advantages remain between whiles. If separate stool and urine

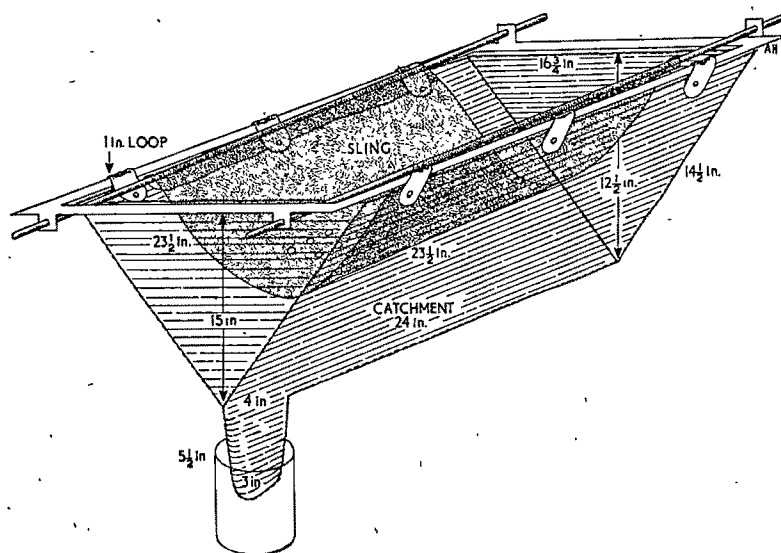


FIG. 2.—Diagram of metabolic cot with dimensions.

irritation occurs over the balance period. This material was selected after other pure plastics and plasticized fibres had been found unsatisfactory because of skin trauma, lack of strength, fraying, or absorption of fluid by fibres.

The cot blanket is encased in non-absorbent plastic and the infant is nursed naked on the sling. The body temperature falls no more than 1° F. (0.55° C.) in a nursery kept at an average temperature of 78° F. (25.6° C.). All excreta either run through the sling on to the catchment or can be washed through. Extra firm stools may be picked off the sling, but as the stool of a newborn infant is usually soft this is seldom necessary. Collection is made into polyethylene bottles continuously mounted below the funnel, and both cot and baby can be swabbed down with deionized water and brush nylon wipes as often as required. The infant is fed in the cot by nurse or mother. During feeding a non-absorbent bib of nylon seersucker is used to catch any regurgitation or vomitus, just as in other study methods, and any wipes used can also be kept in a separate polyethylene bottle for analysis and correction of "intake."

The advantages of this cot are that it allows total collection with minimal handling of the baby and minimal nursing care. The method is fully acceptable by mothers, and

collection is required an adhesive bag technique can be added, and should leakage occur it would probably be more readily noticed in the "open" cot than with a "closed" diaper technique. Occasionally a rather large quantity of deionized water is required for thorough cleansing at the end of the balance study. This makes the analysis more tedious but none the less efficient.

Thanks are expressed to Mr. L. A. McKenzie and Mr. W. Kay, Regional Physics Laboratory, Eastern Regional Hospital Board, Scotland, and Mr. D. M. High, of D. M. High, Waterproof Clothing Manufacturers, Dundee, for their assistance in the construction of this metabolic cot.

This project is supported by a grant from John Wyeth & Brother Ltd.

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Book Reviews

Black Magic

The African Witch. With Particular Reference to Witchcraft Beliefs and Practice Among the Shona of Rhodesia. By Michael Gelfand, C.B.E., M.D., F.R.C.P., D.P.H. (Pp. 227+xvi; illustrated. 30s.) Edinburgh and London: E. & S. Livingstone. 1967.

Everyone knows that witches really do exist—especially physicians who practise in the rural areas of Africa. Many, in due course, achieve a harmonious if unofficial working relationship, each recognizing the value of the other, the one for scientific medicine and the other for faith healing. It is indeed only in the mid-nineteenth century, with its great advances in microbiology, biochemistry, and therapeutics that Western medicine has supplemented faith and the apothecary's bottle of medicine with medical science.

In Africa (where animism is prevalent) mysticism and ritual still rule the lives of the majority in the rural areas, and even in the urban areas they still persist, though to a lesser extent. Some two years ago an article appeared in a Nigerian daily newspaper reporting that a small rural retailer whose business was failing consulted a female witch-doctor and allegedly murdered his wife: to produce a brew with certain fats and herbs to boost the business. In Senegal the "marabout" or sorcerer may be both the religious leader and medicine man of his community. Fetishers also undertake dental excisions, incise abscesses, and make simple prosthetics. There are "spirits" for both good and evil. The Kisii in Kenya still trepan certain patients who are possessed of evil spirits giving rise to headaches, mental disturbance, etc., with primitive tools, making a hole to let out the evil spirit. Such is the belief in the powers of witchcraft.

In brief and general terms, many African tribes believe in an all-pervading and prevailing creator who is everywhere, but remote. Lesser spirits, however, more closely related to man's daily activities, exist for both good and evil. The good is the witch-doctor, who, using bones, stones, spells, or potions, removes spells and alleviates sickness. This is the Mganga of the Wakamba. Evil may be accomplished by two methods: either by the ancestral spirit removing his "protection," or by a witch or fetisher (the Mchawi of the Wakamba) casting spells.

The practising physician in Africa, if he is non-African, learns about the inter-relationship of witchcraft and medicine the hard way—by experience. He learns that the African does not believe in Western ideas of the aetiology and epidemiology of disease. He learns that the African consults both types of healer—the physician for the immediate cure of the disease, and the witch doctor for the eradication of the cause. He learns that these are people whose lives are bound by tribal patterns of behaviour, beliefs, and customs. The individual is an integral part of his community, whose thinking tends to be communal, and is subject to many fears and stresses due to transgression of these rules and the attempt to avoid transgression. Add to this the stresses imposed in an attempt to adopt Western concepts and modes of life, and it is little wonder that anxiety states and psychosomatic ills exist. We per-

haps underestimate these strains, the point at which breakdown occurs, and the resort to tribal healers for reassurance.

Michael Gelfand, in his capacity as a trained observer of facts and as a warm human physician with scientific curiosity, has endeavoured to investigate the interface of medicine and witchcraft. This is a book which dissects and displays the anatomy of witchcraft in relation to one particular people of Africa: the Shona of Rhodesia. He describes the people, their culture, and their spiritual beliefs. He describes the types of witches, good and evil, the means they use, the prevalence of witchcraft, and its effect on individuals and communities. He describes the types of illnesses ascribed to witchcraft, the treatment employed, and the results. He examines the place of the witch and the witch-doctor in the daily routine of life.

Perhaps this book is best described as a field-epidemiologist's analysis of witchcraft. It may not be an expert social-anthropologist's bible, but it certainly should be on the shelf of every practising rural physician in Africa. It should rank with his textbooks of tropical medicine and hygiene, to the greater understanding of the afflictions of his patients and community, not to mention the greater understanding by the physician-administrator—for example, page 68 reveals that requests to attend a funeral are not the proverbial facile excuse of the office boy but a serious matter for the African who is absent from the funeral of his relative. In reading this book physicians may begin to understand some of the reasons for the inevitable slowness of change and to remember the old adage—more haste, less speed.

N. R. E. FENDALL.

Sympathetic Amines

The Uptake and Storage of Noradrenaline in Sympathetic Nerves. By Leslie L. Iversen. (Pp. 253+xiii; illustrated. 57s. 6d.) London: Cambridge University Press, 1967.

This is a remarkable book, consisting as it does of a rewritten Ph.D. thesis, and one wishes fervently that more theses had the same potentiality. It consists essentially of two components. The first is a review of the current state of knowledge about uptake and storage of noradrenaline by sympathetic nerves. This is a most valuable review, with a balanced historical outlook, careful selection of references, and a critical approach which does not debar the author from specifying, on particular issues, on which side of the fence he prefers to sit. Possibly the account of xylocholine (parent of today's adrenergic nerve blocking agents) is a little cursory, but this is a small price to pay for such carefully chosen references in general. The second component is the author's own work, particularly his identification in the heart of two uptake mechanisms, handling the

sympathetic amines. His original papers provide a fuller, more rigorous, and indeed more enjoyable account of this work; but the present book allows him to put it into context—to bring out, for instance, the analogies between his Uptake₁ and the uptake-mechanism of the intracellular particles obtained from sympathetic nerve.

The book reflects strongly the present technology of work on the sympathetic system. Most of our best recent knowledge has come through the development of efficient spectrofluorimetry, of tritiated amines with high specific activity, of differential ultracentrifugation, and (most recently) of fluorescence methods applied to amines. As a result, chemistry and biochemistry bulk large, and there is only one record of a physiological experiment illustrated (that of miniature potentials). Those not chemically minded may find their minds clotted by the formidable chemical arrays of amines and related drugs. Yet it is a fact that, once the discovery of reserpine reawakened research on the adrenergic nervous system, it has been the biochemical pharmacologists who have been making the pace. (An awkward conse-

quence of their rate of progress is that the reader must be warned that views have now changed (for instance, about the site of Uptake₂) in a few respects.)

It is an attractive feature of the book that the author himself looks forward to the time when the various transport, binding, and release mechanisms and the subcellular structures are integrated into a functioning unity. The volume can be strongly recommended, with all praise for the care in its production and its compact, efficient index.

W. D. M. PATON.

First Aid

New Essential First Aid. By A. Ward Gardner, M.D., D.I.H., and Peter J. Roylance, M.B., Ch.B. (Pp. 174; illustrated. 3s. 6d.) London: Pan Books. 1967.

This small paperback is the best book on first aid I have read. It is written expressly for the ignorant amateur and throughout emphasizes that the sole function of first aid is to provide the minimum essential treatment to

keep the patient alive and to get him to a doctor or hospital in the best possible condition. In making this point the authors sacrifice a good deal of the minute detail of bandaging, splinting, etc., which is found in most first-aid manuals, but since this book will be bought and used by those who have no particular interest in the subject—for example, road users and householders—nothing is lost thereby.

After a general introduction there is a most important chapter on priorities in first aid. This is a most difficult problem for the layman when, faced with a number of more or less seriously injured people, he has to decide in what order to treat them. In each individual patient, too, it is important to recognize which conditions need urgent treatment and which may be safely left. Obviously each situation must be treated on its merits, but the authors lay down basic principles which any one with average common sense should be able to apply.

Excellent chapters are devoted to mouth-to-nose artificial respiration and unconsciousness. These are followed by sections dealing with bleeding, burns, fractures and dislocations, head injuries, poisoning, and bandaging. A small section on accidental hypothermia is included and there is a very welcome chapter on organizing the first aid at an accident. Most of what the authors say about this is no more than common sense, but this is so often lacking in those trying to help at an incident.

This book should be in every household and in every car. I can recommend it unreservedly.

E. J. CLEGG.

Neuroradiology

Pneumoencephalography. By E. Graeme Robertson, M.D.(Melb.), F.R.C.P., F.R.A.C.P., F.C.R.A.(Hon.). (Pp. 808 + xxiii; illustrated. \$30.50.) Springfield, Illinois: Charles C. Thomas. 1967.

Nearly 30 years ago Graeme Robertson developed the method of controlled fractional encephalography. Gradually his technique has been taken up by neuroradiologists all over the world. Ten years have passed since the first edition of his *Pneumoencephalography* was published; almost immediately it became the bible for workers in this field. With 10 years of added experience, and with his excellent system of documentation, a much-welcome second edition has appeared. The new text is nearly twice the size of the old, and the number of illustrations has been more than doubled. The list of references has lengthened and has been brought up to date.

The author has left most of the old text more or less intact, but many of the chapters have been considerably amplified covering new work. This applies particularly to injuries of the head, developmental anomalies, and encephalography in childhood. Much of the work in the last of these chapters has been facilitated by the use of a special encephalographic paediatric chair developed by his neurosurgeon colleague Mr. R. S. Hooper. From the photographs it looks good and inexpensive.

The most important addition to the work is the long chapter entitled "Comparative Assessment of Pneumoencephalography in

the Investigation of Neoplasms With and Without Increased Pressure." This has been a very vexed question for many years, and it is salutary to see such an authoritative opinion in print. Graeme Robertson is not only a distinguished neurologist but also a neuroradiologist by partial adoption, and his opinion and judgement on this question cannot be lightly dismissed. All medical men concerned with patients suspected of harbouring intracranial tumours will find this chapter of particular interest.

Generally speaking, the reproductions of radiographs are of a high standard, but the publishers might note that some of the pulls from the old blocks are not as good as in the first edition, and one (Fig. 43b) has been reproduced upside down in the new edition (correctly in the first edition). Taking the text as a whole one can find no major faults. The book has become a classic—one can say no more except to look forward to a third edition in another decade.

J. W. D. BULL.

Old People in Our Social Structure

The Social Needs of the Over-80's. The Stockport Survey. By Fraser Brockington, M.A., M.D., B.Chir.(Cantab.), D.P.H., M.R.C.P.(Lond.), M.Sc.(Manch.), and Susanne M. Lempert, M.B., Ch.B., D.P.H. (Pp. 147 + vi. 35s.) Manchester: Manchester University Press. 1966.

The Social Needs of the Over-80's is the report of a survey of all people over 80 years of age in the County Borough of Stockport. When preparing the survey, great difficulty was experienced in identifying the old people. Inquiry from general practitioners, for example, produced only 801 names, whereas it was finally estimated that there were 2,516 persons over 80 years of age in the county borough. This difficulty in finding the aged until their health has completely broken down runs like a thread through the whole book, which becomes an implicit and sometimes explicit plea for preventive care of the aged.

The general characteristics of the aged and the way they fit into the social structure is investigated and analysed under the following headings: sociability, diet, housing, incapacities and illness, mobility, and survival.

To those who have worked with the aged the book brings no surprises, but many impressions are confirmed by factual evidence documented in great detail. This is a healthy exercise because impressions without factual correction often imperceptibly become fantasies and, on occasion, hobby horses. The authors find that the domiciliary services fall short in many aspects in meeting the needs of the over 80s, partly because many old people were unaware of the help available, and partly because the services themselves were sometimes inadequate. They report that prevention as a primary object hardly exists even at such special danger points as leaving hospital or bereavement, and that this failure results in unnecessary admission to institutions.

They conclude that the best hope of improvement lies in a real integration of the existing social and medical services, quoting the authority of the W.H.O. for this, while

accepting the great difficulties which will have to be overcome.

E. WOODFORD-WILLIAMS.

Approaches to Anatomy

An Introduction to Functional Anatomy. 3rd edition. By David Sinclair, M.A., M.D., D.Sc., F.R.C.S.Ed. (Pp. 466; illustrated. 52s. 6d.) Oxford: Blackwell. 1966.

Clinical Anatomy. A Revision and Applied Anatomy for Clinical Students. 3rd edition. By Harold Ellis, M.A., M.Ch., D.M., F.R.C.S. (Pp. 381 + xvi; illustrated. 40s.) Oxford: Blackwell. 1966.

These two books have a different approach to anatomy. Both have now reached their third edition and undoubtedly serve a useful purpose.

Professor Sinclair's book is aimed at the medical ancillary staff who require a basic knowledge not only of anatomical structure but also of elementary physiology of the human body. This new edition has been improved by the addition of much new material, and the chapters on joints and the genitourinary system have been completely rewritten and brought up to date. It gives a concise account of the various tissues and systems of the body and discusses the functional topography of the various organ systems. These different aspects are combined in a very readable and interesting way. The text is well set out and there is a full glossary at the end of the book.

Professor Ellis's book, on the other hand, is essentially a book for medical students and sets out to give the clinical approach to anatomy and highlights those features of anatomy which are of importance in medicine, midwifery, and surgery. The text is particularly suitable for the revision of anatomy during the clinical course and for preparation for final examinations. Although unsuitable as a replacement for the larger textbooks necessary for a student during his initial study of human anatomy, it can serve as a very useful supplement to stimulate the student's interest and to demonstrate the relevance of the subject to clinical practice. The diagrams are simple, numerous, and readily reproducible. The entire text has been revised and many of the illustrations replaced or supplemented.

Both books are more than adequate for the purpose for which they are written and can be recommended without reservation.

W. J. HAMILTON.

"Classic" of Pathology

Recent Advances in Pathology. 8th edition. Edited by C. V. Harrison, M.D. (Pp. 414 + x; illustrated. 70s.) London: J. & A. Churchill. 1966.

This book first appeared in 1932 and since then the appearance of every subsequent edition has been awaited with eagerness. It has always been a great favourite with medical students who had become especially interested in pathology, and some of the chapters of previous editions have become classics. *Recent Advances in Pathology* has always seemed to have a double orientation.

It was directed towards a relatively junior audience, at least as far as pathology was concerned, and was based on a structural or morbid anatomical standpoint. The eighth and latest edition, under the able editorship of Professor C. V. Harrison seems to have retained both these traditions.

The book opens with an outstandingly good account of chromosomal abnormalities in man, by Professor B. Lennox, that will be widely appreciated by students and their teachers. Dr. R. H. Heptinstall's chapter on renal disease rather disappointingly avoids discussion of current views on the pathogenesis of glomerulonephritis, although he does mention Goodpasture's syndrome (apparently inappropriately named, like most eponymous conditions), which now occupies a central position in the controversy on the role of immune complexes in renal pathology. Dr. J. G. Azzopardi contributes a very full account of the systemic effects of neoplasia that is extremely useful, but here again a greater digression into pathogenetic mechanisms would have been appreciated. As might be expected, Professor K. Weinbre's chapter on liver disease is of a high standard and topical. Indeed, the same is true of Professor Harrison's own contributions on lymphoid tissue and arterial disease, and of the chapters by Professor K. A. Porter on tissue transplantation, by Dr. D. Hourihane on malabsorption, and Dr. B. E. Heard on lung disease. There is no doubt the eighth edition of this famous book maintains the tradition of providing an up-to-date account of the structural basis of pathological problems of topical interest.

In view of the book's avowed object it may be unfair to ask for more discussion of pathogenetic mechanisms and inclusion of more material from other disciplines (Professor Porter is a notable exception here) or even ultrastructural data. Much if not most of this experimental material may not stand the test of time. Nevertheless, to paraphrase Sir Thomas Lewis, "it may be exciting, even if untrue," and education and intellectual excitement are inseparable.

W. G. SPECTOR.

Paediatric Cardiology

Heart Disease in Infancy and Childhood. 2nd edition. By John D. Keith, M.D., Richard D. Rowe, M.B.(N.Z.), F.R.C.P. (Edin.), and Peter Vlad, M.D. (Pp. 1239 + xvii; illustrated. £15.) London: Collier-Macmillan. 1967.

The appearance of the second edition of this well-known textbook of paediatric cardiology will be welcomed by all those who are interested in the field. Dr. Keith and his colleagues have substantially revised the first edition and added a number of new chapters. In the preface the authors comment on the continuing need for accurate data on the natural history of heart disorders, despite the fact that surgery has altered the prognosis in so many cardiac lesions.

The book opens with a chapter on the incidence of congenital and rheumatic heart disease, and continues with chapters on heart sounds and murmurs, blood pressure, electrocardiography, oximetry, cardiac catheterization, and angiocardiology. In the chapter on cardiac catheterization special attention is devoted to the risks of the procedure, which are shown to be remarkably small with modern techniques. A chapter on the embryology of congenital heart disease has been contributed by J. W. A. Duckworth, and on the familial occurrence of congenital heart disease by I. Uchida. Chapters then follow on specific lesions, starting with patent ductus arteriosus and working through all congenital anomalies and including important chapters on complete transposition of the great arteries, the dextrocardias, single ventricle, and chamber localization by R. Van Praagh.

The second half of the book is devoted to, in the main, cardiac disorders not of a congenital origin, such as rheumatic heart disease, cardiac involvement in the collagen diseases, bacterial endocarditis, pericarditis, congestive heart failure, the arrhythmias, pulmonary heart disease, atherosclerosis, glycogen storage disease, and other topics. Electrolyte imbalance and the electrocardiogram, and the heart in thyroid disorders and in neuromuscular dystrophies, also receive attention. There is a useful chapter on heart disease

associated with chromosomal abnormalities and on Marfan's syndrome. The final chapters include cardiac tumours, sudden death in infancy and childhood, the heart in anaemia, and cardiac involvement in gargoylism.

In each chapter the subject matter is dealt with exhaustively, the incidence, pathology, physiology, aetiology, diagnosis, treatment, and prognosis being clearly set out. The text is authoritative and detailed without being over-dogmatic, and the very extensive experience of the authors, and in particular of Dr. Keith, is evident from the clarity and decisiveness of the writing. The illustrations are excellent, and there is a good bibliography at the end of each chapter, with a comprehensive index at the end of the book. Every chapter is designed especially to throw light on recent advances—technical, physiological, medical, and surgical.

The book concludes with five appendices on diagnostic problems in angiocardiology, and in cardiac catheterization, clinical problems in congenital heart disease, and, perhaps the most valuable of all, drugs and dosages useful in heart disease in infancy and childhood. Finally, the *tour de force* of the book, Appendix 5, is a tightly condensed summary of all the important features of congenital heart disease arranged as a table.

There is little to criticize in this notable textbook, and it is difficult to pick out any particular part as being better than another. Of special interest to many readers will be the results of the researches of Dr. Keith's associates on the natural history of ventricular septal defect, the incidence of spontaneous closure, and the behaviour of the pulmonary vascular system. Essentially it is a reference book which will inevitably be part of the library of cardiologists and cardiac surgeons, as well as of many general physicians, paediatricians, and research workers in other fields. Withal it is an extremely readable book, owing to the excellence of the writing and the presentation of important data. The authors are to be heartily congratulated on their second edition, which will undoubtedly have a wide appeal and create an extensive demand.

J. F. GOODWIN.

Books Received

Review is not precluded by notice here of books recently received.

Symposium: Thyroid Disease and Calcium Metabolism. Royal College of Physicians of Edinburgh. (Pp. 159; illustrated. 25s.) Edinburgh: R.C.P. 1967.

Cutaneous Sensation. By David Sinclair. (Pp. 306 + xii; illustrated. 63s.) London: Oxford University Press. 1967.

French Pensions. Occasional Papers on Social Administration No. 21. By Tony Lynes. (Pp. 163. 25s.) London: G. Bell. 1967.

Radium Dosage. The Manchester System. 2nd edition. Edited by W. J. Meredith, D.Sc., F.Inst.P. (Pp. 134 + viii + appendix; illustrated. 42s.) Edinburgh and London: E. & S. Livingstone. 1967.

Les Prix Nobel. En 1966. (Pp. 182; illustrated. 50 Swedish kronor.) Stockholm: Norstedt. 1967.

Principles of Autonomic-Somatic Integrations. By Ernst Gellhorn, M.D., Ph.D. (Pp. 318 + xiii; illustrated. 80s.) Minnesota: University Press. London: Oxford University Press. 1967.

Progress in Experimental Tumor Research. Vol. 9. Edited by F. Homburger. (Pp. 341 + x; illustrated. £5 10s.) Basle: S. Karger. London: Academic Press. 1967.

Contact Lenses. Symposium in Munich-Feldafing, 1966. Edited by O. H. Dabiezies, H. Laue, A. Schlossman, and G. P. Halberg. (Pp. 173; illustrated. £4 11s.) Basle: S. Karger. London: Academic Press. 1967.

The Kidney. An Outline of Normal and Abnormal Structure and Function. 3rd edition. By H. E. de Wardener, M.B.E., M.D., F.R.C.P. (Pp. 408 + viii; illustrated. 60s.) London: J. & A. Churchill. 1967.

Allgemeine Chirurgie. Ein Lehrbuch für Studierende und Ärzte. By Professor Max Saegesser. (Pp. 411; illustrated. DM. 55.) Bern and Stuttgart: Hans Huber. 1967.

Current Medical Research. Reprint of the Articles in the Medical Research Council's Annual Report, April 1966–March 1967. (Pp. 83 + iv; illustrated. 8s.) London: H.M.S.O. 1967.

Lecture Notes on Cardiology. By J. S. Fleming, M.D., M.R.C.P.(Lond. and Edin.), and M. V. Brainbridge, M.A., M.B., B.Chir.(Cantab.), F.R.C.S.(Eng.). (Pp. 317 + x; illustrated. 35s.) Oxford and Edinburgh: Blackwell. 1967.

Dento-facial Development and Growth. By James Henderson Scott. (Pp. 205 + xii; illustrated. 63s.) Oxford: Pergamon. 1967.

Vademecum der Fettsucht. By Professor Walter Krebs. (Pp. 90. No price given.) Berlin: Volk und Gesundheit. 1967.

Contractions of the Tympanic Muscles in Man. By Gisle Djupesland. (Pp. 113; illustrated. 45s.) Oslo: Universitetsforlaget. 1967.

Cellular Aspects of Membrane Permeability. By E. Schoffeniels. (Pp. 266 + xiii; illustrated. £5.) Oxford: Pergamon. 1967.

Middle Articles

MEDICAL HISTORY

Queen Elizabeth Hospital for Children, London: Centenary of "The Queen's," 1867-1967

VALENTINE A. J. SWAIN,* F.R.C.S.

Brit. med. J., 1967, 4, 733-735

One hundred years ago the Queen Elizabeth Hospital for Children was established in Bethnal Green by the Misses Mary Elizabeth and Ellen Phillips. Their social conscience was stirred by the terrible scourge of Asiatic cholera in 1866 which spread rapidly through the east of London. This epidemic threw a pitiful light on the way children of the poor lived. In the squalor and overcrowding the sick, ill-clothed, and ill-fed children drew attention to the urgent need for a special hospital. The population of Bethnal Green and Shoreditch was nearly a quarter of a million. In the hospitals' annual report of that time we read: "In the great city of London, which till a few years ago possessed no hospital for children, out of every 100 children 24 die annually during the first 2 years of life, and during the next 8 years 11 die out of the remaining 76. These children perish, not because there is in them (in most cases) any dangerous sickness but for want of sanitary and medical knowledge in respect of their tender lives."

Early Days

In the first part of the nineteenth century the establishment of special hospitals met with opposition, especially in the case of children's hospitals, for many thought that it was essential for the mothers to care for their own children. Florence Nightingale in 1860 wrote that "the causes of the enormous

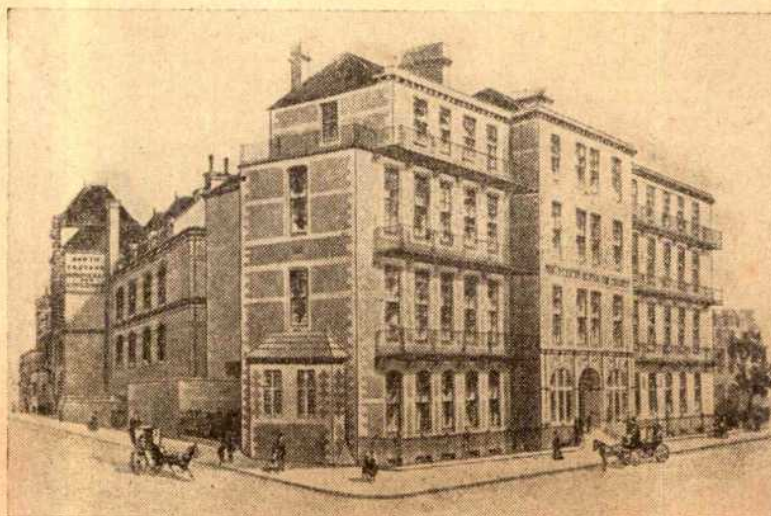
child mortality are perfectly well known, they are chiefly want of cleanliness, want of ventilation, and want of whitewash: in one word, defective household hygiene."

On 12 July 1867 the Misses Phillips rented a house in Virginia Row, Bethnal Green, and set up the "Dispensary for Women and Children." As the patients so thronged the building, it was decided that children only would be treated. The next year the work was transferred to 125 Hackney Road, near to Shoreditch Church, where in addition 12 cots were provided. Soon this building too became inadequate, and in 1870, with the financial help raised by a bazaar at Cannon Street Hotel, the freehold of 327 Hackney Road (part of the present site of the hospital in Goldsmith Row) was purchased. From this humble beginning the hospital enlarged to its present size. In the early days annual subscribers had the privilege of recommending a number of children as outpatients and/or inpatients in proportion to the amount subscribed. Otherwise the charge of two-pence was made for an outpatient attendance and inpatients paid 2s. 6d. per week. This payment had a salutary effect, permitting genuine cases to be seen, and "upheld the self-respect of people, so that they would not be regarded as paupers." The children had to be brought in the arms of their parents, but when too ill to be so transported nurses visited their homes. In 1898, owing to the large number of the more prosperous parents seeking treatment, an inquiry officer was appointed to check the abuse, and in 1903, with the appointment of Miss Miller Jones, this post became that of lady almoner.

* Senior Surgeon, Queen Elizabeth Hospital for Children, London E.2.



Miss Mary Elizabeth Phillips.



The North-Eastern Hospital for Children, Hackney Road.



Mrs. Alex Fox (née Ellen Phillips).

Raising of Funds

The Phillips sisters were members of the Society of Friends, and likewise the Foundation Committee under the Presidency of Joseph Gurney Barclay consisted of prominent members of that fraternity—William Beck, John D. Fry, J. Lister Godlee, Edmund Pace, and Nathaniel Tregelles. Thus from the beginning the hospital benefited by the benevolent philanthropy, wisdom, and business initiative of this pioneer committee. At first, in 1868, there was only a handful of generous benefactors, but gradually funds were sought for expansion. Bazaars, concerts, and dinners were organized to meet the cost of new buildings. Soon Royal Patrons, Queen Victoria and the Royal Princesses, and civic and ecclesiastical dignitaries graced these efforts. Voluntary subscriptions and funds increased to pay for future projects. City companies, merchants, bankers, and also friends of the hospital contributed, and individual gifts were numerous. In 1877 the Children's Association was established "to promote an interest among children of the upper classes in the welfare of children of the poor, to provide funds for the maintenance of the hospital and to encourage the use of the talents and leisure time of children to benefit the hospital and its patients." Later such funds as the "Stamp Collectors' Fund" started by Mr. Glenton Kerr, the secretary, and the "Little Folk's Fund" did much to spread the name of the hospital abroad. In 1893, through the generous gift of £10,000 by Mr. John Horniman, the building fund was set up. In 1897 a three-day bazaar was held at Queen's Hall to raise funds for the additional building. The Duchess of Connaught, the Duchess of Marlborough, and the Duchess of Newcastle performed the opening ceremonies. Many other distinguished personages and friends took an active interest in the hospital. At the turn of the century H.R.H. Princess Louise opened the new building and 134 beds became available.

Medical and Nursing Staffs

From the beginning the hospital was equally fortunate in having a distinguished medical staff. In 1867 (Sir) Jonathan Hutchinson and (Sir) Morell Mackenzie became the first consulting surgeon and physician respectively, and (Sir) Wilson Fox's name was later added as consulting physician. He was a fellow student of Joseph Lister, and, like Hutchinson, was also a Quaker. These great clinicians introduced promising colleagues to serve on the staff, such as the erudite Dr. William B. Woodham, Dr. A. E. Sansom, and Dr. W. Cayley as physicians. The last two actively served the hospital for 15 years.

The surgeon, Mr. Waren Tay, was appointed in 1868, as a friend and collaborator with Hutchinson; both contributed much to general surgery and ophthalmology. Also the two eponymous diseases, Tay-Sachs disease and Hutchinson's triad, reflect a small part of their wide interest as writers, teachers, and clinicians. They had the distinction in 1871 of being the first to successfully operate on an infant suffering from intussusception. During Waren Tay's 21 years on the staff (Sir) Rickman J. Godlee in 1881 became the second surgeon for the next seven years and consulting surgeon till his death in 1925. Godlee, Joseph Lister's nephew and assistant, "did much to enhance the reputation of the hospital." All these physicians and surgeons were also on the staff of teaching hospitals—the London, University College, or Middlesex. These set the pattern for future years.

The nursing staff was also of high standard. Miss Anne Elizabeth Horne, trained at St. Thomas's Hospital, was the first Lady Superintendent and Matron in 1870. She had "general charge and management of the hospital" and looked after the housekeeping and household accounts and held "the position of mistress of the family." The nurses had to be "able to read as well as write with facility, and each nurse should attend to the children with care and kindness and use every endeavour to make them happy." "The Matron's and Servants' wages" amounted to £117 16s. 8d. a year. On her marriage to Yardley Warner in 1877 Miss Horne went to America to undertake philanthropic work. She was succeeded by Miss E. W. Curno (1877–1902) and Miss Ann Bushby (1902–27). Miss Bushby was trained at the East London Hospital for Children and King's College Hospital; her outstanding interest in children's nursing led to her election to the General Nursing Council, and she was Vice-President of the British College of Nursing. Many of the nurses trained at the hospital became matrons at other children's hospitals and many served overseas.

Specialties

Gradually during the century general medicine and surgery made way for special disciplines, and the hospital kept abreast of medical progress. Though anaesthesia and antiseptic methods were adopted in the hospital in the early days, the scope of surgery was limited at first to opening abscesses, removing necrotic bone, treating injuries and deformities, and an occasional tracheostomy and lithotomy operation. The first "chloroformist," Dr. John Poland, was appointed in 1880; before this the residents were instructed in anaesthesia, and in fact Dr. Sansom, who was a friend of John Snow, in 1865 wrote his book, *Chloroform: Its Action and Administration*. In some hospitals an extra salary was paid to the anaesthetist, but it was not until 1870–80 that the specialist posts were established. Later other specialists followed, for in 1895 Mr. Sydney Stephenson became the first ophthalmologist, and two years later Mr. John W. Pare started a pioneer special dental clinic for children.

In 1898 electric lighting was installed throughout the hospital, and the 7th Duke of Newcastle, who was a Life Governor and later a member of the Management Committee, in the same year presented the gift of the "complete and very powerful Roentgen Rays apparatus." It was to be supervised and examined at the cost of two guineas annually. By this gift the hospital was the first children's hospital to possess such an apparatus. This event was celebrated by a soirée—"plants for decoration, an extra porter, and a band were engaged" for the ceremony.

In 1910, the ear, nose, and throat and the skin departments were started by Mr. W. G. Howarth and Dr. H. G. Adamson. Other specialties followed, so that now most of the special branches of paediatrics are represented.

Before the first world war in 1914 women became eligible for two of the resident medical appointments, and the late Dr.

NEW HOSPITAL FOR CHILDREN AT SHOREDITCH

This morning a fancy bazaar is held at the Cannon-street Hotel, concerning which it may be useful to give a few heads of information. Under the special patronage of their Royal Highnesses the Prince and Princess Christian, the Prince and Princess of Teck, and the Princess Louise, it is to be opened by the latter in person, who, in a certain sense, is acting for the Queen; for her Majesty has taken the deepest interest in the labour in hand, and has contributed personally to the stalls, while the Princess of Wales, the Crown Princess of Prussia, and other members of the Royal Family have sent goods worked by their own hands, or collected by themselves, in the hope of increasing materially the fund on behalf of which the bazaar is held. It is desired to increase the scope of a Children's Hospital, now working in Shoreditch, and her Majesty and family who, as is well known, send annual presents of toys, and in other substantial modes, testify their interest in the excellent establishment in Great Ormond-street, are earnest in their wish to aid the project for which to-day's bazaar is held, in the most direct and unmistakable way. We have just visited the modest little establishment now open, have endeavoured to master the principle upon which it is carried on, and have come away profoundly satisfied that those who show themselves of the Queen's way of thinking by supporting the bazaar to-day will further an institution which is admirable in its

was necessary to limit it to children only. In April, 1868, the present house was taken in 11 Hackney-road, the services of a second medical officer and of a qualified dispenser were procured, and a dispensary opened four days in the week. Before this, it must be understood, a lively interest had been roused in the neighbourhood, and the appointment of an influential committee, and the receipt of handsome donations and subscriptions gradually followed. The good things grew and prospered. The benevolent impulse and constant care of its far founder met with their reward, and in February last year two small wards, containing two beds, were provided, in addition to the out-patients' department, and the new hospital for children was established. It has not yet been able to exceed the limit named, though the little beds are arranged so near to each other as to be almost in contact with sanitary conditions, and though most pitiable cases are pleading for admission within its doors. Up the narrow stairs, and down a light and cheerful bottom on the first floor, where a stout and motherly-looking nurse reigns over her little charges with a loving hand, and where toys and picture-books are being played with and turned over by wee little fellows, who turn a wistful eye to the new comer while such of them as are strong enough ask questions as to their condition and treatment of a grateful smile. They are eminently well behaved. The refining influence of all health is embodied what is coarse and elevated what is tender in their little faces, until no visitor could suppose them to be of other than gentle nurture and blood. We shall again avoid the description of their complaints. Why distress

Excerpt from the *Daily News*, 16 May 1870.

Helen Mackay (paediatrician 1916–59) recalled that the hospital served both “as general practitioner as well as consultant for children miles around.” In the neighbourhood there was still much poverty and undernourishment. Rickets was very common and so also were anaemia and dental caries. Gastro-enteritis then had a death rate of about 50%. “No treatment, other than skilful nursing, was available for very many of the patients in the medical wards.” Between 1920 and 1930 there was a “grim period of unemployment,” after which the living standard gradually rose, and because of better feeding and care the health of children improved. About that time paediatrics became a specialty, and some 25 years later paediatric surgery was established as an entity. In the 1930s additional buildings were completed—Princess Elizabeth Ward (1930) to accommodate infants and nursing mothers; an enlarged dental department, massage and light department (1934); a new outpatient department (1938); and new casualty, pathology, and x-ray departments and observation ward (1939)—thus 160 beds were available in London and 44 beds at Bexhill.

At the outbreak of the second world war the Queen's was designated as a hospital for civilian casualties only, on the assumption that there would be a mass evacuation of all children from London; but gradually the child evacuees returned to East London, and so the children's outpatient and casualty department were reopened. In the Battle of Britain period of 1940 large-scale evacuation of children returned. The sick children of the Queen's Hospital with those from Princess Elizabeth of York, Shadwell, were accommodated at an improvised hospital at Ashendene in Hertfordshire and at Bayford. Both of the main hospitals received their share of the air raids and bombs that fell heavily on East London, but the buildings survived without major damage.

When in 1868 the hospital first moved to Hackney Road it was named the “North-Eastern Hospital for Children,” becoming “The Queen's” in 1908. With the amalgamation in 1942 of the “Princess Elizabeth of York Hospital for Children” (formerly the East London Hospital for Children, Shadwell), the new title the “Queen Elizabeth Hospital for Children” was acquired under the patronage of H.M. the King and H.M. the Queen and H.R.H. Princess Elizabeth. Other branches of the

hospital are the Little Folk's Home at Bexhill (1930) and the country hospital at Banstead, Surrey—a gift from Mr. Stanley Garton—completed in 1948. In 1948, with the National Health Service Act, the hospital became part of the N.E. Metropolitan Regional Hospital Board. In 1963 the Shadwell branch was closed for economic reasons. That hospital, formerly the “East London Hospital for Children,” had a parallel beginning with the Hackney Road branch, but its history is another story. Since 1946 regular postgraduate teaching has been undertaken in association with the Institute of Child Health, and more recently undergraduate students attend for paediatric training.

The Hospital Today

The Queen Elizabeth Hospital today is a busy general children's hospital for acute cases, and with its 270 beds serves the neighbourhood, and by reason of its special interests young patients also come from all parts of the country and overseas. Through the close links with maternity units, many newborn babies are admitted, and their congenital disorders and malformations are a special study in the hospital. The changing pattern of disease in children today shows a large increase in the work among the youngest age groups. The special investigations, techniques, and modern treatment call for increased space and staff. The present and future generation of nurses, doctors, and patients will find encouragement in the very generous support given by the Hayward Foundation to the hospital's Research Appeal Fund for the building of a new diagnostic unit and research laboratories. These new additions will help to keep the hospital in the van of medical progress. Funds are still needed to endow these enterprises. Furthermore, it is hoped that a new operating-theatre suite with an intensive care unit and a new nurses' home, to replace the old residence, will be built, and that perhaps additional wards will be planned by the next decade.

The fulfilment of these plans would be a legacy worthy of those members of the Society of Friends who founded the hospital 100 years ago.

MEDICAL EDUCATION

Training of Nephrologists

Two recent publications^{1,2} have recently appeared dealing with the training of nephrologists. A memorandum¹ by the Renal Association defines nephrology as “the study of renal structure and function in health and disease, including the prevention and treatment of diseases involving the kidney and urinary tract at all ages.” The memorandum envisages two types of renal unit—*major units*, which would serve a population of about 2 million and would usually be situated at teaching or major district hospitals; and *subsidiary units*, which would serve a population of about 200,000, and would preferably be associated with a major unit. The major unit would contain 60 beds, including 10 for intermittent haemodialysis. It would undertake the full management of all types of renal disease, including renal trans-

plantation; the training of nephrologists and urologists; research; and the co-ordination of the subsidiary units in the area. The subsidiary units would be mainly concerned with intermittent haemodialysis.

The staffing envisaged in the memorandum comprises two or three consultant nephrologists; two or three urologists; two or three whole-time senior registrars (one surgical); and six medical registrars/senior house-officers (divided between medicine and surgery). Staff to provide a 24-hour specialist ancillary service would also be necessary.

The report of the Royal College of Physicians' Committee on Nephrology² recommends that nephrology should be recognized as a specialty of medicine. It considers that it will be necessary to provide special training for both nephrologists—that is, consul-

tant physicians almost wholly engaged in the specialty—and general physicians with a special interest in nephrology. The committee suggests that after the pre-registration year nephrologists should spend a year in gaining further experience in a hospital post, or in a laboratory or research post. Thereafter two years should be spent in general clinical medicine at registrar (or equivalent) level, and four years at senior registrar (or equivalent) level, with at least six months' experience in dialysis at some stage of training.

REFERENCES

- ¹ *Training of Nephrologists*, Memorandum of the Executive Committee of the Renal Association, 1967.
- ² *Committee on Nephrology: Report*, 1967. Royal College of Physicians of London.

CONFERENCES AND MEETINGS

Exploration of Teaching in General Practice: Conference at R.C.G.P.

[FROM A SPECIAL CORRESPONDENT]

A one-and-a-half-day conference on the exploration of teaching in general practice was held at the Royal College of General Practitioners in London on 8 and 9 December.

Dr. D. L. CROMBIE (general practitioner and Director of the College Records and Statistical Unit, Birmingham), speaking on "The Problems of Teaching in General Practice," said the general practitioner's function was primary assessment of undifferentiated clinical material. A personal doctor practising continuing care, he relied on the assessment of probabilities. Classical teaching of medical students, based on diagnostic procedures suitable for selected hospital cases, was unsuitable for this material, and young general practitioners had to learn appropriate methods when they got into practice. A rational medical education should teach both methods of diagnosis, but would do so only when general practitioners themselves became teachers. The discipline of general practice could become reproducible and transmissible only after research into general practitioners' methods, which should be initiated by academic departments.

Dr. KEITH HODGKIN (general practitioner, Redcar), on "Factual Observations," demonstrated that the clinical material in general practice differed in both quality and quantity from that seen in hospital. Teaching based on hospital material gave a false bias. A survey into acute appendicitis in Newcastle had shown that 49% of children had perforated appendices on admission to hospital because of delay in diagnosis by parents and general practitioners. He showed from figures in his practice that this delay was due to confusion with gastroenteritis: a general practitioner saw about 150 cases per annum, of which one or two had appendicitis. Improvement in diagnosis would come by recognition of this confusion. It could be taught only in general practice because gastroenteritis is not a hospital disease.

View of the Medical School

Professor Sir BRIAN WINDEYER (Dean of the Middlesex Hospital Medical School, London), speaking on "As the Medical School sees the Problem," gave the consensus of opinion in one school, though he said that each school must evolve in its own way. Undergraduate education no longer hoped to produce a complete doctor, but to teach basic knowledge of causation, manifestations, and history of disease, as well as the effects of the behaviour of individuals. In the past the school had concentrated on sick people in hospital and did not teach students enough about the common illnesses dealt with by personal family doctors. These illnesses could be taught in a teaching general practice which was part of a department of social medicine. He questioned the assumption that if students knew more about general practice they would be attracted to it: ultimate careers depended on circumstance, though personalities among

teachers could motivate students towards their particular branch of medicine.

Dr. IAN McWHINNEY (general practitioner, Stratford-on-Avon) said that general practice dealt with clinical decisions about individuals, and social medicine with epidemiology and the medical care of communities. The general practitioner must know about epidemiology and sociology, but his discipline lay between social and clinical medicine. It should be taught in a department which was separate from, though closely linked with, a department of social medicine.

The chairman, Professor Sir MAX ROSENHEIM, P.R.C.P., summing up the morning session, said that undergraduate education gave students a good basic training and a critical attitude to innovation. The conference should, in his opinion, concentrate on vocational training, for which Dr. Hodgkin's paper seemed to him an impassioned plea.

Present Teaching in General Practice

With Dr. John Hunt, President of the Royal College of General Practitioners, in the chair at the afternoon session, Dr. ANDREW SMITH (general practitioner and clinical tutor in family medicine at Newcastle upon Tyne University) discussed "Present Teaching in General Practice." He described the family and community medicine course at Newcastle, which involved all students in their first clinical year for five weeks, half of which was spent in general practice with one of 12 clinical tutors (general practitioners working in partnership or group practice) and half in community medicine with district nurses, health visitors, and other community workers. The content of the course evolved at regular meetings of the teaching group, which included six senior consultants as well as the general practitioners and public health doctors. The teaching general practices were organized so that the tutor could devote time to teaching undistracted by routine work. The course had been conspicuously successful in that students are matured by their experience in general practice and had asked for and been given an extra week of it. Another test of success, an increase in the number of students who wanted to enter general practice, had yet to be faced.

Professor RICHARD SCOTT (professor of general practice at the University of Edinburgh) said that general practice was an integral part of a community health service in that it offered everyone direct and continuing access to a doctor. Its major activity was application of existing knowledge, and everything in the undergraduate curriculum was relevant to it. It should be taught by involving students in delegated clinical responsibility at the patient's home or the general practitioner's consulting-room. Some of the resources of general practice might contribute to a division of community medicine in a medical school, and he cited

as an example how a medical student could become involved in obstetrics by questioning the expectant mother about her own and her family's emotional attitude to her pregnancy and listening to her replies.

Clinical Content

Dr. P. S. BYRNE (general practitioner and lecturer in general practice at Manchester University) discussed "The Clinical Content of General Practice." The need for definition became apparent when the National Health Service divorced general practice from hospital medicine and medical knowledge advanced so rapidly. General practice had become a discipline in its own right and research was needed to discover both its present content and its projection into the future. The general practitioner was a generalist and his skills were sharpest in conditions which did not need hospital techniques.

Dr. Byrne saw the general practitioner as the general physician of the future who would practise in groups and develop a medical hobby. Academic departments of general practice were needed to define clinical content, and to teach the continuing advances which had changed many diseases from hospital to domiciliary ones.

Professor J. C. VAN ES (professor of general practice at the University of Utrecht, Holland) described the new curriculum at his medical school, now in its third year. General practice was taught to all third-year students. There were lectures on topics such as the doctor-patient relationship and the morbidity patterns in general practice. Each student was attached to a general practitioner, when he studied in detail the non-clinical impact of illness on specific families. Clinical aspects were demonstrated in the final year, when students accompanied general practitioners on urgent visits. Specific training for the expected 70-80 would-be general practitioners was planned after graduation and was expected to take one year, though experience might show that a longer period was necessary.

Professor JOHN ANDERSON (professor of medicine, King's College Hospital, London) spoke on the "Role of the Universities in General Practice." In his view, though the universities aimed to teach students the importance of flexibility and change, they were themselves bound by the traditions of the Middle Ages. The whole medical curriculum ought to be changed. Medicine was dominated by science to the exclusion of psychology and sociology; dissecting animals was irrelevant to understanding human behaviour, and anatomical diagnosis to solving problems. Old rituals needed to be discarded in favour of new attitudes based on the doctor's role in society. Medicine was the most conservative profession, and nowhere more so than in the University of London, where Oxbridge amateurism and dilettantism obstructed reform.

Application of Teaching Methods

On 9 December, with Professor H. W. ROBSON (Vice Chancellor, Sheffield University) in the chair, Mr. A. E. TUBBS (Department of Education, University of Birmingham) spoke on "The Application of Teaching Methods." The general practitioner's work, he said, differed from that of other doctors in that he was concerned with patients—the detection of departures from normal, long-term management, and emotional problems—rather than with disease. Learning should include discrimination and explaining situations, as well as acquiring skills and retaining originality. It was likely to occur best in small groups in which the learners played an active part and there was an adequate system of feed-back. Objectives of teaching must be clear and feed-back must occur quickly enough to allow modification of teaching methods.

Dr. J. R. ELLIS (honorary secretary of the Association for the Study of Medical Education) spoke about "Future Teaching of General Practice." There would, he said, be enormous changes in general practice in the next decade. The increasing gap between demand and supply would force general practitioners into groups, where delegation of work was easier. He would need 10 years' training, half of which would be under-

graduate and half vocational. Vocational training would be done more efficiently in hospital than in general practice itself because human behaviour, of the relatives as well as the patients themselves, was concentrated there. The general practitioner was mistaken in thinking he knew the community: he dealt with only a selected section of it.

Dr. J. R. REVANS (senior administrative medical officer, Wessex Regional Hospital Board) dealt with "General Practice and the Hospitals." He said that general practitioners needed continuing postgraduate education, and described the Wessex facilities, which included a postgraduate dean, a medical centre, and a library. He thought that cottage hospitals should be converted into health centres with preconvalescent beds and facilities for minor surgery. General practitioners must play a part in the whole of medical care, perhaps through general-practitioner beds in district hospitals as well as clinical assistantships.

Dr. W. KERR HENDERSON (senior medical officer, Department of Health for Scotland) said that teaching health centres could achieve some of the objectives outlined. They could provide material for the teaching of community medicine which was suitable for both undergraduates and postgraduates and would be the natural location for a department of community medicine. They

should be closely associated with the teaching hospital.

Dr. GEORGE SWIFT (Chairman of Council of the Royal College of General Practitioners and general practitioner, Winchester) spoke about vocational training, of which he thought a general practitioner needed a minimum of three years—two in hospital and one in general practice. He estimated that 940 new entrants to general practice were needed each year, and suggested that some should be married women at present employed as assistant county medical officers, who would need vocational training. Recruitment to vocational training was at present exceptionally poor because untrained young doctors could earn twice as much in general practice. A national policy was needed in which vocational training would be an essential prerequisite to becoming a principal in general practice, and the General Medical Council and the Ministry of Health should initiate it.

Summing up the conference, Professor H. N. ROBSON said that nobody was satisfied with the present education of doctors. It must be improved by the inclusion of the body of knowledge of the undifferentiated mass of human discomfort and illness in the community. In his opinion this should be taught in a department of general medicine, headed by a generalist with a background of general practice and community medicine.

Mathematics in Medicine: B.M.A. Symposium

A symposium on the application of mathematical and computer methods to problems in medicine was held under the joint auspices of the British Medical Association and the Institute of Mathematics at B.M.A. House on 6 December.

The chairman for the morning session, Dr. RONALD GIBSON (Chairman of the B.M.A. Council), introduced Dr. BRIAN THWAITES (President of the Institute of Mathematics and Principal of Westfield College). Dr. Thwaites spoke of the difficulties involved in the analysis of data, taking aortic blood flow as an example. The medical profession was prone to force data to fit into some kind of linear relationship, commonly by using logarithms. Nevertheless, the restriction and categorization of data often allowed more useful relationships to be shown than those resulting from indeterminate selection. Finally, he drew attention to the difficulty of mathematical predictions in a biological system owing to the enormous number of variations that could be introduced.

Dr. PERCY CLIFFE (Westminster Hospital, London) expressed concern with the lack of mathematical knowledge among doctors. He illustrated the value of mathematical models with some examples of varying complexity. The measurement of the coronary blood flow by an infusion technique was compared to a simple inflow-outflow system, and he also described the predictions obtained from a model of the control of schistosomiasis, which were accurate even in assessing the lack of control during the second world war.

Biological Wave Forms

Dr. H. R. A. TOWNSEND (Western General Hospital, Edinburgh) spoke on wave forms of biological origin. The simplest observations were those made on unit potentials where a series of events could be observed during the course of a base-line tracing. The number and sequence were analysed, grouped, and an attempt was made to determine their relation to other phenomena. Data were presented graphically, and it was often necessary to transform them in order to obtain linear relationships. In the electrocardiogram the waveform was evidently related to the underlying physiology of the heart, and quantitative measurements could be derived from it. In the electroencephalogram, on the other hand, irregular waves were produced, and the unaided human eye could pick out only outstanding features—for example, the specific changes associated with epilepsy. Mathematical transformation into more regular waveforms would enable further understanding and prediction of future events in the electroencephalogram.

Mr. J. E. HAILSTONE (Atlas Computers) gave a warning of the difficult task of analysing waveforms. A clearly defined account could not be made even by mathematicians.

With Dr. Thwaites in the chair, at the afternoon session Professor J. ANDERSON (King's College Hospital, London) opened by pointing out that the new vocabulary facing the medical student fresh from strictly

scientific disciplines had not sufficiently interested the medical teacher. Not only did they have to learn a new terminology but also the process of reorientation. Clearly the process was without end. Already the number of articles published had outstripped the capacity of the individual doctor even to select the worth-while topics for study. Nevertheless, the use of a computer as the store and devices such as "key words" in articles would enable an adequate survey of the world literature to be carried out. A source of confusion was that the many syndromes and synonyms might cause "noise," but this could be remedied by careful selection of headings and careful definition of terms. There was a special need for doctors' thoughts and opinions to be speedily transferred into a permanent record.

In the discussion one speaker emphasized that a computer only recodified thoughts from one language to another. Problems arose from the alternative meanings which were prevalent in medicine. Dr. Townsend produced a list of 300 words used in electroencephalographic terminology, but considered that another 700 would cover most situations.

Use in Diagnosis

Professor PAUL HALL (Karolinska Hospital, Stockholm, Sweden) began with a warning, saying that he considered "automated medical diagnosis" to be a misnomer. On the one hand, the diagnosis proper corre-

sponded to the definition of disease. On the other hand, the computer gave rise to a statistician's probability diagnosis. At his hospital they had obtained 10 years' experience. The computer system allowed for a central library which contained all records. This had solved the difficulty of inadequate and slow retrieval of information. Search was made for cases with similar symptoms, signs, and progress; thus the diagnosis, therapy, and prognosis could be used as a guide for new cases. In 1962 they had introduced a standardized questionnaire to be completed by patients, and they had also been greatly helped by a new type of aide, who was both a secretary and a computer operator. Professor Hall emphasized that they had avoided making doctors into computer technicians. Once the questionnaire was completed a summary was prepared; the doctor then obtained

any other details required and proceeded to physical examination and the relevant ancillary investigations. It had been found that effective action could be taken as a result of the questionnaire alone in up to 85% of the cases. The essential role of the computer was to store information and to allow its rapid retrieval. The cost of the new system was twice as much as with the conventional methods, but the saving in time was about 60 times.

Professor G. A. BARNARD (University of Essex) spoke of an impressive questionnaire he had seen used in an allergy clinic in Wisconsin. The patients sat in front of the computer and answered a series of questions by pressing the appropriate buttons on the machine. The output of the machine was presented in the form of an abbreviated medical history. This had led to speeding

up of the diagnostic service. Professor W. J. H. BUTTERFIELD (Guy's Hospital, London) said that he was worried that this extreme form of mechanization would not be comprehensible to the less intelligent patients.

Discussing the problems of storage and data retrieval of information, Dr. J. HOWLETT (Science Research Council's Atlas Computer Laboratory) said that the retrieval of literature was aided by the use of "key words" in articles. There was no real need to learn computer language, for an understanding of the process was sufficient. Problems were more likely to arise in insufficiently restricting the computer, with the possible result of a deluge of unwanted data. He demonstrated the use of a computer in producing a 10-foot roll of references to the work of an author and the author himself.

Current Trends in Epilepsy

[FROM A SPECIAL CORRESPONDENT]

Opening the British Epilepsy Association's symposium on current trends, held in Manchester on 25 November, the chairman, LORD COHEN OF BIRKENHEAD, introduced the first speaker, Dr. JOHN HUNT (London), whom he congratulated upon his recent election as President of the Royal College of General Practitioners.

Dr. Hunt spoke from the viewpoint of the family doctor and emphasized the widely differing forms taken by epileptic attacks. One type of special interest was the convulsive epileptiform fit sometimes seen during vasovagal fainting attacks. Such fits were due to cerebral ischaemia and used to be regarded as unmasking an epileptic tendency, but many people now thought that cerebral ischaemia was just one of a number of factors able to induce epileptiform convulsions in normal subjects. If full investigation revealed no evidence of idiopathic epilepsy, such patients could lead a normal life avoiding known precipitating factors.

Continuing, Dr. Hunt pointed out that practitioners seldom witnessed single fits, but their presence was often vital in serial attacks or status epilepticus, when maintenance of an airway, assisted respiration when necessary, and intramuscular injection of an anti-convulsant could be life-saving. Between attacks treatment had to be scrupulously regular, and the practitioner's task was to exert a stabilizing, common-sense influence and ensure that his patients received the best possible education and employment. Restrictions should be kept to a minimum, for everyone had to be prepared to accept some degree of calculated risk. Patients with epilepsy who wished to marry should always reveal their true condition before becoming engaged, but there was only a slight possibility that children would be affected.

Temporal Lobe Epilepsy

Speaking on temporal lobe epilepsy, Dr. MAURICE PARSONAGE (Leeds) outlined earlier studies of its natural history and gave preliminary results of a follow-up study being carried out in Leeds. Among 103

patients with temporal lobe epilepsy—the commonest single variety seen in clinical practice—the aetiology was uncertain in 60; 12 had cerebrovascular disease, 10 tumours, and six a history of trauma. Other less common causes were degenerative disease, post-infective or infantile brain damage, and neurosyphilis. Fourteen patients had remissions, probably unrelated to treatment, lasting for periods ranging from three to 25 years. In general, the results of therapy were disappointing; drug treatment, mainly with phenytoin, controlled fits in only 45%, while elective lobectomy reduced rather than abolished attacks in three out of the four patients submitted to the operation.

About two-thirds of the patients in Dr. Parsonage's series had personality changes—depression in 42 of the 103 studied, neurotic behaviour in 17, and psychosis or aggression in nine each; four patients were inadequate personalities and two persistently criminal.

Discussing the treatment of temporal lobe epilepsy, Dr. CHRISTOPHER OUNSTEAD (Oxford) emphasized the importance of prevention. Better management of birth injury or other trauma, encephalitis, meningitis, and status epilepticus might have prevented the development of temporal lobe epilepsy in 50% or more of one series of children with the condition. Some children appeared to have an inherited predisposition to status epilepticus in early childhood. Often precipitated by fever, these attacks differed from the more familiar febrile convulsions, damaged the temporal lobe, and caused subsequent temporal lobe epilepsy.

Another problem, mentioned by Dr. Ounstead in the subsequent discussion, was the management of hyperkinetic children, who made up 8.2% of all those with any sort of convulsive disorder in childhood. Of these 80% were boys; they usually slept well, but were hyperactive by day with euphoria and a brief attention span. They did badly at school, and their treatment required special care since phenobarbitone made them even more lively and amphetamine produced a retarded depression. As they grew up, hyperkinetic children usually became slow and stolid.

Childhood Epilepsy

Childhood epilepsy was subdivided into three age groups by Dr. BRIAN BOWER (Oxford). Attacks in the neonatal period seldom took the form of fits, and ranged from limb or face twitching to tonic episodes with cyanosis. They were most commonly due to birth injury, including anoxia (now a commoner cause than trauma) and hypoglycaemia; while hypocalcaemic convulsions occurred at the end of the first week of life, often after changing from breast milk to cow's milk. Infants with the hypoglycaemia of dysmaturity, on the other hand, showed the features of intrauterine starvation, being underweight and deficient in subcutaneous fat with papery, scaly skin. In about half there was a history of maternal pre-eclamptic toxæmia, and convulsions usually took place on the second day when the blood sugar fell below 20 mg./100 ml. Even vigorous treatment at this stage could not prevent a high incidence of permanent brain damage.

Fits were common between the ages of 1 month and 3 years, about 2.5% of children having one or more at this age. It had also recently been shown that pertussis antigen could cause brain damage. While most children with febrile convulsions did not have epilepsy later, those with fits following pertussis immunization fell into a much graver prognostic group, in which the aetiology was frequently unknown and 85% became moderately or grossly subnormal.

The administration of corticosteroids suppressed the fits and might be able to prevent brain damage if started within a day or two of the first spasm.

Concluding, Dr. Bower said that fits in children of 3 years and over took the form of grand or petit mal or temporal lobe epilepsy, the last being particularly difficult to diagnose and treat.

Behaviour Disorders

Mr. CHRISTOPHER BAGLEY (London) described a recent study of behaviour disorders—mainly aggression, anxiety, or

"mixed"—in 118 epileptic children referred for neurological investigation. Disturbance of a severity comparable to that seen in non-epileptic children referred to child guidance clinics was found in 43%. Brain damage and minor motor fits were significantly associated with aggression, while stressful environmental factors—poverty, overcrowding, and disturbed parental behaviour—were related to aggressive and mixed disorders. On the whole, a high intelligence quotient was associated with normal or anxious behaviour, and a low one with hyperactivity or aggression. The study had included an excess of children from the upper social classes, which suggested that those from lower classes who lived away from a teaching hospital did not receive adequate investigation of their epilepsy. This point was taken up later by Lord Cohen, who pointed out that the 1956 Committee under his chairmanship had for this very reason proposed the setting up of special diagnostic centres for epilepsy. Unfortunately, hardly any were yet in existence.

Legal problems associated with epilepsy were covered by Dr. NORTHAGE MATHER (Manchester), who spoke on epilepsy and

crime, and Dr. L. A. LIVERSEDGE (Manchester) on driving. The latter claimed that Britain was at the bottom of the international league for liberality to epileptics; the present yardstick—it was not a regulation—demanded that a patient should have been free from attacks for five years, and without medication for the last two of them, before he could receive a licence. This situation forced epileptic patients to concealment, and it had been estimated that over 80,000 were on the road. It would be safer for them to drive *on treatment* than to stop drugs in order to get a licence, and Dr. Liversedge proposed a three-year period without an attack and regular medication under supervision, as conditions for a driving licence.

Importance of Accurate Diagnosis

Referring to epilepsy as a symptom not a disease, Dr. P. M. JEAVONS (Birmingham) emphasized the importance of accurate diagnosis and outlined the drugs at present in use for each type of fit. The aim of treatment was to enable the patient to lead a normal life. Statistics on employment, accidents, heredity, and other factors showed

that the attitude of society, and even of doctors, towards epilepsy was not justified by the facts. Each patient had to be considered as an individual; it was important to avoid saying "No."

Lord Cohen summed up the proceedings and reminded participants that epilepsy was a symptom of an underlying lesion, which should always be sought; failure to find one was due to our ignorance. Every nerve cell, whether in the brain or elsewhere, had its own level of stability, and trigeminal neuralgia might be regarded as epilepsy of the Gasserian ganglion, for instance. Lord Cohen concluded by discussing the ethical problems posed by epilepsy. There was no code of ethics laid down by the General Medical Council governing medical practice in England. The doctor had duties to his professional brethren, to society, and to mankind in general, as well as to the individual patient. Information about patients was already divulged every day for the good of the community. The doctor should reveal that a patient suffered from epilepsy when it was necessary for the public safety to do so. And the public should be educated to eliminate prejudice about epilepsy.

Pharmacists and the Sainsbury Report

[FROM A SPECIAL CORRESPONDENT]

On 10 November the School of Pharmacy of the University of London organized a meeting to bring together different viewpoints on the Sainsbury Report on the relation of the drug industry to the National Health Service.

Welcoming the report, Dr. F. HARTLEY (Dean of the School of Pharmacy) mentioned everyone's feeling of relief that full-scale nationalization was not proposed. Although approving the proposals to ensure some measure of price supervision by the Ministry of Health, he wondered just how expensive these new measures would be. He pointed out that British drug firms were, with their exports, responsible for over £30m. to the good in our balance of payments. Hence it would be short-sighted to try to limit the legitimate profits made by British firms, especially those who introduced new drugs. On the other hand, the very large foreign drug firms in this country, principally American and Swiss, were responsible for a small deficit in our balance of payments.

Development of New Drugs

Continuing, Dr. Hartley emphasized that the industry depended for its prosperity on the development of new drugs, and that in future the worth-while research groups would probably be found in as few as five or six large firms. He felt that there should not be much support for the firms producing imitation, or "me too," drugs, nor for those producing polypharmaceuticals, often in the guise of new drugs. These firms tended to be the smaller firms, and with the encouragement of the true innovators in the industry he felt that it was inevitable that the smaller

firms would not prosper in the next few years.

Mr. J. A. BAKER (chief pharmacist, Westminster Hospital, London S.W.1) spoke of our dependence on the drug industry for safe and cheap medicines. The incentives of the industry should not be removed. He welcomed the proposed Medicines Commission as inevitable, and likely to receive strong support from hospital pharmacists. He felt strongly that the Commission should be truly impartial and independent. More especially the Commission should not be responsible to the Minister of Health.

Mr. Baker thought that some firms were able to make what he considered to be excessive profits because the present periods of patent protection were too long. While protection was very necessary, a shorter period of protection might, he thought, lead to a greater incentive to firms to produce new drugs. He himself was very happy to see the adoption of one name for a drug with the abolition of brand names. From the nursing staff's point of view the proliferation of names made it very easy for nurses to prescribe the wrong drug, and for this reason it was found necessary for the hospital pharmacist to check every prescription in the hospital to make sure that it was clear.

Brand Names

While he agreed that the abolition of brand names had much to recommend it from the point of view of the hospital pharmacist, Dr. CHARLES STEVENS (with a background of international law and his work as an industrial pharmacist with Imperial Chemical Industries) felt that the Medicines Commission should have a certain amount of indepen-

dence, though it would not work well if it was responsible to no one at all. The best practical solution, he thought, was responsibility to the Minister, who in turn was responsible to Parliament. In Britain Ministers always had to answer Parliamentary questions which brought their departments' work into the light of day.

So far as brand names were concerned, Dr. Stevens pointed out that while these might seem unnecessary in Britain they were essential for a drug firm's overseas sales. A product could be patented in Britain, but generally abroad it was the process that was patented and not the final product. Once a new drug was released it was not long before a clever chemist had found a new route to the final product.

Discussing brand names, Dr. HARTLEY brought up the question of drug formulation—that is, presentation of drugs so far as particle size was concerned. The latter could have a profound effect on the biological availability of a drug, and this was a field in which there was much useful work to be done.

Dr. G. R. FRYERS (Bayer Products Ltd.) emphasized that the Sainsbury Report concerned itself with the *innovating* pharmaceutical industry. Competitive research teams were the basis of the industry, and large firms in the international market were needed to find new drugs—and these firms in turn depended on the sale of drugs internationally. Firms would succeed only if they did so internationally; unless changes in the regulation of the British drug firms now contemplated made for the prosperity of British firms in the United Kingdom they would fail internationally.

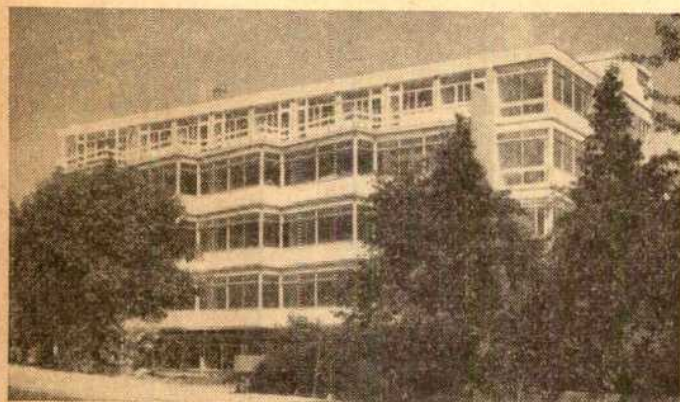
Christmas Quiz

(Answers at p. 755)

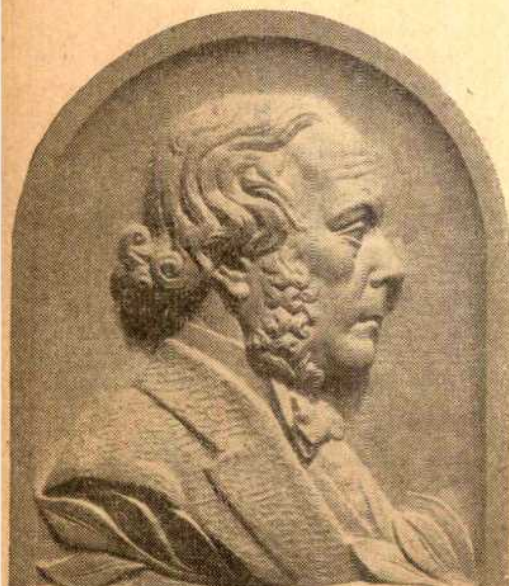
- What is ?
(a) Pigeon fancier's disease. (b) Pigeon crammer's disease.
- Who are ?
(a) the Amish, (b) the Jumpers of Maine, (c) the clay-eaters of North Carolina, (a) the orange people ?



A



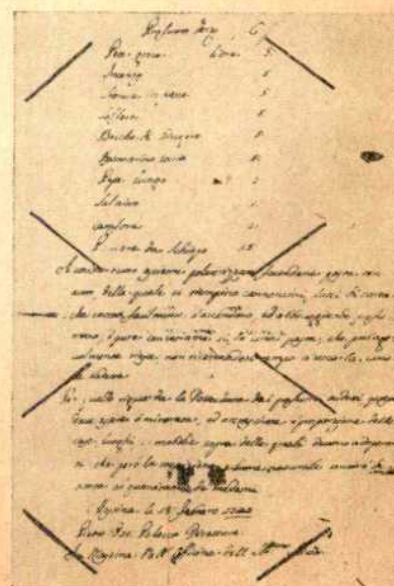
B



C



D



E

- Name the following whose anniversaries were remembered in 1967:

- The founder of a famous teaching hospital and of a specialist hospital in London.
 - A man whose father was a famous neurologist and who gave up medicine for polar exploration.
 - The originator of a staining method for histological and parasitic preparations.
 - The winner of two Nobel Prizes for physics and chemistry, whose contributions to medicine are still being exploited.
- And the following, the centenary of whose discoveries was celebrated:

- The originator of the antiseptic principle.
- The discoverer of amyl nitrite as a treatment for angina.

- See the illustrations:

(A) and (B) Both these buildings were opened in 1967. What are they, and where are they situated ?

(C) Whom does this relief commemorate, and where is it situated ?

(D) Whom does this statue commemorate, and what famous saying is associated with him ?

(E) What has happened to this document ?

- What are the following ?

(a) Straight back syndrome. (b) Stiff man syndrome. (c) Pickwickian syndrome. (d) Heart failure of the hunchback.

- What do the following children suffer from ?

(a) The happy puppet. (b) The bobble-head doll. (c) The Pekinese child. (d) Collodion babies. (e) Stinking infants.

- Who are patron saints of the following ?

(a) Spas. (b) Sufferers from toothache. (c) Nurses. (d) Sufferers from gout. (e) Doctors. (f) Epileptics. (g) Medicine.

- What are the dangers of:

Sniffing puff balls, gathering mushrooms, sawing maple logs, and collecting hay ?

- What do the following abbreviations stand for ?

(a) "Bilge." (b) R.D.S. (c) S.T.P. (d) E.C.F. or E.F.E. (e) D.D.D. (not an insecticide).

- In what literary works do the following characters appear ?

(a) Dr. Slop. (b) Dr. Gideon Gray and Dr. Adam Hartley. (c) "Doctor" Sganarelle. (d) Edwin Ingleby. (e) Dr. Andrew Manson.

- What diseases were:

(a) First described by the sufferer, (b) first described in the writer's son, (c) named after the original patients ?

Correspondence.

Letters to the Editor should not exceed 500 words.

Renal Glucose Threshold

SIR,—The paper by Professor W. J. H. Butterfield and his coworkers (2 December, p. 505) showing that the diagnosis of diabetes mellitus can be made in the absence of glycosuria is of especial importance in the field of geriatrics. I now have records of about 20 elderly patients presenting with neurological symptoms and signs where the diagnosis of diabetes mellitus has been previously dismissed because of the absence of glycosuria. Subsequent glucose tolerance tests have established the true aetiology, and appropriate treatment invariably results in satisfactory improvement.

One of my patients, a woman of 72 years, had increasing difficulty in rising from a sitting position and going up steps. She had been seen by a consultant physician and neurologist and, after extensive investigations, diagnosed as suffering from "thrombosis of the anterior spinal artery." The urine was sugar-free. The disability grew progressively worse and she became depressed. As a last resort her general practitioner referred her to the geriatric department, where weakness and wasting of the pelvic girdle muscles with depressed leg reflexes were found. A glucose tolerance test revealed a diabetic curve with aglycosuria, and treatment with tolbutamide resulted in full recovery.

A man of 78 being treated for osteoarthritis of the lumbar vertebrae developed progressive difficulty in walking, with signs of pyramidal tract disease, followed by severe bilateral wrist drop. There was no sugar in the urine, but the glucose tolerance curve was typical of diabetes mellitus. He quickly recovered with appropriate treatment. The radiological appearance of the lumbar vertebrae was consistent with Charcot's disease of the spine.

Another elderly patient was referred recently as suffering from "senile wrist-drop," and the diabetic origin of this was dismissed by her doctor because of the absence of sugar in the urine.

Professor Butterfield's recommendation that the idea of diabetes mellitus always being associated with glycosuria be abandoned is timely. The increasing numbers of elderly patients in our population and the easy acceptance of "senility" as the aetiological factor for many of their symptoms and signs, especially those involving the neurological and cardiovascular systems, should make us beware of overlooking the presence of diabetes mellitus even in the absence of sugar in the urine.—I am, etc.,

LEONARD ROSENTHAL.

St. James's Hospital,
Leeds 9.

SIR,—I have read with interest and appreciation the article on renal glucose threshold variations (2 December, p. 505) by Professor W. J. H. Butterfield and his team from Guy's. They have proved what I suggested in *The Diabetic Life* (15th edition) that the sugar threshold rises as age increases. My own

threshold (age 75, insulin for 45 years) has been proved by simultaneous blood-sugar and urine tests to have risen and is the first thing that has convinced me that, if not quite senile, I am getting on.

There is one point they do not mention which I wish they would investigate—the variability of the threshold. From my experience with many glucose tolerance tests the threshold is higher when the curve is rising than when it is coming down. I wonder if the rise after carbohydrate food or the fall after insulin affects the threshold in the same way? Of course, it's up to the investigators to practise and overcome the difficulties of getting small quantities of urine at the times required.

An old experiment years ago (unpublished) has a bearing on threshold discovery. A normal aglycosuric student volunteered to have a catheter passed into his bladder, and I filled it with 5% of glucose and let it out immediately. The next urine he could pass contained 0.3% of glucose by a titration method.—I am, etc.,

London W.1.

R. D. LAWRENCE.

Transfusion Malaria

SIR,—Dr. Angela E. Vartan's description (25 November, p. 466) of a case of *Plasmodium malariae* infection following blood transfusion was of much interest, as the high incidence of such accidentally induced cases of quartan malaria has created some concern, especially in countries where malaria eradication has been achieved or is in its final stage. In addition to the data from Yugoslavia published by Lepeš¹ and quoted in Dr. Vartan's article there are more recent reports from Romania and from the U.S.S.R. which indicate the extent of the problem. Thus in Romania during the period 1959–65 there were no fewer than 112 cases of *P. malariae* infections subsequent to blood transfusion.² In 86% of these cases the donor's blood was conserved at 4°–6° C. for one to five days, but in three cases of induced malaria infection the blood had been kept for 12 days.

In the U.S.S.R. Sergiev and his colleagues³ reported that during the period 1963–5 out of 47 cases of *P. malariae* infections 33 were due to blood transfusion or to "haemotherapy." The latter procedure, quite common in Eastern Europe, consists of intramuscular injection of 10–20 ml. of blood taken from another person, usually the mother, for protection of children against measles. Six cases of *P. malariae* in children were due to such an occurrence.

The detection of the latent or asymptomatic infection with *P. malariae* is very difficult, though the fluorescent antibody test may be of value in this respect and should be more

widely used for the exclusion of some potentially infective blood donors.

Parasites of *P. malariae* can remain dormant for many years, and the presence in Britain of an immigrant population coming from countries where quartan malaria is not uncommon makes Dr. Vartan's paper particularly timely and important.—I am, etc.,

L. J. BRUCE-CHWATT.

London School of Hygiene and
Tropical Medicine,
London W.C.1.

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Viruses in Diarrhoeal Disease

SIR,—Despite a widespread impression to the contrary, there is little evidence to incriminate enteric viruses detectable by current diagnostic techniques as significant causes of diarrhoeal disease. In order to illustrate the unrewarding results of testing routine faecal specimens from patients with uncomplicated diarrhoea or gastroenteritis, we have analysed the results of testing 748 such specimens, mostly from children, during the past seven years.

Viruses were isolated from 93 (12%) in monkey kidney or human amnion tissue cultures, the percentage positive in different years ranging from 7% in 1966 to 18% in 1962. At least 25 different virus types were represented: 8 polioviruses, 11 Coxsackie viruses, 51 E.C.H.O. viruses, 13 unidentified enteroviruses, and 7 typed and 3 untyped adenoviruses. The largest groups of typed viruses were E.C.H.O. 14 (11 cases), E.C.H.O. 11 (9 cases), and E.C.H.O. 8 (8 cases). Most of the E.C.H.O. 14 isolations were made in 1962, when the same virus was also isolated from cases of neurological disease.¹ The E.C.H.O. 11 isolations were scattered over five different years, and no clearcut association of this or other types of enterovirus emerged from an analysis of all isolations of enteroviruses in 1960–4.² No viruses were isolated from various outbreaks affecting children or adults in nurseries, schools, colleges, and factories. Although an earlier study from this laboratory³ suggested a special association of E.C.H.O. virus 7 with diarrhoea, we have not found this again. In a comparison of closely matched children with respiratory or diarrhoeal disease in this hospital, similar viruses were isolated from the stools of both groups.⁴ Type 3 adenovirus was associated with gastrointestinal and respiratory symptoms in a small outbreak investigated in 1960,⁵ but we have encountered no similar episode in later years.

Chance coincidence of an outbreak of diarrhoea with a period of high prevalence of an enterovirus may explain some of the reported associations of enteroviruses with diarrhoea.^{6–8} No evidence of the importance of enteroviruses or adenoviruses

emerged from large studies in Texas⁶ and South Africa.¹⁰⁻¹² Altogether it seems unlikely that enteroviruses or adenoviruses are significant causes of uncomplicated diarrhoeal disease. Routine virological investigation by present techniques of stools from diarrhoeal patients is an unrewarding diversion of effort. Perhaps when the technical trick of demonstrating hepatitis virus has been discovered a new group of agents may be found responsible for that large majority of diarrhoeal illnesses in which neither virological nor bacteriological tests are currently successful.—We are, etc.,

ELEANOR J. BELL.

Regional Virus Laboratory,
Ruchill Hospital,
Glasgow N.W.

N. R. GRIST.

Department of Infectious Diseases,
University of Glasgow.

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Withdrawal of Heroin

SIR,—The biochemical mechanisms of physical dependence on drugs remain obscure. We wish to record a phenomenon in which marked manifestations of withdrawal followed a change from intravenous to intramuscular administration of a fixed dose of heroin in a long-standing addict, with recovery on returning to the intravenous route.

A 52-year-old woman was admitted to St. Stephen's Hospital, Chelsea, on 11 December 1966 with bronchial asthma. She had become addicted to morphine given for postoperative pain following accidental ligation of the right ureter at ovariectomy in 1936. She changed to heroin several years later, and at the time of admission was receiving 2 gr. (120 mg.) of heroin with 12.5 mg. cocaine intravenously five times daily.

She was treated with tetracycline, bronchodilators, and later A.C.T.H., with marked improvement in her bronchospasm.

Her general condition, nevertheless, did not improve, and though her chest was no longer troublesome she became confused, restless, and agitated. She became increasingly disorientated and developed a coarse tremor of the upper and lower limbs. During her asthmatic attack she had been experiencing difficulty in "fixing" herself, and had been receiving her heroin and cocaine intramuscularly. It was felt, therefore, that though she was in fact having her normal dosage she was suffering from withdrawal symptoms due to a change in the method of administration. At this time her condition was critical, and though heart action, lungs, and blood

pressure appeared to be normal she was moribund. A Gordh's needle was therefore inserted and intravenous administration of heroin and cocaine begun at the same dosage. She improved rapidly and was soon able to resume her own intravenous injections.

The practical problems of opiate addiction appear to be related mainly to the psyche of the addict; withdrawal, if desired, is usually easy in the early stages at least, but relapse is very frequent. Experience in prison suggests that withdrawal symptoms may be of psychic origin. Nellans and Masee¹ reported from the Atlanta State Penitentiary in 1929 that complete withdrawal could be accomplished with only minor symptoms, and suggested that the most powerful therapeutic agent was the absolute certainty that no further drug would be given. On the other hand, withdrawal can be reproduced in animals, and, though differences in route of administration do not influence effectiveness, monkeys given morphine for two months become moribund following withdrawal, and recover when the drug is given.²

It is striking that death from withdrawal does not seem to be a hazard for the present-day addict, though he is at risk for many other reasons. Helpers and Rho³ reported 1,561 deaths in addicts, none related to withdrawal. It is said that "exhaustion" may occur; treatment, with insulin for instance, may contribute.⁴ We felt that our patient would have died from withdrawal symptoms if she had not been returned to intravenous from intramuscular therapy. This, however, remains speculative.

This case emphasizes the physical aspect of withdrawal. If drugs of dependence become essential to some metabolic process, it may be that a certain concentration is required which would explain the effectiveness of intravenous heroin. This may have therapeutic implications, though such a severe reaction to withdrawal appears to be very rare.—We are, etc.,

F. DUDLEY HART.

MARGARET H. GIBSON.

E. C. HUSKISSON.

St. Stephen's Hospital,
London S.W.10.

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Carcinogenic Properties of Ortho-dianisidine

SIR,—In his letter (21 October, p. 172) Dr. D. G. Illingworth states that Occultest and Hematest reagent tablets (Ames) contain ortho-tolidine, but doubts whether, if used according to the manufacturer's instructions, any risk is incurred in their use. The manufacturer's leaflets which accompany the tablets confirm that both preparations contain ortho-tolidine. In view of the fact that they state "hands, droppers, and working area must be clean and free from any traces of blood," it is clear that a technique which involves the tablets coming in contact with the skin is envisaged.

Ortho-tolidine (dimethylbenzidine) is listed in the *Prescribed Industrial Diseases Regulations No. 39*¹ as a carcinogen in man, and is

also listed in the *Carcinogenic Substances Regulations*, which become law on 9 December.² It is known that the aromatic amines as a class can be absorbed through the skin.³ These tablets may be handled occasionally (for example, by doctors) or up to several times each working day (for example, by certain nurses or laboratory technicians).

According to the *British Medical Journal* (22 July, p. 189), "although it is not possible to say that there is a level of exposure to the carcinogenic aromatic amines below which there is no risk, the hazard to trained laboratory workers must be small." It may be that all that is necessary to obviate the risk is that a no-touch technique be employed. If so, clear instructions to this effect are necessary on the leaflet. Those interested are referred to *Precautions for Laboratory Workers who Handle Carcinogenic Aromatic Amines* published by the Chester Beatty Research Institute. However, the moral argument seems irrefutable that the persons concerned should have an opportunity of knowing that the tablets may contain a carcinogen (for example, by means of a label on the container), so that they may choose whether or not to use them.

The analogy which Dr. Illingworth makes with cigarette-smoking is a poor one. There may or may not be merits in having their carcinogenic action marked on the packet as he suggests. But employees are rarely instructed by employers to smoke as part of their duties, and in any case this hazard is already public knowledge.—I am, etc.,

DONALD ACHESON.

Department of Clinical
Medicine,
University of Oxford.

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Streptomycin, I.N.H., and Thiacetazone

SIR,—We have read with interest the letter by Dr. S. N. Dutta and colleagues (7 October, p. 55) on streptomycin, I.N.H., and thiacetazone. We are concerned lest this should deter others from using thiacetazone in the treatment of tuberculosis in developing countries. The cheapness of the drug has made it possible for people to have effective treatment, whereas before the expense of streptomycin and P.A.S. often led to inadequate courses of treatment. We are convinced of the value of thiacetazone and isonicotinic acid hydrazide (I.N.H.) alone in the majority of cases.

In 1965-6 we conducted a trial on 90 patients in order to investigate the development of drug resistance in the treatment of pulmonary tuberculosis with thiacetazone and I.N.H. During this trial there were six patients who had a rash, one having exfoliative dermatitis. One patient had jaundice, thought to be due to the drugs.¹ The rash was mostly of the maculopapular type; it left behind a black pigmented area which persisted for many months. The case of exfoliative dermatitis was of a very severe type. The rash appeared usually about the end of the third week. It did not regress quickly with the cessation of the drug. There was some relief of severe skin irritation when treated with antihistamine drugs and corticosteroids. It is now thought advisable to stop the drug immediately

on the appearance of any type of rash. Most of the patients who developed the rash were later treated with streptomycin and I.N.H., and still later with I.N.H. and P.A.S. without recurrence of the rash.

Provided a watch is kept for these complications, there is no reason why I.N.H. and thiacetazone should not form the basis of treatment for most cases, but we would recommend a smaller dose than that used by Dr. Dutta and his colleagues (that is, thiacetazone 225 mg. and I.N.H. 450 mg./day). The commonly accepted dose for an adult is thiacetazone 150 mg. and I.N.H. 300 mg./day. This has been found to produce a satisfactory clinical response; and this dose of thiacetazone is as effective as P.A.S. 10 g./day in preventing the emergence of resistance to I.N.H.²⁻⁵ The dosage of 150 mg. thiacetazone and 300 mg. I.N.H. for an adult is thought to be critical, and lower doses seem less effective.⁶ A higher dosage of thiacetazone (200 mg.) was found to be toxic in the early 1957 East African/B.M.R.C. trial,³ and also by Bunn.⁷ Leprosy workers also have recommended not exceeding the 150-mg. daily dose.⁸⁻¹¹

If it is possible to determine drug resistance it is better to avoid the combination of thiacetazone and I.N.H. if primary I.N.H. resistance is present or develops early in the course of treatment. Thiacetazone resistance is less important and often only temporary.—We are, etc.,

FRANK I. TOVEY.
NARAYANA SETTY.
R. M. BARTON.

Weston-super-Mare,
Somerset.

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Sarcoid Myopathy

SIR,—The bald statement in the medical memorandum by Dr. P. S. Talbot that "The skin lesions of sarcoidosis were first described by Boeck (1899) . . ." (25 November, p. 465) is incorrect. It is surprising that the Editor of the *British Medical Journal*—of all editors—does not challenge such a remark, for the skin lesions of sarcoidosis were first described by a predecessor of his in that office.^{1,2}

Even more pitiful is the fact that a miliary granuloma, extracted by blind biopsy of an anonymous muscle, should be magnified, with no other evidence, into the multisystem disease sarcoidosis. This is reckless devaluation of a noble disorder.—I am, etc.,

D. GERAINT JAMES.

Royal Northern Hospital,
London N.7.

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Pseudomonas Infection in Hospital

SIR,—In their description of sterilizing the Engström ventilator your correspondents from the Karolinska Hospital (2 December, p. 548) said that they use ultrasonically nebulized 70% ethyl alcohol. We should like to draw your attention to a hazard in this technique, because the method, while bacteriologically effective in killing all bacteria except spores, will give a remarkable explosion if the alcohol mist is sparked in an oxygen-enriched atmosphere. This alcohol mist is also inflammable in air. None of the ultrasonic nebulizers we have examined can be considered flame-proof, and therefore this method of sterilizing ventilators cannot be recommended.

For these reasons we are currently investigating methods of sterilizing such ventilators using ultrasonically nebulized, non-toxic, liquid halogenated hydrocarbons, and hope to publish our results shortly.—We are, etc.,

JOHN S. ROBINSON.
JAMES WHITBY.
P. J. TOMLIN.

Department of Anaesthetics,
Queen Elizabeth Hospital,
Birmingham.

Achilles Tendon Reflex Time

SIR,—Dr. M. Zachmann (2 December, p. 528) suggests that the shortening of the Achilles reflex time that occurs during insulin hypoglycaemia may be due to adrenaline release. We have confirmed Fejér and Kun's observation¹ that adrenaline does reduce Achilles reflex time. The intravenous infusion of adrenaline (10 µg./min.) reduces the time to half-relaxation of the human calf twitch by some 15%, whether elicited by an ankle tap or by stimulation of the medial popliteal nerve. This effect is abolished by prior β-adrenergic blockade; which also significantly prolongs the duration of the Achilles reflex in thyrotoxicosis. The results of these studies are to be published elsewhere.^{2,3}—We are, etc.,

C. D. MARSDEN.
J. C. MEADOWS.

Departments of Medicine and Neurology,
St. Thomas's Hospital Medical School,
London S.E.1.

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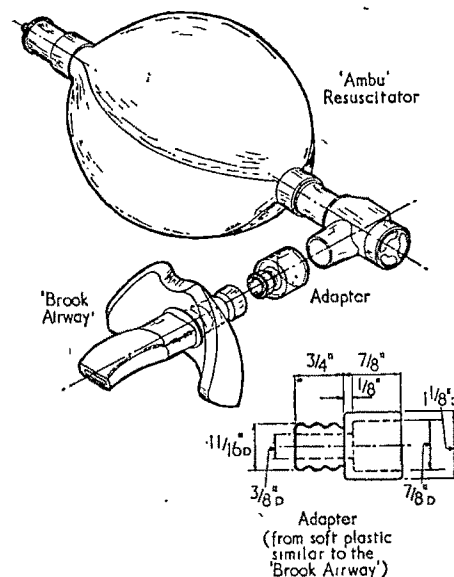
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Resuscitation Appliance

SIR,—When using the Brook airway or the Ambu bag for resuscitation certain problems arise. With the Brook airway considerable energy is required to blow down it for any length of time, and the problem is magnified if external cardiac massage is being performed at the same time. The Ambu bag is commonly used in conjunction with a face-mask, and it can be difficult to place the mask over the patient's face with an airtight seal and at the same time ensure elevation of the chin and backward tilt of the head.

We have devised an apparatus to overcome these problems. It consists of an adaptor to allow the use of an Ambu bag attached to the mouthpiece of a Brook airway, keeping

the advantages of both instruments and avoiding some of the disadvantages. At present we are using a brass adaptor which is both airtight and easily removable. It is hoped to produce a plastic one incorporating a small side-arm extension to allow catheter suction through the airway, without the need for temporary disconnection of the apparatus.



With this apparatus it is easy to produce an airtight fit round the patient's mouth. The tongue can be kept well out of the way. There is less risk of airway obstruction therefore, and should it occur it may be easily recognized by feeling the resistance in the compression of the bag. The device is simple to operate, and the bag can be disconnected easily from the airway to allow catheter suction through the airway.

It is safe for paediatric use. Over-inflation of the infant's lungs is a well-recognized risk of expired air resuscitation. Using an Ambu bag with a smaller Brook airway, the maximum pressure reached when the bag is squeezed with one hand is 35 cm. of water. This is generally recognized as being safe for infants.

Oxygen may be administered by the Ambu bag, allowing an enrichment of air with up to 50% oxygen, compared with ordinary expired air respiration which contains 14% to 18% oxygen. The small risk of infection with expired air resuscitation is eliminated.—We are, etc.,

M. L. CHISWICK.
G. FOY.

Hope Hospital,
Salford.

Body Building on Drugs

SIR,—My attention has recently been drawn to your leading article on this subject (11 November, p. 310) and also to the letter from Dr. D. E. Pearsons (same issue, p. 353) and the letter of Dr. J. R. Owen (25 November, p. 484). This is becoming a very real problem among those closely associated with strength athletes of all kinds.

Unfortunately, my experience in weight-lifting and body-building circles suggests that these drugs do in fact tend to augment muscle bulk in men who are concomitantly engaged in a strength or body-building

regimen of heavy exercise and at the same time are on a high food intake with protein supplements. I write "unfortunately" because the success of these athletes in increasing their muscle size by these means is being copied by more and more young men in the hope of finding an easy pathway to massive muscle size and strength. The tendency often is to rely more on the drugs than increased exercise.

The amateur organizations with which I am associated have heard of many cases of young weight-lifters and body builders being prescribed anabolic steroids more or less on request from their general practitioners. There certainly does seem to exist a "black market" of these drugs, particularly in the U.S.A., according to athletes I have spoken to when I have been serving as international judge at contests of amateur athletic physique. We are very concerned indeed about this trend, and many articles have been written in the official journals of the organizations to which I am medical adviser deploring the use of drugs and pointing out their dangers. As far as the strength and physique contests held by these organizations are concerned, we now make it a rule that no athlete on these drugs is allowed to enter. However, it is very difficult, if not impossible, to determine which athletes are using drugs, and so our ban is rather an empty threat and not much of a deterrent.

I would like to use the medium of your columns to urge that all doctors approached to prescribe anabolic steroids for this purpose refuse to do so. Wide publicity of the very positive dangers of using these drugs, particularly when taken by mouth, would also be welcomed.—I am, etc.,

I. J. MACQUEEN,

Medical Adviser to the Society of
Amateur Weight Lifters and the
National Amateur Body-Builders'
Association.

Croydon, Surrey.

Why Sternal Marrow?

SIR,—Dr. M. W. P. Carney (2 December, p. 512) in his interesting article on serum folate values in psychiatric patients mentions the uncomfortable and frightening procedure of sternal marrow puncture.

I wonder why the iliac crest is not more widely regarded as the site of choice for this procedure. It is certainly less disturbing for the patient and can be performed with safety even in the absence of complete co-operation and in the presence of severe osteoporosis.

It is particularly simple to perform where musculature is lax and subcutaneous tissue scanty, as in the case of the majority of geriatric patients.—I am, etc.,

Perth Royal Infirmary,
Perth.

MARY SHAW.

Investigating Hypertension

SIR,—Having written to you (26 August, p. 557) about a paper on the investigation of hypertension (29 July, p. 306), I was pleased to see your sensible leading article on that subject (9 December, p. 569) based on the reported experience of the Royal Postgraduate Medical School.

Our experience has been similar, and from the beginning we have had no enthusiasm for the more complex forms of investigation

except in those patients in whom some relevant abnormality was likely to be found and which might lead to special treatment. The disappointing results of surgical treatment in most patients are well known. We have also been impressed with the efficacy of antihypertensive drugs properly given to patients with renal hypertension who are not suitable for surgery. Adequate control of the blood pressure can usually be obtained by paying sufficient attention to detail in the individual patient, and often by giving appropriate combinations of antihypertensive drugs.

I agree that all that is required in the majority of patients are serial recordings of the blood pressure, examination of the retinae with fully dilated pupils, a 12-lead electrocardiogram; examination of the urine for protein, abnormal constituents on microscopy, and culture; a specimen of blood for estimation of the blood urea, the erythrocyte sedimentation rate, electrolytes; and a good intravenous pyelogram. In the well-recognized small group of patients in whom renal arteriography is indicated the need for this can be assessed by an isotope renogram, for which the patient can always if necessary be referred to a special centre.

Most of the above tests can, of course, be carried out on an outpatient basis, but if it seems probable that some underlying disease is present or that treatment is indicated the patient should be admitted to hospital for the necessary investigations and the assessment of renal function. If treatment is indicated the institution of an appropriate regimen with antihypertensive drugs can be established, and then be continued by the general practitioner with occasional reassessment at hospital by an interested and experienced physician.—I am, etc.,

R. W. D. TURNER.

Department of Medicine
Annexe,
University of Edinburgh,
Edinburgh 8.

Primigravida or Primipara?

SIR,—I feel it is at times at least misleading when the words "primigravida" and "primipara" are used as though they were synonymous. Surely a primigravida only becomes a primipara when she gives birth, and prior to labour is nulliparous.—I am, etc.,

Port Talbot,
Glam.

R. S. SAXTON.

Obstetric Forceps or Vacuum Extractor?

SIR,—I had hoped to avoid taking any further part in this correspondence, but I feel that I cannot let the letter of Mr. A. F. Clift (2 December, p. 553) go unanswered.

I use the vacuum extractor to deliver the child in cases of either maternal or foetal distress when this arises before full dilatation of the cervix, provided the cervix is half or more dilated. I do not "drag the baby through an undilated cervix" and I do not admit that the procedure carries with it "the serious risks of brain damage, uterine rupture, and ruined uterine supports with subsequent prolapse." If I thought these risks were present I should certainly abandon the use of the instrument in the first stage. I believe that the *modus operandi* of the vacuum

extractor applied before full dilatation of the cervix is to stimulate better co-ordinated uterine contractions by bringing the presenting part into improved contact with the cervix and so to promote rapid dilatation of the cervix in an almost physiological manner. The results obtained in our series of over 1,000 deliveries in Worcester, as well as those from many other centres, show that this can be achieved with a minimum of risk to the child, and in a follow-up study of mothers delivered during the first stage of labour the incidence of cervical trauma and of relaxation of the uterine supports was no greater than in a similar series of spontaneous deliveries. Furthermore, we have seen no case of cervical incompetence in any of our cases delivered by vacuum extraction in the first stage. These results have been obtained not only by "a busy registrar or an active consultant" (Mr. D. B. Brown (25 November, p. 487)) but by some 45 different operators, including house-surgeons and postgraduate students with little or no experience of operative obstetrics. J. Chassar Moir in *Kerr's Operative Obstetrics* suggests that much of the opposition to the vacuum extractor comes from those who have no experience of its use, and I am confident that this opposition would be much less if senior obstetricians would put it to the test.

The most recent major study of this question comes from Helsinki, where Sjostedt,² in a series of approximately 800 forceps deliveries compared with the same number of vacuum extractions, found the perinatal mortality three times as great in the former group. It is not surprising, therefore, that the vacuum extractor has very largely displaced the forceps throughout the Scandinavian countries and Germany, as well as in many parts of the British Isles.—I am, etc.,

J. A. CHALMERS.

Worcester Royal Infirmary;
Worcester.

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β -Adrenergic Blockade and Cardiac Arrhythmias

SIR,—Dr. G. Sloman and Dr. Mary Stannard's paper (2 December, p. 508) lists among the treated arrhythmias only two examples of atrial flutter. Previous reports on the use of pronethalol¹ and propranolol¹ have suggested that atrial flutter is less responsive to β -adrenergic blockade than are other supraventricular arrhythmias. Sloman and Stannard's Case 13, further, cannot be held to be typical of atrial flutter in general, since the underlying disease was thyrotoxicosis. Since thyroxine is known to sensitize the heart to sympathetic stimulation, it would be expected that atrial flutter due to thyrotoxicosis might be more responsive to sympathetic blockade than would flutter due to other causes. Of particular interest, therefore, is the other case (Case 17) of atrial flutter, whose response is described thus: "... the ventricular rate slowed initially, and later there was reversion to sinus rhythm."

I have recently had occasion to treat three patients admitted to hospital with "tachycardia" which subsequently proved to be due to atrial

flutter with 2 to 1 block. Full digitalization regimens failed to control the ventricular rate. In each case, and subsequently propranolol was given intravenously in a dose of 3 mg. over a period of 10 minutes with continuous electrocardiographic monitoring. In all three patients the immediate effect was to increase sensitivity to vagal stimulation by carotid sinus massage, which produced a much greater degree of ventricular slowing than before propranolol; slowing which persisted for some seconds after cessation of massage. Oral propranolol was then given in a dose of 10 mg. every four hours. By the next day the degree of atrioventricular block in all had become 3 to 1 or even 4 to 1, without any alteration in the flutter rate. However, at some stage between 48 and 72 hours after beginning propranolol sinus rhythm was found to have returned, and no further flutter episodes occurred. In two patients the underlying cause was chronic myocardial ischaemia, and the third had rheumatic mitral valve disease with recurrence of acute rheumatism.

At first it seemed that the restoration of sinus rhythm in a possibly paroxysmal atrial flutter might be spontaneous and unrelated to therapy. However, the similar pattern in these three cases, and in Drs. Sloman and Stannard's case, suggests that propranolol does in fact have a dual mode of action in atrial flutter, the first being the depression of ventricular excitability or of atrioventricular conduction, so that there is an increase in the degree of A-V block, without any fall in atrial rate. At a later stage, presumably following a cumulative increase in drug effect, the abnormal atrial discharge is suppressed, and sinus rhythm is restored.

It is apparent that propranolol may well be a worth-while addition to the list of drugs for the treatment of atrial flutter.—I am, etc.,

Stobhill General Hospital, D. A. L. WATT.
Glasgow N.1.

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Postgastrectomy Problems

SIR,—In his most helpful article on post-gastrectomy problems (18 November, p. 403) Mr. J. A. Williams states that "the treatment of gall-bladder disease presents few problems" when it is found to be the "cause" of recurrent dyspepsia after gastrectomy. It is a common experience that in patients with gall-bladder disease alone cholecystectomy fails to relieve dyspepsia in a large proportion of cases, and the treatment of this symptom is anything but free of problems. I wonder if Mr. Williams has had a different experience with postgastrectomy patients. If so, may this not be a significant observation?—I am, etc.,

ALAN G. JOHNSON.

West London Hospital,
London W.6.

Coxsackie B5 Virus

SIR,—It was stated in the leading article "Outbreaks of Coxsackie B Infection" (9 December, p. 570) that no Coxsackie B5 virus infections were reported from Northern Ireland during 1965. In fact, eight Coxsackie B5 infections occurring during 1965 were reported to the Central Public Health

Laboratory at Colindale and were published in the weekly summaries of the Public Health Laboratory Service. The details of these patients were as follows:

Patient	Age	Sex	Illness	Month of Illness
1	5	M	Healthy excreter	August
2	34	F	Aseptic meningitis	September
3	4	F	Aseptic meningitis	October
4	3	M	Aseptic meningitis	November
5	29	F	Aseptic meningitis	November
6	39	F	Pericarditis	November
7	60	F	Bornholm disease	November
8	25	M	Aseptic meningitis	December

Coxsackie B5 virus was isolated from faeces of the first seven patients, while in Patient 5 virus was also isolated from the cerebrospinal fluid. Patient 8 was diagnosed by finding a rising titre of Coxsackie B5 virus antibody.—I am, etc.,

J. H. CONNOLLY.

Department of Microbiology,
Queen's University,
Belfast.

Congenital Dislocation of the Hip

SIR,—I read Dr. C. O. Carter's letter (9 December, p. 618) with considerable interest. With an incidence of abnormally lax hips as high as 1 in 40 at birth in certain parts of Britain, it obviously must happen fairly frequently that two or more children with congenital dislocation of the hip are born into one family, either in the same generation or spanning the generations. The suggestion that such children merit specially careful examination is not right. There are no first- and second-class citizens in congenital dislocation of the hip. Every baby at birth is entitled to the most careful examination available to it.—I am, etc.,

Hope Hospital,
Salford 6.

T. G. BARLOW.

Which Stethoscope?

SIR,—Dr. B. J. Peck (9 December, p. 620) describes a transistorized stethoscope which would no doubt cost very little to make from parts of an old hearing-aid. But surely anyone but the most penurious practitioner would be better advised to invest in a cheap electronic stethoscope such as I myself have been using almost exclusively for the last two years.

My own hearing has deteriorated only marginally, but nobody could hope to hear as well with an ordinary stethoscope as one can with the neat little instrument I carry round in my pocket. Its general shape and size are similar to the old-fashioned instrument, but with it one can hear heart sounds beautifully even through layers of an old lady's clothing that it would take much time and grumbling to remove. A foetal heart can be heard in circumstances where no old instrument could pick it up. Amplification is variable and there is a choice of high and low tone chest-pieces, though I find the latter generally useful. To me it is quite amazing that neither

Dr. Peck nor the article to which he refers makes any mention of the modern transistorized stethoscope. On the other hand, it is fair to say that in this day and age of hearing-aids and all sorts of sound-reproducing appliances in patients' homes I have yet to meet a colleague who has anything better than two old "speaking tubes" joined to a little funnel to enable him pick up various sounds from the human body.—I am, etc.,

Eye, Suffolk.

SHACKLETON BAILEY.

"Mediflash"

SIR,—Those of us who deal with emergencies, especially road accidents, should be grateful to Dr. R. Snook (2 December, p. 556) for having made it possible for us to carry a warning/protective device on our cars.

Our own chief constable welcomed its introduction and would favour an even brighter light which could be seen more clearly in daylight, fog, or storm. If we are circumspect in the use of this lamp it will be respected by police and public alike. I and my colleagues have already proved its efficacy during the recent spate of accidents from ice and fog. May I add two comments on Dr. Snook's excellent letter?

In Britain emergencies are an everyday occurrence, a thousandfold so. Emergency work is dangerous and those undertaking it deserve co-operation. Dr. Snook and the B.M.A. officials must not be thwarted in their endeavours to further the humanitarian services of our profession, nor be discouraged by the apparent lack of comprehension of others.—I am, etc.,

KENNETH C. EASTON.

Catterick Village,
Richmond, Yorks.

Megaloblastic Anaemia and Ascorbic Acid

SIR,—We have read with interest the claim by Dr. P. Asquith and his colleagues (18 November, p. 402) that the megaloblastic anaemia in a scorbutic patient responded to ascorbic acid alone. The diet of this patient before admission was obviously low in folate as well as ascorbic acid. He had a low serum folate activity associated with megaloblastic erythropoiesis, and it is difficult to avoid the conclusion that his anaemia was, in part at least, the result of folate deficiency. The authors state that he returned to haematological normality when given ascorbic acid 500 mg. daily and "a folate-deficient diet composed of tea, bread, jam, eggs, fish, chicken, minced meat, and potato." The last five items in this diet contain significant amounts of folate; without details of a cooking process designed to reduce the folate content and assays of the food as eaten, this diet cannot be described accurately as folate-deficient.

We have assayed various foods using *Lactobacillus casei* as the test organism, and have found eggs to contain up to 50 µg. per yolk and potatoes 6.8 µg. per 100 g. The *Agricultural Handbook* of the U.S.A. gives the following folate concentrations¹:

Bread (white)	...	13.8 µg./100 g.
Fish (raw)	...	164 " "
Chicken	...	3.1 " "
Minced meat	...	4.3 " "

The observation that the fasting serum folate activity remained low does not disprove that the haematological response was the result of folate in the diet after admission, as it is possible to treat megaloblastic anaemia without replenishing body folate stores.³

Any relationship between folate metabolism and ascorbic acid remains obscure, but it has been shown that patients with only slight evidence of folate deficiency may become frankly megaloblastic when treated with ascorbic acid alone and a folic acid-free diet.^{4,5} The contradictory reports of ascorbic acid converting megaloblastic erythropoiesis to normoblastic and normoblastic erythropoiesis to megaloblastic are probably explained by the former studies not being conducted on folate-free diets, and by an increased utilization and low intake of folate in the latter.

As a patient who has scurvy is likely to be folate-deficient, it seems sensible to give folic acid to all scorbutic patients and also to ensure that they are not deficient of vitamin B₁₂ and iron.—We are, etc.,

R. E. DAVIS.

Department of Haematology,
Royal Perth Hospital,
Perth, Western Australia.

A. F. FLEMING.

University Department of
Obstetrics and Gynaecology,
King Edward Memorial Hospital,
Subiaco, Western Australia.

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Hypercalcaemia and Malignant Tumours

SIR,—The spirited reply (11 November, p. 355) to my earlier letter (23 September, p. 799) does not increase the likelihood that the bronchial carcinoma described by Dr. W. E. Medd and his colleagues (2 September, p. 590) was producing a parathyrotropic substance. In stating that hyperplastic parathyroid glands have not been found in patients with hypercalcaemia and non-parathyroid malignant tumours I was quoting from the authoritative paper by Sherwood and his coworkers.¹ Roth² in 1964 reviewed the literature and considered that the case was not proved for the existence of a parathyrotropic substance in any of the papers where this had been suggested as the indirect cause for the hypercalcaemia. He thought that primary chief-cell hyperplasia of the parathyroids³ was the cause for the hypercalcaemia in each of the patients (who had an incidental tumour in another organ).

The two papers that Dr. Medd quotes in support of a mechanism mediated via the parathyroids causing the hypercalcaemia are extremely wispy struts when examined more carefully. In the first,⁴ the patient had primary chief-cell hyperplasia of the parathyroids. Dr. Castleman examined the glands and suggested that there was no need to implicate bronchogenic carcinoma at all in the pathogenesis of the hypercalcaemia, and that it could be considered as a coexisting independent pathologic process. In the

second,⁵ a case-record, two small parathyroids only were found at necropsy, and the evidence for mild hyperplasia was based on the absence of fat in the glands, and this was in a patient cachectic from loss of body fat. The glands, on description, were unlikely to have been of sufficient size to have produced a plasma calcium level in excess of 17 mg./100 ml. More undermining of Dr. Medd's support, however, is the fact that Dr. A. H. Tashjian, jun., made an immunoassay of the primary tumour and found parathormone-like activity in it. These two papers are hardly good evidence when placed alongside the many published reports where no parathyroid hyperplasia was discovered to explain the hypercalcaemia.

If Dr. Medd will get in touch with me I shall be happy to try to arrange that the tumour from his patient be assayed for any parathormone-like activity.—I am, etc.,

MILO KEYNES.

Nuffield Department of Surgery,
The Radcliffe Infirmary,
Oxford.

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Medical Science: Master or Servant?

SIR,—In his reply to Lord Platt's Harveian Oration (25 November, p. 439) Professor W. S. Peart (9 December, p. 616) calls for the provision in university medical departments of more and more sophisticated workers to carry out ever smaller and more refined measurements. With diffidence I suggest that he thus seems to confirm the validity of Lord Platt's contention while attempting to refute it.

For years many of us, remembering the time when doctors were still able to talk to their patients, have been waiting for just such a lead as Lord Platt has now given. We feel that only by restoring a proper balance between the art and science of medicine shall we find true satisfaction for ourselves and our patients.—I am, etc.,

Ringwood,
Hants.

R. VAUGHAN FACEY.

Institutional Care of the Mentally Subnormal

SIR,—Dr. G. B. Simon (2 December, p. 549) takes us (2 September, p. 573) to task (a) for not considering children on waiting-lists and (b) for underestimating the proportion of children requiring "medical investigation or treatment of a kind necessitating hospital admission." Assessment of the needs of children on waiting-lists was not essential to the aims of our inquiry, which Dr. Simon ignores; nevertheless account was taken of them in estimating the number of children needing hospital care (Fig. 2 in our paper). The estimate of patients' requirements was made, not by us, but by the staffs of the hospitals, including Lea Castle. On the same point Dr. Simon seems to confuse the number

of patients (7) said to need hospital care for medical investigation and treatment with the total number (1,007) considered to need hospital care for any reason, mainly for mental and basic nursing.

Nevertheless we agree that Pilkington's estimate¹ (10%) of the proportion of patients who require "detailed specialist day-to-day diagnosis care and treatment" is a more acceptable indication of future needs, and like Dr. Simon we should be sorry to see the lower Birmingham figure misused.—We are, etc.,

THOMAS McKEOWN.

University of Birmingham,
Birmingham.

IAN LECK.

University College Hospital
Medical School,
London W.C.1.

REFERENCE

- Pilkington, T. L., in *Report of the Annual Conference of the National Association for Mental Health*, 1966, p. 50. London.

Patient or Ailment?

SIR,—One gets the impression (*Supplement*, 9 December, p. 71) that the Private Practice Committee have failed to condemn a very curious attitude to general practice. From your report it seems that a general practitioner undertook the care of a patient for a "particular ailment," and that he and the patient conspired to keep this secret from her "N.H.S. doctor"—in other words from her regular general practitioner. May one ask whether a general practitioner can undertake the care of a particular ailment, not of the whole patient? It was evidently not a trivial matter, since she was admitted to hospital, apparently as an emergency. Given the chance, this sort of patient may end up by seeing Dr. Smith for her rapid heart, Dr. Jones for her goitre, and Dr. Brown for her exophthalmos!

And what of the ethical position? Should not the private general practitioner have insisted that if this patient had such little trust in her regular doctor as to deceive him deliberately, she should take steps to remove her name from his list altogether? She could then have truthfully told the hospital that she had no N.H.S. doctor. I would like to make it clear that I am by no means opposed to true private general practice. But for patients to remain on the list of one general practitioner (N.H.S.) and then to have secret consultations with a second general practitioner privately seems to me such an obvious cause of friction and confusion as to be worthy of strong discouragement.—I am, etc.,

Maidstone, Kent.

JOHN B. GLASS.

Hospital Management

SIR,—Once again professions of economy and efficiency (25 November, p. 482) are on the lips of public men. May I make three practical suggestions which would be simple to implement.

Hospital management committees still consist predominantly of laymen innocent of any real knowledge of the highly technical problems of a modern hospital. Admittedly things have improved, but the elderly seeking escape from boredom are still conspicuously

with us. Conversely the senior officers of the hospital on whom efficiency depends are hardly ever consulted. In theory there are advisory committees at which senior staff and hospital management committee members consult. In one case records show that over two years the attendance of the lay members of the hospital management committee was under 25%. At times the hospital staff found themselves without any hospital management committee representative with whom to consult. Is it not time hospitals were run by professionals with sufficient lay representation to prevent abuse? Few of us would care to invest our money in companies run by amateurs.

The medical superintendent is still with us, although in emasculated form. This system of imposing a doctor on others, usually without consulting them, is surely undemocratic and obsolete. Under it only chance decides whether this man can command the loyalty and respect of his colleagues. In the not infrequent cases where he cannot disharmony and frustration result. The elected officers of the senior medical staff committee should replace him.

Staff in efficient hospitals receive the same salaries as those in inefficient hospitals. Some financial incentive needs to be devised, and in this the advice of business consultants and efficiency experts should be taken.—I am, etc.,

Littlemore Hospital,
Littlemore, Oxford.

J. E. DUFFIELD.

Forging Prescriptions

SIR,—We would like to bring to your attention the fact that recently on two separate occasions patients have produced photo copies of their prescriptions given on previous occasions by the doctor. This is obviously helpful to the patients who require only a repeat prescription of their drug, and they could thus tell any strange doctor exactly what medicines they are on. However, the obvious problem arises that this photo copy has an exact signature of the doctor, and recently one of us (G. B. S.) had a quantity of prescription-pads stolen after breaking into his car. Of course the prescriptions were made use of and appeared at chemists with signatures vastly different from the signature of the doctor concerned, but as soon as the doctor's signature can be so easily found and forged then it may be difficult for the chemist to tell that the doctor has not himself prescribed the forged prescription.

Needless to say nearly all of the prescriptions returned by chemists were for drugs of the purple-heart variety. Perhaps it is necessary, as well as having a dangerous drugs register, to have an addicted drugs register.—We are, etc.,

B. D. LASCELLES.
G. B. STURROCK.

London E.1.

Mileage Allowances

SIR,—I am sure we are all grateful to the Negotiating Subcommittee of the Central Committee for Hospital Medical Services for obtaining an increase in the mileage allowances. I am indebted to Dr. N. L. Rowe (11 November, p. 361) for his lucid explana-

tion of the change of basis for calculating the new allowances which came into effect on 1 July 1967. No one can quarrel with the change from horsepower to cubic capacity in determining the class in which a car is to be assessed. I note that the circular announcing the change was issued by the Ministry of Health in July, although I suspect the Scottish Home and Health Department issued the circular later than July. The intimation of the increase in the allowances was published in the *Supplement* on 19 August (p. 121). It would therefore appear that the application of the "no detriment" clause was made retrospective to a date before the announcement, and, if so, I think this was unjustifiable and unfair.

My point is that it was a breach of contract to make the date on which the change became effective earlier than the announcement of the change. Did the Negotiating Subcommittee agree to this, and, if so, why, or did the Health Departments make this decree on their own?—I am, etc.,

Penicuik,
Midlothian.

JOHN G. MCWHIRTER.

Sickness Benefits

SIR,—There must be many general practitioners who believe, as I did, that the new regulations regarding sickness benefits meant that we should be refunded locum fees during sickness up to a maximum of £32 per week.

This is not so. I was recently unfit to work for eight days, and locums were employed for six surgeries at a cost of £18 18s. After completing a number of forms I was told that £7 6s. 3d. would be allowed. This was calculated on the following formula:

$$\frac{12}{60} \times \frac{8}{7} \times 32 = £7 \text{ 6s. 3d.}$$

12 = number of hours worked by locums.
60 = "normal working hours."
 $\frac{8}{7}$ = number of weeks sick.

It will be seen that the amount paid does not enter into the calculation. Presumably a full-time locum working at least 60 hours will attract the full £32. But of sheer necessity most of us can have only part-time help, as there are very few full-time locums available. Incidentally, it is interesting to note that our "normal working hours" are reckoned to be 60 per week.

I was completely deceived, and it is likely that others will have been misled too. I wonder if our negotiators realized the truth? If so, it is a pity that it was not publicized, because, once again, as in the whittling down of the 70% for ancillary help, this is likely to cause irritation and frustration. Finally, it is of great importance that those considering insuring against sickness, or possibly reviewing their present policies on the assumption that they will receive £32 per week, should realize the facts.—I am, etc.,

Harrogate, Yorks.

D. C. WILLIAMS.

Terms of Service—1805

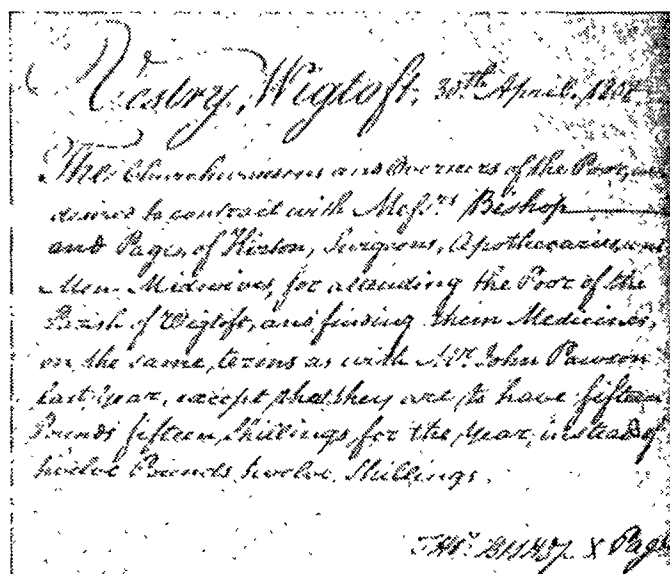
SIR,—In the register of Wigtoft Parish Church in the county of Lincolnshire I found several references to the medical profession. One is reproduced below, and it reads as follows:

Vestry, Wigtoft, 30 April 1808.

The Churchwardens and Overseers of the Poor, were desired to contract with Messrs. Bishop and

fifteen Shillings for the Year, instead of twelve Pounds twelve Shillings.

In another, dated April 1807, it is stipulated "he is not to attend more than three women in childbirth, if he does, that he be allowed for such attendance one guinea each. That venereal cases be excluded. That he attend the poor at Kirton Holme belonging to



Page, of Kirton, Surgeons, Apothecaries, and Men-Midwives, for attending the Poor of the Parish of Wigtoft, and finding them Medicines, on the same terms as with Mr. John Pawson last Year, except that they are to have fifteen Pounds

the said Parish. But that his journeys do not exceed more than three miles from the town of Wigtoft.—I am, etc.,

Boston, Lincs.

G. R. USMAR.

Obituary Notices

Sir ADOLPHE ABRAHAMS, O.B.E. M.A., M.D., F.R.C.P.

Sir Adolphe Abrahams, consulting physician to Westminster Hospital and Hampstead General Hospital, London, died on 11 December after a long illness. He was 84.



[Walter Stoneman]

Adolphe Abrahams, son of Isaac Abrahams, of London, was born at Capé Town on 6 February 1883. He received his education at Bedford Modern School, where he was Exhibitioner, and at Emmanuel College, Cambridge, where he was Foundation Scholar and Prizeman. He took first class honours in the Natural Sciences Tripos in 1906, and went to St. Bartholomew's Hospital for his clinical studies, qualifying with the Conjoint diploma in 1909 and graduating M.B., B.Chir. two years later. He undertook further post-graduate study in Vienna, and proceeded M.D. in 1914. His first appointment was as house-surgeon at St. Bartholomew's Hospital, where also he edited the *St. Bartholomew's Hospital Journal*. From 1915 to 1920 he saw war service and was in charge of the medical division of the Connaught Hospital, Aldershot, and district consulting physician, Aldershot Command. He held the rank of major, R.A.M.C. and was mentioned in dispatches.

After demobilization Abrahams was appointed to the staff of Westminster Hospital in 1920, where he remained for the rest of his career. He retired in 1948, when he became honorary consulting physician to the hospital. At Westminster his influence was deeply felt in the medical school. He was in turn lecturer, tutor, and administrator in medicine, and dean from 1934 to 1940. He was also physician to the Royal Chest Hospital, and consulting physician to the Hampstead General Hospital, the Chislehurst, Orpington and Cray Valley Hospital, and the L.C.C. hospitals before these latter were taken over by the regional boards. He was examiner in medicine to the Universities of Cambridge and Liverpool, and examiner in medicine and applied pharmacology and therapeutics to the University of London. The Royal College of Physicians, of which he became a Fellow in 1930, appointed him censor. In 1951 he delivered the Lumleian Lecture to the College. He was a prominent member of the Association of Physicians of Great Britain and Ireland, and he had been president of the British Association of Gastro-Enterologists. With Sir Arthur Porritt he took a leading part in founding the British Association of Sport and Medicine.

Both medicine and athletics have lost a long-familiar figure by the death of Sir Adolphe Abrahams. The three brothers

Abrahams were renowned in the world of athletics. Adolphe Abrahams, the eldest of them, linked athletics with medicine in a life-long study. He acted as medical officer in charge of the British Olympic team at the various Games from 1912 in Stockholm to 1936 in Berlin, and after that at the European championships in Paris in 1938, and was also honorary medical adviser to the International Athletic Board. His interest in physical fitness was unbounded, and he once described it as "the provision of antidotes to the consequences of modern existence." He had some unorthodox ideas on the subject which he voiced particularly in his Arris and Gale Lectures to the Royal College of Surgeons in 1928 on the physiology of violent exercises. Among other things, he deprecated women entrants in big athletic contests. Physical vigour, in his view, might be purchased at an exorbitant price, at the sacrifice of certain moral qualities and advantages. He declared that all forms of violent exercise, especially when accompanied by the nervous tension of competition, tended to aggressiveness and to the disappearance of that softness which was identified with the charm of women. But for men he insisted on the value of athletic performance, even down to old age. He was one among several septuagenarians who were capable of running 100 yards in 12 seconds. He scoffed at golf for young men; it was an exercise, he said, for the middle-aged and elderly, especially for those mentally overworked and predisposed to introspection and melancholy. His own recreations included riding and motoring.

Alike in the stadium and in the hospital or classroom Adolphe Abrahams was a man to catch the eye. His spare figure, even when approaching old age, had something of the poise and grace of the Greek athlete. His physical endowments were matched by his intellectual qualities. His lectures and even his impromptu speeches in medical assemblies were models of what such things should be—examples of clear thinking, careful and often picturesque phrasing, and pleasant delivery. He was a master of the cogent simile and the faintly sardonic comment.

Abrahams wrote a good deal on general medical subjects, and was for some time editor of the *Postgraduate Medical Journal*. An early work of his, with the late Dr. G. Henschell, was on *Chronic Colitis*. He also produced, with Mr. A. Clifford Morson in 1921, a *Manual of Urinary Diseases*. Among other volumes were *Diseases and Disorders of Digestion* in 1931, *Training for Health and Athletics*, with H. M. Abrahams, in 1936, *The Human Machine* in 1955, *Disabilities and Injuries of Athletics and Sport* in 1960, and *Duodenal Ulcer and Other Alimentary Canal Disorders*, in 1961.

He was appointed O.B.E. in 1919, and was knighted in 1939. He married in 1922 Miss Adrienne Walsh, daughter of John Walsh of County Wicklow, and they had a son and daughter.

S. C. writes: My first recollection of Adolphe Abrahams is as an R.A.M.C. major applying for the vacancy of assistant physician to Westminster Hospital in 1920. His appointment coincided with that of two other Bart's men—Stanley Woodwork and Arnold Stott—all three destined to achieve distinction in the medical scene of London between the two wars.

Much has been said about Adolphe Abrahams as an athlete, and to this I may add two small points which may have escaped notice. When he was past middle age he had a portion of his radial artery excised, sent it to Sharpey-Schafer, and was delighted to get a report that the artery was that of a healthy young man. It was his practice up till the age of 70 and over to run round Regent's Park on Saturday afternoons, regardless of the weather, and it is reported that it was his habit to take his temperature during this exercise and that his performance improved as his temperature rose.

As a general physician he was most interested in fitness and health, and was somewhat cynical as regards ill-health. Both as a colleague, when called in consultation, and as a teacher this cynicism was obvious and was based chiefly on his philosophy that as we knew little enough about normal psychological problems we cannot "throw our weight about" as regards pathological states. He was an accomplished after-dinner speaker, a shrewd critic of the too readily accepted fads in medical practice, and somewhat inclined to rely on the *vis medicatrix naturae*.

The last few years of his life he put up with the physical disabilities of age, and referred to his bodily frame as "an antiquated Rolls-Royce—but still a Rolls-Royce." He was part of the medical scene of London, between the two world wars, and in many ways remarkable, liked by most, and respected by all who knew him.

W. E. L. writes: I remember Adolphe Abrahams's outpatient clinics with their large number of patients. Dr. Abrahams was conscientious in his attendance and never left the clinic, no matter how late the hour, until the last patient had been seen. He was an excellent clinician, and although his manner, from the patients' point of view, might appear rather detached, he took the greatest interest in their welfare. His chief interest was in diseases of the digestive tract, on which subject he wrote extensively, and he had a splendid command of the English language. Students will recall with pleasure his clinical teaching in his outpatient clinics, and later on his ward rounds when he became a senior physician. In fact Adolphe was always interested in students' activities, and often wrote in their journal. It was a great pleasure for him to witness the great strides which the Westminster Medical School had made from his early association with the hospital, and part of this success was due to himself as he was dean of the Medical School from 1934 to 1940.

At Cambridge he was a fine athlete, and throughout his long life he was a great advocate of adequate physical exercise. He did much to foster athletics in this and other countries, and he was medical officer to the British Olympic team on many occasions. In 1951 he delivered the Lumleian Lecture at the Royal College of Physicians, his subject being "Physical Exercise; its Clinical Associations."

Even when greatly advanced in years his boyish athletic figure, always most elegantly dressed, was the envy of his colleagues, and he will be remembered with affection.

G. MACDONALD, C.M.G., M.D.
F.R.C.P., D.P.H., D.T.M.

Professor G. Macdonald, professor of tropical hygiene in the University of London and director of the Ross Institute at the London School of Hygiene and Tropical Medicine, died on 10 December, at the age of 64.

George Macdonald, son of the late John Smyth Macdonald, F.R.S., was born on 22 June 1903. He was educated at the King Edward VII School, Sheffield, and entered the University of Liverpool, where after a distinguished undergraduate career he graduated M.B.,



Ch.B. in 1924 and took the D.T.M. the same year. From the early stage of his career Macdonald was attracted to tropical medicine. From 1925 to 1929 he was research assistant at the Sir Alfred Lewis Jones Laboratories in Freetown, Sierra Leone. He then spent two years

as a research officer for the Malaria Survey of India before returning to England in 1931. A year later he proceeded M.D. and shortly after took the D.P.H. After this he worked for five years as a medical officer for the Mariani Medical Association in Assam before his appointment as assistant director at the Ross Institute in 1937, where in 1945 he succeeded Sir Malcolm Watson as director. He had a distinguished service during the second world war when he was in turn commanding officer of No. 1, No. 2, and No. 3 Malaria Field Laboratories, and then consultant malariologist to the Middle East Forces and to the Central Mediterranean Forces.

After demobilization in 1945 with the rank of brigadier he resumed his work at the Ross Institute, and in the same year was also appointed professor of tropical hygiene at the University of London. He took the M.R.C.P. in 1948. He was appointed C.M.G. in 1953, and in 1954 received from the World Health Assembly the Darling Foundation Award for his studies on epidemiology of malaria. In 1955 he was elected F.R.C.P.

He was honorary consultant malariologist to the War Office, member of the World Health Organization Expert Advisory Panel on malaria and on environmental hygiene,

and leader of the 1952 W.H.O. mission to Korea. From 1953 to 1961 he was a member of the Colonial Medical Research Committee. He was chairman of the malaria committee of the Medical Research Council and a member of the Council's Tropical Medicine Research Board from 1961 to 1964, member of the managing committee of the Bureau of Hygiene and Tropical Diseases, and from 1965 to 1967 president of the Royal Society of Tropical Medicine and Hygiene.

The death of George Macdonald is a grievous loss to tropical preventive medicine generally and to malariology in particular. There are few people among the rapidly diminishing group of senior malaria experts whose impact on the strategy of control and eradication of malaria has been as great. There are even fewer whose scientific concepts of malaria epidemiology have been equally important, and among them no one can match George Macdonald's interest, enthusiasm, and experience in applying modern computer techniques to preventive medicine.

The mathematical models presented in a series of papers during the period 1952 to 1957, and in his 1957 book *Epidemiology and Control of Malaria*, gained immediate acceptance, because they provided a satisfying explanation of one aspect of malaria—namely, the variation of its epidemiological equilibrium. This equilibrium, very sensitive to changes in the mosquitoes' feeding pattern and longevity, has now been fully quantified and adapted to computer calculation, and is now being used for both the design and assessment of control programmes. The theory of malaria control was originally built up on a general basis, but found its confirmation and practical application in the course of field programmes assisted by the World Health Organization. From the very beginning of the global malaria eradication programme Professor Macdonald was closely associated with its planning. He participated in nearly every session of the W.H.O. Expert Committee on malaria, and the impact of his experience and personality are obvious in most of the relevant records. George Macdonald's recent work on assessment of the rate of reduction of the parasite reservoir indicates the possibility of forecasting the interruption of malaria transmission, and has been incorporated into the latest reports of the W.H.O. Expert Committee on malaria for field use.

His method of mathematical analysis has been extended to bilharziasis and a wonderful model devised, several characteristics of the snail vector being treated as parameters. The results of this study run on a computer showed such a striking similarity to the experience gained in the field that it could well be used as guide for various forms of control of bilharziasis.

Until a few weeks before his death George Macdonald worked on other mathematical models that could be applied to many insect-borne infections, and to immunization programmes for control of all types of communicable disease. About a year ago he knew that from then on he lived on borrowed time, but this did not greatly affect his decision to live as normally as possible, and to carry on with his research and teaching. To all those who were close to him during that time this lonely fight against an inexorable fate was a dramatic experience and an inspiring

example. He was a man of many talents and had a tremendous personality that commanded an immediate respect and admiration. A formidable opponent in a scientific discussion, he always listened carefully and weighed fully the argument that challenged his views. His manner could be aloof when he was preoccupied, but whoever worked with him or needed his help appreciated his quiet humour, his ability to understand others, and his infinite kindness. He was loved by his staff, who were intensely loyal to him and proud of his and their joint achievements. In international circles, where he was immensely respected, he represented the best tradition of British science and its applications to problems of tropical public health.

He is survived by his wife, whose affection and understanding helped him so much during all their married life, and by his son and two daughters, one of whom is a practising physician. We offer them our deep sympathy in their bereavement.—L. J. B.-C.

BÉLA SCHICK, M.D.

Dr. Béla Schick, the well-known paediatrician, died in New York on 6 December, aged 90. His name is inseparably connected with the test he devised in 1913 for estimating susceptibility to diphtheria; and among immunologists he will be remembered for the fundamental work he carried out with von Pirquet, in Vienna, in the early years of the century on the subject of allergy.

Béla Schick was born as a premature infant at Boglár, in Hungary, on 16 July 1877. He received his medical training at Graz, in Austria, where he graduated M.D. in 1894. He remained at the university till 1900, and then, after approximately a two-year period of military service in the medical division of the Austrian army, proceeded, like his great fellow-countryman Semmelweis before him, to the larger world of Vienna. There in the university and the children's clinic he worked in collaboration with Clemens von Pirquet and Theodor Escherich. In 1918 he was made professor of paediatrics. He retained this position till 1923, when he emigrated to the United States to take up a post that had been offered him at the Mount Sinai Hospital in New York. The rest of his life was spent in his adopted country, where he was naturalized in 1929. He practised as a consulting paediatrician in New York City. In this capacity he was attached among others to the Mount Sinai Hospital, the Sea View Hospital, and the Willard Parker Hospital; and later, from 1938 to 1942, was appointed clinical professor and lecturer in diseases of children at Columbia University. After his retirement in 1942 at the age of 65 he continued his paediatric work at the Bethel Hospital, in Brooklyn, and the Albert Einstein College of Medicine, where he acted as visiting professor.

Schick married in 1925 Catharine C. Fries, a doctor of jurisprudence. Though denied children of his own, he was intensely fond of children, and his ways with them are commemorated in a book *Béla Schick and the World of Children*, by Antoni Gronowicz, published in 1954. Every year, partly in response to a nostalgic home call, Schick spent two or three months in Europe attending paediatric congresses and renewing

acquaintances with friends and colleagues. For this purpose he kept an old open Ford car in permanent storage, which he picked up when he came over. He was fond of travelling, and it was on a South American cruise last month that he contracted pleurisy, from which he died shortly after his enforced return to New York.

Honours were showered upon him too numerous to name. Among them, however, was the Addingham gold medal awarded him at Leeds in 1938, and the Semmelweis medal of the American Hungarian Medical Society in 1955. To celebrate his 80th birthday papers by authors from different parts of the world were published in four successive numbers of the *International Archives of Allergy and Applied Immunology*, and later published in collected form as a Festschrift entitled *Current Problems in Allergy and Immunology*, edited by William Kaufman (S. Karger, Basel, 1959).

Schick came into prominence in 1905 when, with von Pirquet, at Vienna, he described the phenomenon of serum sickness. As has so often happened in similar circumstances, von Pirquet and Schick were not the first to recognize the disease. This had been done already in Lublinski in 1894, but it was they who coined the term "serum sickness." Schick's association with von Pirquet was most beneficial. They worked together in harmony and laid much of the foundations of our knowledge of allergy. Von Pirquet, in 1907, introduced his tuberculin scratch test; and, working along the same lines, Schick in 1913 introduced the skin test that bears his name. Though both tests are carried out on the skin, they are quite different in principle. The one is a test for delayed hypersensitivity to the tubercle bacillus, and when positive indicates the existence of infection. The other is a test for the presence or absence of serum antitoxin; it does not depend on allergy, and when positive indicates susceptibility to the diphtheria bacillus. The Schick test was taken up by Park and Zingher in New York, in 1925, as the basis of the city's programme to eliminate diphtheria. Thousands of children were tested, and much valuable information was obtained about the epidemiology of the disease. The original purpose of the test was to find out whether a child in contact with diphtheria needed to be passively protected by an injection of diphtheria antitoxin. Later, when neutralized toxin and toxoid preparations became available for active immunization, it was used to find out which children required immunizing. Now, with routine immunization of infants, all of whom after the disappearance of maternal antibody can be regarded as susceptible, the Schick test is no longer needed. Apart from epidemiological survey work and the testing of the antigenic potency of various prophylactic agents, its only use is to serve as a detector of hypersensitivity of older persons to foreign proteins in the toxin preparation—a purpose quite different from that for which it was originally intended.

In addition to allergy, Schick was interested in a variety of subjects mainly relating to infectious diseases of children. While at Vienna he wrote a book in 1912 on scarlet fever with his colleague Theodor Escherich—of *Escherichia coli* fame—and during his long life he wrote on tuberculosis, diphtheria, child care, and the nutritional problems of

children. He realized the danger of cross-infection to an infant admitted to the general ward of a hospital, and insisted on all infants under 1 year being nursed in isolation in special cubicles from which even the residents were barred. He put the welfare of his child patients before everything else, and their clinical care and treatment before research investigations. He will be remembered with affection and respect by medical and scientific workers throughout the world, and particularly by those who had the privilege of sitting under him as a teacher. —G. S. W.

A. R. S. VICKERS, C.M.G., O.B.E.
M.B., CH.M.

Dr. A. R. S. Vickers, medical superintendent of the Royal Flying Doctor Service of Australia, Queensland Section, died at Cape Town, South Africa, on his way back to Australia from England at the end of October. He was 66.

Allan Robert Stanley Vickers was born on 3 June 1901, and received his medical education at the University of Sydney, graduating M.B., Ch.M. in 1926. He was appointed resident medical officer at Albury Hospital in 1927, and in 1931 was recruited as medical officer to the Flying Doctor Service by its founder, the Rev. John Flynn, of the Australian Inland Mission. He served with the Flying Doctor Service in many parts of Australia, becoming in 1935 the medical superintendent and controller of bases at the Queensland Section. During the second world war he served with the Australian Army Medical Corps as officer commanding the 110th Australian Military Hospital. For much of this period he was vice-president of the West Australia Section of the Flying Doctor Service. After being discharged in 1943 with the rank of lieutenant-colonel he returned to his duties with the Flying Doctor Service in Queensland, where he opened a new base at Charleville, remaining there until 1954. In addition, he was appointed senior medical officer of the Queensland Section, and was closely associated with the establishment and supervision of new bases. In recognition of his services he was appointed O.B.E. in 1951 and C.M.G. in 1955. In 1955 the Flying Doctor Service was granted permission to use the prefix "Royal."

Dr. Vickers, who came to Britain in 1954 under the auspices of the Nuffield Foundation to undertake postgraduate study and to stimulate interest in the flying doctor services in the Commonwealth countries, again visited Britain in 1967, this time in a private capacity to attend the wedding of his son—also in the medical profession. It was on the return journey by sea to Australia that his death occurred.

In 1934 he married Lillias Whitman, and they had two sons.

N. A. D. writes: From the early thirties until his death Dr. Allan Vickers had been for most Australians the epitome of the "Flying Doctor." In the years of drought and depression he voluntarily cut his salary while refusing to allow the Flying Doctor Service to be curtailed, and then was sent by the founder, "Flynn of the Inland," on a lecture tour of the Australian cities that put the service back on its feet. It was in London

during 1954 that I met Allan, and his enthusiasm took me to Queensland as a flying doctor. His support and encouragement helped to see a Flying Doctor Service started in Nigeria, and at the time of his death he was helping initiate a service in Ethiopia. His death is a loss both personal and to the Services in Australia and Africa.

BESSIE M. PLAYFAIR, M.D., D.P.H.

Dr. Bessie M. Playfair (née Davidson), formerly medical officer in charge of the V.D. department at the Royal Free Hospital, London, died in Dundee Royal Infirmary on 21 November. She was 70.

Bessie Morrison Davidson was born on 13 December 1896, and received her medical education at St. Andrews University, graduating M.B., Ch.B. in 1920 and proceeding M.D. three years later. She took the D.P.H. in 1930. After holding several appointments in Scotland, including that of medical officer to the public health department at Dundee, she came to London in the late 1930s to take up an appointment in the venereal diseases department of the Royal Free Hospital, becoming medical officer in charge of the department in 1957. She was also part-time medical officer to the public health department, Deptford, and to the women's welfare centres in North Kensington and Goswell Road, London. In addition, she was medical officer in charge of the special clinic at the Mothers' Hospital in Clapton, which was run by the Salvation Army. She retired in 1960.

M. R. writes: Dr. Playfair came to London from Dundee, where she had been doing antenatal and V.D. work, to be second assistant of the V.D. department at the Royal Free Hospital, and eventually became director of the department. She did valuable work there, being a keen, hard-working Scots-woman, devoted to her work and to her patients. On retirement she went to Plympton, Devon, to be near her son—also in the medical profession—and her grandchildren.

J. S. writes: I first knew Dr. Playfair in 1945 when she was senior assistant in the department of venereology at the Royal Free Hospital. She was also in charge of the special clinic at the Salvation Army's Mothers' Hospital at Clapton and visiting venereologist at Avalon approved school. In 1957 she became the medical officer in charge of the clinic at the Royal Free Hospital, retiring in October 1960. She was an excellent venereologist, and much beloved by her patients, however difficult they might be. Her delightful sense of humour was never at a loss in dealing with difficult situations. For many years she lectured in her special subject to pupil midwives at the Royal College of Midwives.

A. CAMPBELL HILL, M.A., M.B., CH.B.

Dr. A. Campbell Hill, for many years a general practitioner in Kensington, died at his home in Hove on 15 November after a long illness. He was 72.

Alexander Campbell Hill was born in Aberdeen on 17 October 1895. He was educated at Gordon's College and Aberdeen

University, graduating M.A. in 1914. His medical studies were interrupted during the first world war by service with the Gordon Highlanders in France, where he was wounded and sent home. He completed his medical course, graduating M.B., Ch.B. in 1918, and immediately joined the R.A.M.C. and was sent out to Mesopotamia.

After demobilization with the rank of captain he started in general practice in Tottenham, at the same time working at the Prince of Wales' Hospital and the Chelsea Hospital for Women. He obtained a diploma in ophthalmology, a subject in which he was particularly interested, and he worked at the Western Ophthalmic Hospital. In 1931 he moved to Kensington, where he remained until he retired in October 1964.

Campbell Hill belonged to that school of family doctors who, by unremitting devotion to their professional work, earn the whole-hearted trust and affection of their patients. He was an excellent practitioner, and always kept himself fully up to date with medical progress. He was more than usually self-sufficient, taking his own x-rays, doing his own clinical side-room work, and maintaining an exceptional expertise in ophthalmic work. He had a quiet and unassuming manner, appearing never to hurry; but no one was more alert and observant, or quick in an emergency. He had few interests outside his work and his family life. He read widely, and had a well-stocked and orderly mind. Very much a Scot, with the gentle enunciation of his northern origins, he did not seek companionship; but those of us who had the privilege of knowing him and enjoying his kindly friendship are grieved that he did not live longer to enjoy his well-earned retirement.

He married in 1924, and is survived by his wife and one son, who joined him in his practice.—J. D. W. P.

T. E. S. LLOYD, M.A., M.B., B.CHIR.

Dr. T. E. S. Lloyd, one of the senior medical practitioners in Luton, died suddenly at his home on 5 December. He was 59.

Thomas Edmund Seymour ("Tom") Lloyd was born in Luton on 11 October 1908, and was educated at Uppingham and Queens' College, Cambridge. His clinical years were spent at St. George's Hospital, London, where he qualified with the Conjoint diploma in 1932, and held early resident appointments. He proceeded to M.A. in 1934, and graduated M.B., B.Chir. in 1937. He joined his father's practice in Luton in 1935, and remained in general practice until his early retirement in 1966. For more than 30 years he was a popular, kind, diligent, and highly esteemed family doctor. His patients found in him not only a medical adviser but a friend and counsellor. Respected by his medical colleagues he played a leading role in many medical activities. He was chairman of the South Bedfordshire Division of the British Medical Association in 1953, and for many years was a member of the social committee, devoting much of his spare time to B.M.A. affairs. His fondness for children and experience in paediatrics led to his appointment to the children's annexe of the Luton and Dunstable Hospital as assistant physician, and later as clinical assistant.

In addition to his dedication to medicine, Dr. Lloyd had wide interests in many other spheres. He was a most talented musician, and not only did he compose and produce the exceedingly popular cabarets for the annual B.M.A. dinner but also, in a more serious vein, composed church music, one of his compositions being recently played as a hymn in the Luton Parish Church. He was an enthusiastic supporter of local government affairs and served on the Bedfordshire County Council, of which he later became an alderman, for a period of 12 years. One of his lesser known hobbies was collecting wild flowers, and he was most knowledgeable on this subject. His reticence about his own abilities was in keeping with his modest demeanour. During the last five years he had bravely faced two serious illnesses, and it is sad and ironic that shortly before his untimely death he had apparently regained his former health and vigour. It is hard to think of medical practice in Luton without Dr. Lloyd in our midst, and to his widow and five children we extend our very deepest sympathy.—T. P.

K. M. FOSTER, M.R.C.S., L.R.C.P.

Dr. K. M. Foster, formerly in general practice at Ancaster, near Grantham, Lincolnshire, died at his home on 28 October. He was 65.

Kenneth Macdonald Foster, the son of a doctor, was born on 6 February 1902, and was educated at Oundle and Birmingham University, qualifying with the Conjoint diploma in 1927. He set up in practice at Worcester, where he became honorary anaesthetist at the Royal Infirmary. He was a founder member of the Worcester Rugby Football Club and a member of the cricket club. He worked undirigly, often operating late in the evening after a long day in his practice. In 1937 he moved to Ancaster. During the second world war he joined the R.A.M.C., and was medical officer in charge of two hospital ships in the Middle East, and was twice torpedoed. After demobilization with the rank of lieutenant-colonel he returned to his practice at Ancaster, and threw himself into his work and into the life of the village so energetically that by 1947 he had received the first warnings of the heart trouble that was to dog him for the rest of his life.

Kenneth Foster was a born committee man, and at various times served on the Grantham Hospital Management Committee, was secretary of the local medical committee, and vice-chairman of the National Health Service executive council. He was a founder member of the (now Royal) College of General Practitioners, and became at one time chairman of its council, having been a member of council since its inception. In 1959 he paid a visit to Australia as representative of the College, a trip which he found completely fascinating. The College was always one of his most cherished objects. He was provost of the North Midlands faculty of the College, and a member of the selection board of Sheffield University. He was largely responsible for starting the Ancaster branch of the British Legion in 1946, and was founder president, remaining in this office until his partial retirement about eleven years ago. A member of the British Medical Association, he was a

representative at the Annual Representative Meetings in 1930 and 1932, and again in 1951.

Kenneth enjoyed a number of hobbies. He kept a motor-cruiser on the Norfolk Broads; a caravan, in which he toured his beloved Highlands; and a market garden which he ran for some years in Ancaster. He loved shooting, but had to give this up because of his health. He will be missed by many as a kind and understanding personal physician, and by his colleagues, as well as his patients, for his wise and prudent counsel in many crises of their lives.

He leaves a widow and a son and daughter.—F. C. C.

J. W. LINNELL, M.C., M.D., F.R.C.P.

T. A. W. writes: Jack Linnell (obituary, 16 December, p. 686) and his brother Rob were second- and third-year men when I went up to St. John's, Cambridge, in 1902. Jack distinguished himself by getting a first in both the first and second parts of the Natural Science Tripos. When the first world war started he already had his foot firmly planted on the consultant ladder at the London Hospital. On the day after the outbreak of the war, however, he walked into the War Office and offered his services. He was accepted immediately, and was in France within a very short time. He was involved in all the major battles, choosing front-line duties in preference to consultant base duties for which he was well qualified. His bravery was recognized by the award of the Military Cross. For many years after the war he had a flourishing consultant practice in London, and made a special study of thyroid diseases, being a co-founder of the Thyroid Society.

His father was rector of Pavenham, Bedfordshire, and Jack read the lesson in his father's church from his undergraduate days until shortly before his death. He had a beautiful voice, and his reading was so much appreciated that one of his admirers made a recording of one lesson reading. Among his many distinguished friends were authors, including Francis Brett Young, and men in many different walks of life. He took great delight in entertaining them in his home.

B. W. P. writes: When he left his London consultant practice to spend week-ends in his lovely country home at Pavenham—so aptly named the Retreat—Dr. Jack (as he was affectionately called by the villagers) did not always leave his work behind. Local general practitioners were glad to call him in for consultation in their difficult cases, and Dr. Linnell would always give of his best. The time he spent with these patients would reveal to him not only their personal problems but many of their personal problems too. Few went away unhelped, and so he added to his already wide circle of friends. An avid reader, a wise countryman, an inspiring talker, and an even better listener, his Sunday teas gathered in a fascinating cross-section of people who were his friends. Those who are left will sadly miss his radiant personality and his true Christian charity, as well as regret the end of a long line of Linnells in North Bedfordshire.

News and Notes

MEDICO-LEGAL

Blood Tests and Paternity

[FROM OUR LEGAL CORRESPONDENT]

The Court of Appeal has affirmed the order of Mr. Justice Ormrod¹ directing the Official Solicitor to arrange for a child to be blood-grouped to assist in determining the child's paternity (*The Times*, 15 November). Both the child's mother, the mother's former husband, and another possible father had themselves consented to submit to a blood test.

The trial judge in making the order claimed to rely on the jurisdiction of the Court as custodian of the child. He held that that jurisdiction was unaffected by an earlier decision of the Court of Appeal that the Court had no power to order the parties to a suit to undergo blood tests.

The judges of the Court of Appeal were divided about the reasoning employed to support Mr. Justice Ormrod's decision. Lord Denning held that the Court had the power to direct that a blood test be done on a child

in custody proceedings, in a paternity suit, or in a divorce action based on the ground of adultery. But Lord Justice Willmer and Lord Justice Davies, while supporting the judges' decision on the particular facts of the case, held that the jurisdiction existed only in proceedings concerning custody of a child, and not in paternity or divorce suits.

Strong views are held on this subject. While some favour the use of all available forms of evidence, even if compulsion is necessary, others see blood tests as an invasion of personal liberty and a significant step along the road to totalitarianism. But fears that the courts will not know where to draw the line show a distressing lack of confidence. It is perhaps not insignificant that the trial judge in this case is medically qualified.

REFERENCE

¹ *Brit. med. J.*, 1967, 2, 120.

Dangerous Patients

[FROM OUR LEGAL CORRESPONDENT]

Once again concern has been expressed from the Bench at the release from a mental hospital of a man who subsequently committed a crime.

On 31 October at Lincolnshire Assizes a man aged 25 pleaded guilty to manslaughter on the grounds of diminished responsibility in respect of a 65-year-old woman. The woman was stabbed to death two months after the man had discharged himself from a mental hospital.

Replying to an inquiry from the Assize Judge, a prison medical officer said that he understood that the man, who had suffered from mental illness for some time and had been treated at Rampton Hospital, had been considered to have improved sufficiently to be transferred from strict supervision to another hospital, where he had been treated as an informal patient.

An order was made committing the man to Rampton Hospital indefinitely.

EPIDEMIOLOGY

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 2 December (No. 48) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	3	0	0	0		1	0	0	0	
Dysentery ..	505	58	115	11	13	564	55	157	9	6
Encephalitis, acute ..	1	0	0	0		1	0	0	0	
Enteric fever: Typhoid ..	1	1	0	0	1	2	1	0	0	1
Paratyphoid ..	0	0	1B	0	0	0	0	0	0	0
Food-poisoning	114	25	15	0		108	26	173	0	
Infective enteritis or diarrhoea under 2 years				17	61				23	26
Measles*	1,257	48	47	19	78	12,287	2177	467	145	101
Meningococcal infection ..	6	1	0	0		3	0	0	0	
Ophthalmia neonatorum ..	4	1	0	0		6	1	0	0	
Pneumonia† ..	149	17	145	7	2	156	27	73	11	1
Poliomyelitis, acute: Paralytic ..	0	0	0	0		0	0	0	0	
Non-paralytic ..	0	0	0	0		0	0	0	0	
Puerperal fever§	80	32	3	0		91	42	0	0	1
Scarlet fever ..	378	61	25	11	8	503	62	30	15	12
Tuberculosis: Respiratory ..	216	46	43	5		227	59	43	3	
Non-respiratory ..	37	12	5	0		48	8	4	0	
Whooping-cough	922	118	48	14	45	649	104	72	6	13

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	2	0		0		1	0		0	
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	2	2	1	0	12	2	0	0	2
Influenza ..	27	2	1	0	1	12	3	1	1	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	933	156	24	15	5	785	141	17	25	16
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	28	5	2	0	2	51	5	2	0	3
Non-respiratory ..				1	0				0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	302	43	24	5	7	305	53	16	10	19
Deaths (excluding stillbirths)	12,016	1896	658	138	141	11,320	1859	576	148	220
LIVE BIRTHS	14,859	2389	843	243	274	14,709	2450	853	237	393
STILLBIRTHS	233	18	17			237	36	18		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.

PARLIAMENT

Questions in the Commons

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Devaluation and Government
Expenditure

Mr. M. MACMILLAN (Farnham, Con.) asked the Minister of Health on 11 December what additional funds were to be made available to maintain the hospital building programme in view of rising costs as a result of devaluation.

Mr. ROBINSON said that the effect of devaluation on Government expenditure was still under consideration and it was too early to make a statement.

Mr. P. DEAN (Somerset, North, Con.) drew the Minister's attention to the fact that there had already been a cut—last year—of £3m. on local authority capital programmes. Unless more money was made available, he said, the Minister's plans for local authority services would fall even further behind his original plans.

Mr. ROBINSON: "It is not expected that devaluation will result in costs of the local authorities' capital programmes rising by all that much, or, indeed, very rapidly."

Mr. P. HOLLAND (Carlton, Con.) asked for a categorical assurance that rising costs would not cause any delay in the establishment of the university hospital in Nottingham.

Mr. ROBINSON said he was unable to give a categorical assurance while the matter was under consideration.

Dr. J. DUNWOODY (Falmouth and Camborne, Lab.) asked whether, in view of suggestions that there might be cuts in expenditure on the Health Service, the Minister would assure the House that he would resist any efforts to reduce expenditure not only on the hospital building programme but on the Health Service as a whole.

Mr. ROBINSON replied that he would take note of what had been said.

Treatment Centres for Drug Addicts

Mr. J. TILNEY (Wavertree, Con.) asked the Minister of Health what he was doing to expedite the setting up of treatment centres for drug addicts and whether special funds would be granted to regional hospital boards for the purpose.

Mr. ROBINSON informed him that additional facilities for the treatment of heroin addiction were being set up as quickly as possible, mainly in the London area. His department, he said, was in close touch with the hospital authorities. The cost was not expected to be very large in relation to the funds available to regional hospital boards. Consideration was given to any case of difficulty.

He added, in answer to another question, that outside London there was no evidence that current demand for treatment was not being met. This was very largely a London problem.

Mr. M. LIPTON (Brixton, Lab.) asked the Minister if he was aware that facilities in the London area for the treatment of drug addicts were "woefully inadequate." Could the Minister say what they were likely to be within the next few weeks?

Mr. ROBINSON said that he did not accept that they were woefully inadequate. "We have not yet completed the total of facilities which we want to be available for the time when the new arrangements come into operation." At the end of October, he said, there were about 70 patients receiving inpatient treatment and 180 receiving outpatient treatment for heroin addiction in some 40 hospitals.

Mr. W. DEEDES (Ashford, Con.) asked the Home Secretary when he expected to publish the necessary regulations under the Dangerous Drugs Act, 1967.

Mr. J. CALLAGHAN said in a written answer on 11 December that he aimed to make the regulations about notification early in the new year and those about prescribing in the spring. "I hope to consult the medical profession on these regulations shortly."

Doctors Returning from N. America

Mr. A. DAVIDSON (Accrington, Lab.) asked the Minister of Health if he had received the report of the board which recently visited the United States and Canada to interview British doctors who had expressed interest in returning to National Health Service practice.

Mr. ROBINSON: "Yes, and I am considering the best way of making these comments available for publication. The board found a substantial number of British doctors now working in North America anxious to return to this country. Arrangements for the return of some 50 doctors are well advanced and the number ultimately returning is likely to be higher. In the light of the report I shall consider further action to diminish the loss of British doctors through emigration."

Industrial Deafness

Dr. M. P. WINSTANLEY (Cheadle, Lib.) asked the Minister of Social Security on 4 December if she would add industrial deafness to the list of conditions qualifying for benefit under the industrial injuries scheme.

Mr. C. LOUGHLIN, Parliamentary Secretary: Before industrial deafness can be prescribed for industrial injuries benefit purposes the requirements of Section 56 (2) of the National Insurance (Industrial Injuries) Act, 1965, have to be satisfied. The large-scale Government research project into the effects of industrial noise, which is aimed at resolving the issues involved, should be completed in July 1968. Until its results become available the Minister cannot come to any conclusions on the question of prescription.

Pay-bed Revenue

Mr. PAUL DEAN (North Somerset, Con.) asked the Minister of Health on 5 December what was the total revenue from Section 5 beds and Section 4 beds, respectively, in the latest year for which figures were available.

Mr. K. ROBINSON: For the year ended 31 March 1967 the totals for England and Wales were: Section 5, £6,100,375; Section 4, £342,482.

Sale of Quinine

Mr. E. LUARD (Oxford, Lab.) asked the Home Secretary on 12 December whether he had yet taken a decision on the recommendations of the Poisons Board concerning the sale of quinine.

Mr. J. CALLAGHAN, in a written reply, stated: "The Poisons Board has considered representations against its earlier recommendations concerning quinine, and is reporting to me shortly. Further consultations may be necessary, but I wish to bring this matter to a conclusion as soon as possible."

Centralization of Operations

Mr. P. WOLRIGE-GORDON (Aberdeen, East, Con.) asked the Minister of Health on 13 December whether he was satisfied that the increasing centralization of operations, including minor operations, in large hospitals was still in the interests of the rural population.

Mr. ROBINSON: "There is no doubt that the most effective service can be given in large hospitals based on large catchment areas and able to offer a wide range of facilities. My policy is therefore, as stated in Cmnd. 3000, to provide a network of district general hospitals of this type. Planning will, however, take into account the communications problem in scattered rural areas."

Heroin and Cocaine Prescribing

Sir MYER GALPERN (Glasgow, Shettleston, Lab.) asked the Minister of Health on 13 December what inquiries were made by his department before doctors were authorized to prescribe heroin and cocaine to drug addicts; and what was the number authorized to do so.

Mr. ROBINSON: "Pending new regulations under Section 1 of the Dangerous Drugs Act, 1967, all doctors may prescribe heroin and cocaine unless their authority to supply and administer these drugs has been withdrawn by the Home Secretary following conviction for an offence against the Dangerous Drugs Act, 1965, or certain sections of the Customs and Excise Act, 1952. The question of preliminary inquiries therefore does not at present arise."

Pay-beds in Scotland

Mr. W. BAKER (Banff, Con.) asked the Secretary of State for Scotland on 13 December how many pay-beds were currently available in each of the regional hospital board areas of Scotland; and how many were available in 1964 and 1951.

Mr. W. ROSS, Secretary of State, gave the following figures in a written answer:

Region	Available Private Pay-beds in Scotland		
	1951	1964	1967
Northern ...	15	14	14
North-eastern ...	141	67	64
Eastern ...	196	115	116
South-eastern ...	140	50	50
Western ...	435	369	327
Scotland ...	929	615	571

Questions in the Lords

Breathalyser Tests

LORD NUGENT OF GUILDFORD (Con.) asked the Government on 11 December how many drivers had been required to submit to a breath test in connexion with the new drink and driving laws and the reasons why, indicating how many had been involved in accidents; how many were alleged to have committed traffic offences; and how many were suspected of having alcohol in the body.

LORD STONHAM, Minister of State, Home Office, said that during the period 9 to 31 October the police in England and Wales required breath tests under Section 2 of the Road Safety Act, 1967, in 2,724 cases. In 811 cases the person concerned was suspected of having been driving or attempting to drive at the time the vehicle was involved in an accident; in 1,049 cases of having committed a traffic offence while the vehicle was in motion; and in 864 of having alcohol in his body. These categories were not mutually exclusive, however. Chief officers of police believed that nearly all the drivers recorded as having been required to take the test because of a moving traffic offence were also suspected of having been drinking.

LORD NUGENT OF GUILDFORD also asked for the numbers of drivers who had been required to go to a police station for a blood or urine test; and the numbers of such cases in which it had subsequently been discovered that the blood alcohol level was not in excess of the prescribed limit.

LORD STONHAM said that in 927 of the 2,724 cases the driver was required to provide a blood or urine specimen for a laboratory test. Of 729 blood specimens analysed the forensic science laboratories reported 157 as being below the prescribed limit; of 96 urine specimens analysed 11 were reported as being below the equivalent level.

LORD NUGENT OF GUILDFORD asked whether Lord Stonham thought that 157 out of 927 was a "rather high proportion" of breathalyser tests which showed a positive reaction yet on blood or urine tests showed that the accused person was innocent.

LORD STONHAM said he did not agree. "There always must be a time lag," he said, "between a person's taking a breath test which shows a content above the level and his then going to a police station, taking a second breath test, having a doctor summoned, and having a blood test sample taken. During the passage of an hour there can be a fall of from 10 to 20 mg. of alcohol content per

100 ml. of the blood. Then, when the samples of capillary blood are taken there is the chance of some evaporation. Containers may not be firmly fixed down, and there may be some further evaporation. And finally, with the extremely accurate tests taken at the laboratory—several are taken and the results averaged—in cases where the blood content is less than 100 mg. per 100 ml., 6 mg. are deducted, which is three times the normal margin of error, and where it is over 100 mg. per 100 ml. 6% is deducted. So there is a great bias in favour of the person who is being tested. Indeed, after the second test, when it still shows evidence of being above the equivalent level, there is in many cases no prosecution by the police."

Points from Parliament

► The number of staffed beds in the hospital service on 30 June 1967 was 467,907. In 1964 it was 471,961. The number of patients on waiting-lists at inpatient departments was 540,876 on 30 June 1967. In 1964 it was 491,488. (Minister of Health, 4 December.)

MEDICAL NEWS

M.R.C. Appoints New Secretary

Dr. J. A. B. GRAY has been appointed by the Medical Research Council to succeed Sir HAROLD HIMSWORTH, F.R.S., who will retire from being secretary of the Council next year. Dr. Gray is 49, and has been immediate deputy and alternate to Sir Harold since May 1966.

Cox Chair of Anatomy, Oxford

Dr. D. A. T. DICK, lecturer in anatomy at Oxford University, has been appointed to the Cox chair of anatomy. Dr. Dick was educated at Hillhead High School, Glasgow, and Glasgow University, where he graduated M.B. in 1949. After service in the R.A.M.C. he was appointed demonstrator in anatomy at Glasgow in 1953. He moved to Oxford University in 1955, being awarded the degree of D.Phil. in 1958. From 1958 to 1959 he was a Carlsberg-Wellcome Research Fellow at the Carlsberg laboratory, Copenhagen. Returning to England he became Junior Research Fellow of Merton College, Oxford, and was appointed to his present post. He was elected a Fellow of St. Cross College, Oxford, in 1965. His book on *Cell*



(B. J. Harris)

Water was published in 1966. During the academic year 1966-7 he was visiting professor of physiology at Duke University, Durham, North Carolina.

Glasgow Honours Professor

Professor W. F. ANDERSON, who holds the David Cargill Chair of Geriatric Medicine at Glasgow University, has been awarded the St. Mungo Prize. The prize (£1,000 and a medal) is awarded every three years to the person judged to have done most to make Glasgow more beautiful, healthier, or more honoured. Commenting on the award, Professor Anderson said it was a tribute to the voluntary workers among the elderly.

1966 Census

Nearly a third of Great Britain's 53 million population lives in south-east England, according to the 10% sample census of England, Wales, and Scotland taken in 1966. The summary results were published this week (*Sample Census 1966, Great Britain, Summary Tables*, 1967, H.M.S.O., 32s. 6d. net). People born outside the British Isles numbered 1.9 million (compared with 1.5 million in 1961), 1 million in the Commonwealth and 0.9 million outside it. Household amenities were found to have improved since 1961. In the present census the proportions of households with the stated amenities were as follows (with 1961 figures in parentheses): exclusive use of own hot water 86% (76%),



Mr. R. V. Cooke, President of the B.M.A., in Helsinki with Dr. Väinö Pensala (right), Secretary of the Finnish Medical Association. Mr. Cooke addressed Finnish doctors at the opening session, on 19 November, of the F.M.A.'s Medical Week.

exclusive use of a fixed bath 80% (73%), and exclusive use of an inside water-closet 77% (1961 figure not available). Of the 17 million households in Great Britain 7½ million (45%) had at least one car, and 1 million (6%) had two or more cars.

Renal Transplantation under N.H.S.

The Minister of Health, Mr. KENNETH ROBINSON, announced in a written answer on 14 December that an Advisory Committee on Renal Transplantation had been appointed with the following terms of reference:

"To advise the Minister of Health and the Secretary of State for Scotland on the development of renal transplantation under the National Health Service, and in particular to examine and advise upon any proposals to establish renal transplantation units at new centres."

The members of the committee are: Professor Sir HEDLEY ATKINS, P.R.C.S. (chairman), Professor J. R. BATCHELOR, Professor D. A. K. BLACK, Professor R. Y. CALNE, Professor H. E. DE WARDENER, Professor A. W. KAY, Professor R. MILNES WALKER, Professor W. S. PEART, Professor R. SHACKMAN, and Professor M. F. A. WOODRUFF.

Cancer Studies in Birmingham

The Birmingham branch of the British Empire Cancer Campaign has reviewed its arrangements with the University of Birmingham for the conduct of research in the B.E.C.C. laboratories adjacent to the Queen Elizabeth Hospital and the Medical School. The branch will put an annual sum of money at the disposal of the university for the staffing and maintenance of the laboratories, which, subject to the approval by the branch of the general research policy to be followed, will then be administered by the university.

Instead of being, as hitherto, under the direction of the professor of pathology as honorary director, the laboratories will be in the charge of a full-time director, to be appointed. The university will shortly advertise a new chair of cancer studies, combined with the directorship. The intimate association of the laboratories with the department of pathology will be replaced by a broader association with the division of pathological studies in the medical school (comprising morbid anatomy, experimental pathology, virology, and other subjects). No firm decision has been taken on the area of cancer studies into which the laboratories will be expected to move: the faculty has in mind an approach through molecular biology, through immunology, through genetics, or through cell experimentation, but other approaches are not excluded.

British Association of Otolaryngologists

At the annual general meeting of the British Association of Otolaryngologists on 1 December the following were elected officers of the association for 1967-8: *president*, Mr. J. ANGELL JAMES; *vice-president*, Mr. G. H. BATEMAN; *honorary treasurer*, Mr. IAN G. ROBIN; *honorary secretary*, Mr. D. RANGER.

M.I.A. Dinner

The Medical Insurance Agency held a dinner in the Great Hall at B.M.A. House on 14 December to celebrate the Agency's diamond jubilee (see p. 696). Mr. A. M. A. MOORE, F.R.C.S., chairman of the M.I.A., presided, and the guests included representatives of the medical charities it supports and of the insurance companies with which it deals. Dr. RONALD GIBSON, chairman of the

B.M.A. Council, proposed the health of the M.I.A., Mr. MOORE responding. Mr. N. V. P. SEAL, the Agency's general manager, toasted the guests, and Mr. G. H. BATEMAN, F.R.C.S., honorary treasurer of the Royal Medical Benevolent Fund, replied. Between and after the speeches there were carols by the Consortium Medicum from Guy's Hospital.

Anniversary Exhibition

Charing Cross Hospital is to celebrate its 150th anniversary next year by holding a special week beginning 13 May. An exhibition illustrating past history is now being arranged. Readers who have photographs, records, or other items of interest and are willing to lend them for the period of the exhibition are invited to communicate with the House Governor.

Guild of Medical Bell Ringers

At the annual meeting of the Guild of Medical Bell Ringers, held in London on 18 November, the following were elected officers: *president*, Dr. J. B. WILLIAMSON; *master*, Dr. P. A. F. CHALK; *secretary*, Dr. D. L. GULLICK.

Services for the Disabled in Edinburgh

The Edinburgh Committee for the Co-ordination of Services for the Disabled set up in 1964 now represents some 70 voluntary, statutory, and professional organizations working with the disabled in the city. A notable event last year was the showing of the committee's film, "Working Together," at the Congress in Wiesbaden of the International Society for the Rehabilitation of the Disabled. Another was the opening of a

Answers to Quiz (p. 740)

1. (a) An allergic alveolitis due to sensitivity to antigens in pigeon droppings. (b) Pulmonary aspergillosis acquired from the habit of French pigeon breeders of transferring grain directly from their mouths to the bird's mouth.

2. (a) A Dutch religious sect in Pennsylvania and Ohio, who live as far as possible uninfluenced by the modern world. Because of this isolation and intermarriage they provide valuable genetic information. (b) Abnormal sensitivity, usually in men, to unexpected noise or touch, which results in an uncontrollable motor reaction of jumping or hitting. (c) A form of pica in pregnant women, who develop a compulsive craving for clay. (d) Persons addicted to tomatoes, carrots, and other foods containing yellow and red pigments.

3. (a) William Marsden, 1796-1867. (b) Jean Baptiste Charcot, 1867-1936. (c) Gustav Giemsa, 1867-1948. (d) Marie Curie, 1867-1934. (e) Lord Lister, 1827-1912. (f) T. Lauder Brunton, 1844-1916.

4. (A) Tenovus Institute at Cardiff. (B) St. Christopher's Hospice, Sydenham. (C) Lister, Royal College of Surgeons. (D) Edward Trudeau; "Guérir quelquefois, soulager souvent, consoler toujours." (E) It has been slit to allow disinfection against the plague.

5. (a) Loss of the normal dorsal curve of the spine, giving the impression of cardiac enlargement and systolic murmurs. "Pseudo heart disease." (b) Progressive, painful spasm of muscles of unknown cause. (c) Attacks of somnolence occurring in excessively obese subjects, possibly due to carbon dioxide narcosis. Typified by Mr. Wardle's boy Joe in the *Pickwick Papers*. (d) Cor pulmonale, often resulting in sudden death.

6. (a) A form of mental defect associated with epilepsy, microcephaly, and uncontrollable laughter. (b) Tremor of the head due to a cyst of the third ventricle. (c) Facies associated with idiopathic hypercalcaemia, sometimes accompanied by aortic stenosis. (d) Babies, usually premature, covered at birth by a shiny membrane which eventually cracks and peels. (e) Certain inborn errors of amino-acid and fatty acid metabolism, such as maple syrup urine disease, the oasthouse syndrome, and disorders of methionine metabolism.

7. (a) St. Chad. (b) St. Apollonia—martyred by having her teeth pulled out and jaws broken before being burnt. (c) St. Agatha. (d) St. Wolfgang. (e) SS. Cosmos and Damian. (f) St. Valentine. (g) St. Luke.

8. They all cause an allergic alveolitis, of which farmer's lung is the best known. Puff balls (*lycoperdon*) are used as a household remedy for stopping nosebleeds, and the pulmonary disease has been called *lycoperdonosis*.

9. (a) Boston Inter-Hospital Liver Group. (b) Respiratory distress syndrome. (c) Serenity, tranquillity, and peace. The hallucinogen more powerful than L.S.D. (d) Endocardial fibro-elastosis. (e) Dynamic dysentery device—an electronic weapon that emits a low vibration which causes loss of control of bowel action, thought to be of potential value in riot control.

10. (a) *Tristram Shandy*—Laurence Sterne. (b) *The Surgeon's Daughter*—Sir Walter Scott. (c) *Le Médecin malgré Lui*—Molière. (d) *The Young Physician*—Francis Brett Young. (e) *The Citadel*—A. J. Cronin.

11. (a) Thrombophlebitis migrans—Armand Trousseau, 1801-1867. (b) Salaam spasms, a variety of infantile spasms—W. J. West, 1841. (c) Christmas disease, Hartnup disease.

recreational and social centre at Cameron House, the property of the Edinburgh University Settlement. In its report for the year the committee provides an analysis of 5,000 cases of disability on the central register, an increase of 856 on the figure for the previous year.

People in the News

► Dr. F. AVERY JONES is to succeed Dr. G. F. ABERCROMBIE, who retires from the chairmanship of the Emergency Bed Service Committee of the King's Fund at the end of the year.

► Professor G. F. MILLS has been appointed to the chair in biochemistry at the medical school, Auckland University.

News in Brief

During 1967 the Variety Club of Great Britain has raised £642,000 for children's charities. Among projects supported are centres for medical research.

Grants and Awards

Professor D. F. N. HARRISON, professor of laryngology and otology, London University, has received a grant of £12,391 from the Medical Research Council to carry out an investigation over three years into changes in the inner ear due to administration of ototoxic and cytotoxic drugs.

The department of psychiatry of Liverpool University has been awarded a grant of £13,484 by the Medical Research Council for a clinical investigation of acute schizophrenia. The grant will be held jointly by Professor C. A. CLARKE, professor of medicine, and Professor F. J. FISH, professor of psychiatry; and Dr. B. K. BROOKER, lecturer in the department of psychiatry, will conduct the investigation.

Coming Events

North Staffordshire Medical Institute and British Occupational Hygiene Society.—International symposium on health conditions in the ceramic industry, 27–29 March 1968, Stoke-on-Trent.

Cambridge University School of Clinical Research and Postgraduate Medical Teaching.—Meeting, "Growing Points in Paediatrics," 8–10 April 1968. Fee £7 7s. Details

and registration forms from the Secretary, the Medical School, Tennis Court Road, Cambridge.

Royal Society of Health.—Health Congress, 29 April to 3 May 1968, Eastbourne.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Thursday, 28 December

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m. Mr. P. Martin: Raynaud's Phenomenon.

Friday, 29 December

ROYAL POSTGRADUATE MEDICAL SCHOOL.—10.15 a.m. Professor R. S. Shackman, Mr. J. R. Batchelor, Professor W. S. Peart, Mr. W. J. Dempster: Profile on Renal Transplantation.

Universities and Colleges

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council on 14 December, with Sir Hedley Atkins, president, in the chair, the election of Professor Sir Robert Macintosh, of Oxford, to the Honorary Fellowship in the Faculty of Anaesthetists was reported.

The Mitchiner Medal for 1963 was awarded to Lieutenant-Colonel W. C. Moffat.

Mr. N. L. Rowe was appointed Webb-Johnson Lecturer for the period 1967–9.

Professor I. R. H. Kramer was appointed the Charles Tomes Lecturer for 1969.

The Hallett Prize for 1965 was presented to Dr. N. V. Perera, of the University of Ceylon.

The Begley Prize was presented to Dr. M. M. Bowen, of St. Bartholomew's Hospital Medical College.

The award of the Evelyn Sprawson Prize to Mr. J. B. Phillips was reported.

A Diploma of Membership was granted to W. P. Garson.

A Licence in Dental Surgery was granted to R. H. J. Milliner.

After the meeting the Cecil Joll Lecture was delivered by Professor R. Y. Calne, on "The present position and future prospects of Organ Transplantation."

Diplomas of Fellowship were granted to the following candidates:

J. W. Carter, D. T. Goradia, A. B. J. Miller-Williams, J. C. D. Plant, M. J. Hunter, E. R. Norton, N. C. Roles, D. Booth, A. C. Bird, R. C.

Lallemand, L.-R. Priault, M. S. Bell, J. P. Pryor, J. D. Carr, D. H. Gordon, E. R. Li. Jones, N. W. Harrison, J. M. Kelly, K. M. Paghera, A. N. Nicolaides, A. C. Warr, A. G. Zahit, F. D. H. Birkett, J. J. Kanski, J. A. H. Bootes, C. F. Ruoss, S. J. Karan, J. R. Salaman, C. B. T. Adams, D. G. Stock, A. Mannan, S. J. Lawrence, M. M. Akl, R. C. Buchanan, M. M. Ali, J. D. C. Anderson, K. K. Mukhopadhyay, T. K. Ghoshal, A. S. Chhabra, C. C. Diddott, J. T. G. Renney, M. K. Sen, K. L. Sethi, S. A. A. Gilani, A. O. Robertson, M. F. Wazna, H.-U. Yaqin, S. N. Barik, H. K. Deb, M. A. M. El Mahdi, P. S. Hunter, J. D. Johnston, S. R. Nowbar, M. K. Shah, D. R. Chhatre, J. T. Cummins, M. M. El-Sheikh, R. F. Evans, J. C. McGrand, G. Mah, L. Singh, N. F. Angley, R. P. Ellis, M. H. G. Hennein, M. T. Husain, R. Iyengar, E. A. Jangda, J. C. O'Sullivan, L. L. W. Peters, C. Savarirayan, R. A. N. Welham, P. D. G. Wilson, S. T. Al-Mufti, G. E. D. Brown, P. I. Condon, D. J. du Temple, A. M. El-Kashan, G. H. Foster, K. B. Jannarkar, I. M. Kamal, P. E. Kiely, T. D. Kretzmar, G. M. Macdonald, M. G. Machayya, J. L. Nicholas, C. C. Rigby, J. S. Salis, M. A. Shanbhag, N. D. Sherson, A. C. Talwalker, M. Thambirajah, D. W. Walters, M. A. Amin, P. K. Basu, G. A. Bunch, R. K. Carruthers, T. F. Chow, B. Cruickshanks, A. Cushman, R. L. W. Fink, S. Hayat, R. Husain, D. Li. Jones, R. O. Jones, H. Kabir, M. A. Legge, Judith McKenzie, P. W. A. Mansell, H. P. Marshall, B. A. Martin, D. D. Meikle, R. Naim-Ur, J. R. Roke, H. K. Roy, K. M. Silva, H. D. Smith, J. A. Spencer, A. R. Undre, B. W. Yeo, G. Zipser, M. Ahmad, P. M. Atkinson, D. Bardsley, D. W. G. Budd, B. G. Clendinning, A. G. A. Cowie, R. Donovan, J. M. Fox, J. W. Hamilton, R. H. Jago, J. F. Kelly, J. Lendrum, P. C. McCarthy, K. A. A. Osting, D. J. Parker, S. A. H. Rizvi, R. J. Shearer, S. R. Sillar, D. G. Thomas, D. C. Williams, O. O. Bassey, C. D. Collins, W. T. Davies, M. A. Edgar, M. J. Glasson, R. F. Jones, R. F. X. Noronha, J. B. North, K. D. Okey, B. Prakash, A. Segal, P. R. Singhi, C. R. Williams.

Correction

The Worshipful Society of Apothecaries of London (2 December, p. 540). The name of Mr. G. T. Willoughby Cashell was omitted from the caption of the picture of the Court in Session. Mr. Cashell was seated between Sir John Richardson and Dr. Peter Bishop.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY 30 DECEMBER 1967

Pointers

Neurological Damage in Parturition: Minor damage is not necessarily detected by classical neurological examination. Standardized quantitative observations are suggested to reveal handicaps and facilitate rearing these infants (p. 763). Leader at p. 761.

Obstetric Analgesia: Assessment by anaesthetist, patient, and midwife indicate that 0.35% methoxyflurane is suitable for intermittent self-administration during labour (p. 767).

Oral Contraceptives: Undesirable menstrual side-effects of microdoses of chlormadinone diminished by addition of oral oestrogens (p. 771).

Pneumoconiosis: Gas transfer defect of lungs found in 10 out of 16 patients whose radiopacities were of pure pinhead type, but in none of 11 men whose opacities were micronodular in type (p. 772).

Febrile Illness in General Practice: E.C.H.O. virus type 3 incriminated as causative agent in a geographical epidemic, which mainly affected children (p. 774).

Intermittent Claudication: Calf muscle denervation gave encouraging results in patients with inoperable femoropopliteal occlusions (p. 776).

Gynaecomastia: Observed in 6 patients with chronic renal failure during early stages of regular dialysis treatment (p. 779).

Pyloric Stenosis and Blood Groups: Lowered incidence of group A demonstrated in 303 patients with infantile hypertrophic pyloric stenosis. Salivary ABH secretor status showed no significant difference from controls (p. 781).

Case Reports: Ureterosigmoidostomy and neoplasia (p. 783); Nail-gun fatality (p. 784).

Congenital Heart Disease: Clinicopathological Conference at Royal Postgraduate Medical School (p. 785).

Upper Alimentary Bleeding: Surgical management (p. 790).

School Health Service: Trial of using general practitioners (p. 797).

Health Centres: Conference of doctors working in them (p. 800). Leader at p. 759.

Nursing Services in General Practice: Letters (p. 803).

Requests for Abortion: Said to be increasing (p. 802).

C.C.H.M.S.: Debates Welsh area health board plan (*Supplement*, p. 89).

Board of Science and Medical Education: Chairman of Council's proposals (*Supplement*, p. 92).

Public Health Pay Dispute: Agreement reached (*Supplement*, p. 94).

Cardiac Transplantation

On 3 December Professor Christian Barnard and his colleagues replaced the heart of 55-year-old Louis Washkansky with that of a 25-year-old girl mortally injured in a road accident. On 21 December Washkansky died, apparently from pneumonia. It is worth noting that the rejection process itself can cause pulmonary disease, but according to press reports the disease was infective in the present case. After a necropsy showing that death was due to pneumonia Professor Barnard was reported¹ as saying that there was no clinical evidence to suggest that rejection played a part in the death, and there was no evidence for human heart transplants to be discontinued. Despite its sad conclusion this was an outstanding surgical feat by the staff of the Groote Schuur Hospital at Cape Town. It was the application to man of a technique which had before been tested in animals and was a courageous operation that was bound to be attempted sooner or later.

How do the problems differ from those of the transplantation of kidneys? Successful matching of the tissues of the donor and the recipient is much more crucial for transplantation of the heart than of the kidney. The kidney is a complex structure, but its function is secretory and a fraction of its potential function will suffice for life. The heart is a unique organ; its vital activity must not falter for more than minutes and there is no artificial substitute which can preserve life for more than a matter of hours. Ischaemic damage may be incurred during transfer of a kidney, but recovery of such tubular necrosis may be confidently awaited. Meanwhile the artificial kidney takes over. A rejection crisis may be surmounted in the same way. Even total failure of function leaves the patient little worse off, for he can return to the intermittent dialysis which had preserved his life before operation, and further kidney grafts can be attempted later.

The heart is a richly innervated organ, but transplantation brings about complete extrinsic autonomic denervation, resulting in near total loss of the myocardial stores of catecholamines.² If the heart is removed from a dog and then replaced (autotransplantation) this denervation may be only temporary, and signs of reinnervation may be found as early as 26 days after reimplantation. It has been shown that after one to three years the response to stimulation of the vagosympathetic trunk is normal, though the actual number of intact neural connexions is probably small if judged by the still depleted catecholamine content of the various chambers of the heart.³ Reinnervation of hearts transplanted from one animal to another seems far less likely, and so the physiological consequences of chronic denervation of the heart have been extensively studied. The exercise tolerance has been shown to be nearly normal in animals with hearts surgically denervated by Cooper's technique,⁴ and W. M. Daggett and his colleagues found that the work capacity of dog hearts 6 to 12 weeks after autotransplantation was remarkably close to that of normal hearts.⁵

Unlike the normal hearts which were studied, autotransplanted hearts utilized exogenous circulating catecholamines. This may be an important adaptation to cardiac denervation, for Daggett's team found no alteration in myocardial contractility after transplantation, though the weight of the heart increased, suggesting that its efficiency was reduced. The retention of fluid and the rise in blood volume which occur early after autotransplantation⁶ are unexplained by these studies. This pseudo-heart-failure may be due to the loss of afferent vagal impulses from atrial stretch receptors and is easily countered by diuretics. Daggett has concluded that the autotransplanted and denervated heart achieves a similar level of performance to the normal heart and that total denervation of the heart, with its concomitant depletion of myocardial stores of catecholamine, does not preclude successful transplantation. Thus the main barrier to successful transplantation of the heart in man seems to be the question of rejection. Further advances will depend on either better immunosuppressive drugs or more probably the perfection of tissue-matching techniques, so that donor can be exactly matched to recipient.

Over the past two years leucocyte antigen groups have gradually been defined. Antisera obtained from multiparous women, patients who have had multiple transfusions, and recipients of skin and kidney allografts have been characterized and can be used to test for leucocyte-group compatibility.⁷⁻⁹ So far no prospective studies have been reported, but a retrospective study of donors and recipients after renal transplantation between relatives has recently been carried out by F. T. Rapaport and his colleagues and has shown that there is a considerable correlation between good leucocyte-group compatibility and success of the graft.¹⁰ The success of some kidney grafts despite apparent leucocyte incompatibility, and rejection of others despite apparent compatibility, underlines the fact that tissue typing is still in its infancy, but even at this stage the success of kidney transplants should become more predictable.

If tissue antigens do have some degree of overlap cardiac homotransplantation (from one person to another) will certainly be practicable. Furthermore, tissue compatibility may exist between different species, so that heterotransplants (between species) may become possible. This would solve some of the ethical and logistical obstacles to homotransplantation that have been discussed.

The diagnosis of death first became a problem with the use of elective cardiac arrest during cardiopulmonary bypass, for until then the issue had been simple: a patient was dead when the heart stopped. But it is the brain which determines whether life continues. If cerebral function has been destroyed the patient is really dead, and the artificial preservation of tissue integrity by a machine does not alter the fact. The difficulties stem from the need to know for certain

whether cerebral damage is irreversible. Relatives of patients with irreparable brain damage have to give permission for organs to be removed, and it would be understandable if some at a time of great distress were hesitant over a request to remove a heart. The coroner's permission is also needed. The short period for which organs can be maintained in good condition outside the body greatly limits the possible scope of large-scale transplant surgery at present, but soon it will be possible to keep organs viable for up to 48 hours after removal, and organ banks will eventually be developed. Until that time there will inevitably be many more potential recipients than there are organs available. But during the next decade cardiac transplantation will probably begin to save lives.

Disease from Monkeys

Wild animals, particularly primates, imported either for sale as pets or for use in laboratories may introduce a wide variety of infections into Britain. A joint committee of the British Veterinary and British Medical Associations reviewed the problem in 1962, and a leading article in these columns¹ drew attention to the problem. The committee thought that legislation and proper quarantine arrangements to control the importation of wild animals (particularly primates) were essential, but that it would be necessary to collect more evidence of the hazard before a strong case could be made for official action probably requiring substantial public expenditure.

Occasional cases of herpes virus B encephalomyelitis due to monkey bites continue to be reported.² An imported monkey recently developed rabies in a laboratory animal house.³ But lately serious outbreaks of infection in Marburg, Frankfurt, and Belgrade have at last focused more official attention on this problem in many countries. Vervet monkeys (*Cercopithecus aethiops*) were imported from Uganda through London, and the shipment was divided between laboratories in Marburg and Frankfurt. An acute febrile illness with rash, varying degrees of lung and liver damage, gastrointestinal disorders, and a tendency to bleeding associated with thrombocytopenia occurred in about 28 persons who had had contact with blood or tissue of these monkeys, and 7 of them died. There were a number of secondary cases in hospital staff with some sort of contact with the blood of patients. At about the same time similar monkeys were imported (some through London) to Belgrade. There two cases of the disease occurred: one a veterinarian who carried out necropsies on monkeys which had died in quarantine, the other his wife. A full report of the disease is to be published in *Deutsche Medizinische Wochenschrift*.⁴

Transmission in man seems to be by contact with infected blood or tissue, and a limited experiment⁵ suggests that the agent may be able to pass through the skin. Thus on present evidence general spread of this disease from man to man is unlikely, but the risk of infection must be constantly borne in mind by those who work (or play) with recently imported monkeys and by medical and nursing staffs treating febrile illnesses in such people. In obscure febrile illnesses and especially in cases of encephalitis questions about contact with animals (especially monkeys) should always be asked.

Material from the German cases was sent to laboratories in various parts of the world, and the major investigation of the human material was carried out at the Microbiological Research Establishment, Porton, Salisbury, which has the best

¹ *The Times*, 19 December 1967.

² Cooper, T., Willman, V. L., Jellinek, M., and Haerlon, C. R., *Science*, 1962, 138, 40.

³ Peiss, C. N., Cooper, T., Willman, V. L., and Randall, W. C., *Circulation Res.*, 1966, 19, 153.

⁴ Donald, D. E., and Shepherd, J. T., *Amer. J. Physiol.*, 1963, 205, 393.

⁵ Daggett, W. M., Willman, V. L., Cooper, T., and Haerlon, C. R., *Circulation*, 1967, 35, Suppl. 1, 96.

⁶ Willman, V. L., Merjavy, J. P., Pennell, R., and Haerlon, C. R., *Ann. Surg.*, 1967, 166, 513.

⁷ Dausset, J., Ivanyi, P., and Ivanyi, D., in *Histocompatibility Testing*, Munksgaard, Copenhagen, 1965, p. 51.

⁸ Rapaport, F. T., Lawrence, H. S., Converse, J. M., and Mulholland, J. H., *Ann. N.Y. Acad. Sci.*, 1964, 120, 280.

⁹ Van Rood, J. J., Van Leeuwen, A., Schippers, A. M. J., Voors, W. H., Frederiks, E., Balmer, H., and Eernisse, J. G., in *Histocompatibility Testing*, Munksgaard, Copenhagen, 1965, p. 37.

¹⁰ Rapaport, F. T., Dausset, J., Hamburger, J., Huone, D. M., Kano, K., Melville-Williams, G., and Milgrom, F., *Ann. Surg.*, 1967, 166, 596.

facilities in Europe for safe research on dangerous infectious agents. A preliminary account of this work⁵ shows that the agent was successfully transmitted to guinea-pigs, to monkeys of two species, to hamsters, and to cell cultures of several types. In guinea-pigs and monkeys the disease resembled the human illness—severe damage to the spleen, liver, and lungs, and a marked tendency to bleeding. The general picture is probably of acute disseminated intravascular coagulation,⁶ which has a variety of trigger mechanisms, including infectious diseases. In the livers of guinea-pigs large numbers of intracytoplasmic inclusion bodies with the staining properties of rickettsias have been seen in parenchymal cells. Filtration experiments suggest that the agent is about the size of a rickettsia or a bedsonia, but surprisingly the disease is not ameliorated (in guinea-pigs or apparently in man) by chloramphenicol or tetracycline, and it grows in cell cultures in the presence of penicillin and streptomycin. Collaborating laboratories in Britain, Germany, the United States, Senegal, South Africa, and elsewhere have failed to find an antigenic relationship between this organism and about 200 viruses, several rickettsias and bedsonias, toxoplasma, or other micro-organisms. Electron-microscopy in both Britain and Germany shows that the organism is elongated and pleomorphic, but its precise nature has not yet been elucidated.

These outbreaks occasioned much surprise—but why? Scientists knowledgeable about the zoonoses have been predicting their occurrence for many years. Over 60 adventitious viruses have been recovered from monkeys used in laboratories, and only chance has dictated that the majority were of low or no pathogenicity for man. Moreover, the risk has been steadily increasing. Not only has the rate of importation risen rapidly but monkeys are being more and more widely used by research workers (other than microbiologists) who often know little about the risks, among them physiologists, psychologists, pharmacologists, and experimental surgeons. Furthermore, as the demand for monkeys increases, the trappers are driven further and further afield to satisfy it, and monkeys have to be obtained from areas where they have little if any contact with man and where medical services capable of recognizing the occurrence of sporadic and unusual infectious diseases are absent. Clearly, therefore, quarantine with careful veterinary and microbiological observation of imported monkeys should be enforced before they are released for general use except to vaccine manufacturers and some of the large organizations such as the Medical Research Council with experienced laboratory staff, which can and do perform this task for themselves. Most of the smaller laboratories do not and probably cannot have adequate facilities and staff, and it should be recognized that it will be expensive to provide central facilities on an adequate scale with the high standard of accommodation necessary for quarantine and the highly trained staff essential to run it. Until this is done, every imported animal must be handled as if it may be harbouring a dangerous infection. Potentially most dangerous of all are the monkeys, which can at present be sold as pets within a very short time of arrival, and though their quarantine can probably be achieved cheaply the provision of adequate legislation will be complex. There is also

a need for much better holding accommodation and supervision at airports and other points of import and trans-shipment, and voluntary organizations such as the R.S.P.C.A. cannot be expected to provide these. In transit at London Airport the vervet monkeys for Germany had some contact with other monkeys (one of them sick), with alligators, and with a large number of species of bird. Cross-infection under such conditions is an obvious possibility and has been suggested as the mode of infection of the vervets.

Perhaps the most important implications of the monkey disease itself are in the manufacture of vaccines, as it seems that kidney cultures from infected monkeys are likely to contain the agent. Clearly there is a paramount need (now being met) for sensitive tests to ensure that live vaccines do not contain it. But the broader question remains whether it is really sensible to make vaccines from the tissues of wild animals. Surely a thoroughly tested cell culture system would be safer. Tested diploid cells (not from neoplasms) will now receive serious consideration as substrates for vaccine production, though very careful control will be required to detect possible malignant changes and such infections as hepatitis viruses in them. The present tendency is to think mainly of human diploids, but the story of how scrapie was spread among sheep by using an inactivated sheep brain vaccine,^{7,8} the fact that slow viruses show considerable host specificity, and the lack of methods for detecting human slow viruses suggest that diploids of a species far removed from man may be safest of all.

Health Centre Explosion

In the past many doctors were attracted to general practice because it offered them freedom to organize their work in their own way. Today, owing to political and social pressures, among other things, this freedom has become relatively limited. Hence young doctors are reluctant to think of general practice as a satisfactory career unless it offers them job-satisfaction of another kind—that of having the means to practise the scientific medicine they were taught. Many measures are now helping to provide these means, among them an increasing formation of group practices, the use of appointment systems and ancillary workers, and the recognition of the need for training—both vocational and continuing—for general practice. Another measure is practice at a health centre, and, as was pointed out at a recent conference at the Ministry of Health of doctors working in health centres (see p. 800), it seems that we are on the verge of a health-centre explosion. At present no fewer than 180 are being built or are at an advanced stage of planning.

One of the principal fears has always been that a standardized form of health-centre practice would be imposed on doctors working in them. There is no evidence that this has happened. Speakers at the conference emphasized the importance of flexibility and of asking the help of the doctors concerned before final plans for a centre are drawn up. Indeed, every health centre built is still in the nature of an experiment whose results may answer many of the remaining questions. What is the optimum size of a centre? Should doctors work as one large team or as several small groups? How large should the auxiliary team be, and how can it be used to save the doctors' time without impairing the essential doctor-patient relationship? Should nurses be used for diagnosing and treating simple ailments?

⁵ *Brit. med. J.*, 1962, 1, 1750.

⁶ *Ibid.*, 1966, 1, 878.

⁷ Boulger, L. R., *Lancet*, 1966, 1, 941.

⁸ Martini, G. A., *ibid.*, 1967, 2, 1363.

⁹ Smith, C. E. G., Simpson, D. I. H., Bowen, E. T. W., and Zlotnik, I., *Lancet*, 1967, 2, 1119.

¹⁰ McKay, D. G., and Margaretten, W., *Arch. intern. Med.*, 1967, 120, 129.

¹¹ Greig, J. R., *J. comp. Path.*, 1950, 60, 263.

¹² Wilson, D. R., Ruth, D., and Smith, W., *ibid.*, 1950, 60, 267.

Fortunately the principles of flexibility and experiment are being applied in practice. One speaker at the conference described a one-man rural centre, and another plans for one for 16 doctors. At one relatively remote centre there are good diagnostic facilities and consultant sessions, and at another neither of these is provided, since the district hospital is round the corner. At one centre some patients are initially seen by a nurse, and at another the doctors make it a rule to speak personally to every patient who telephones. At yet another centre a pilot scheme for reducing visiting by bringing the patients to the centre is to be tried. It is clear, however, that even more flexibility is needed. Many speakers complained of sudden large increases in their bills for maintenance and ancillary help, often without notice, and the boundary between local-authority and general-practitioner services in some centres is still too rigid.

Health centres are not the only means of providing facilities for good medical practice. There are a few privately built group-practice centres which look and work as well as any health centre. Nor do health centres necessarily have to be paid for out of public funds—that at Witney, near Oxford, was built with private money. Nevertheless, in future most of them are likely to be financed by the State in one way or another. For this reason alone it is important that experiments should continue. More medical students should be able to see medical practice at health centres. In particular at least one centre should be built adjacent to a district general hospital. Family doctors working there should have access to the hospital diagnostic services and to beds. And they would meet their consultant colleagues on equal terms.

Intra-arterial Chemotherapy for Recurrent Neoplasms

Systemic administration of cytotoxic agents is the most valuable form of treatment for the leukaemias and widespread lymphomas, and useful remissions are regularly achieved. In chorion-carcinoma many reports of cure are now on record. For most solid tumours, however, systemic chemotherapy is of limited value because the local action is overshadowed by its toxic effects, especially on the bone marrow and gastrointestinal epithelium.

C. T. Klopp and his colleagues¹ in 1950 pioneered the use of intra-arterial injection to localize the effects of cytotoxic agents in patients with cancer confined to one region. Almost a decade later O. Creech² and R. D. Sullivan³ and their colleagues elaborated the original simple injection technique along lines predicted by Klopp. They achieved intensification of the local effect combined with limitation of the general toxicity by two methods: either the affected region was perfused through an extracorporeal circulation, or when simple intra-arterial infusion of the drug was used an antagonist was given in the systemic circulation to block toxic effects on normal tissues.

All these workers reported much better regression of disease than that obtained with cytotoxic agents given by the conventional systemic route. Understandably, widespread interest and enthusiasm were engendered and a spate of published work followed. The early impetus is now subsiding and it is becoming possible to view the merits of intra-arterial chemotherapy in truer perspective.

Regional extracorporeal perfusion using a pump-oxygenator has achieved an established place in the management of

uncontrolled malignant melanoma confined to a limb.^{4,5} Worthwhile palliation and sometimes prolonged freedom from signs of local disease can be obtained, so that major amputation is seldom required; the complication rate is acceptably low.

Simple intra-arterial injection or infusion with or without a systemic antidote has been used most often in the treatment of cancer in the head and neck, though it is also of some value in the treatment of pelvic⁶ and hepatic⁷ tumours. In 1962 G. Westbury and his colleagues⁸ reported the results of treatment with intra-arterial methotrexate and intramuscular citrovorum factor in 26 patients with cancer of the head and neck which had recurred after surgery or radiotherapy or both. They noted only one worthwhile response and stressed the considerable morbidity and mortality associated with the method, and suggested that the sclerosing effect of previous irradiation on the vascular bed had impeded access of the agent to the tumour cells. H. J. Espiner and his co-workers,⁹ reporting their own experience, observed the best results in patients in whom chemotherapy was the primary form of treatment; the worst results were in those receiving chemotherapy soon after radiotherapy had failed. Others have since drawn similar conclusions.¹⁰ More recently S. Tindel¹¹ has described a trial of intra-arterial infusion in patients with recurrence of neoplasms after surgery or radiotherapy or both. More than half had tumours of the head and neck; the remainder suffered from lesions of the bowel, bladder, cervix, or liver. He concluded that real benefit was uncommon and that the substantial morbidity and mortality limited the use of the method as a means of palliation. D. F. N. Harrison¹² has attempted to reduce the dangers of intra-arterial therapy in certain types of cancer of the head and neck by giving short-term infusions under whole-body hypothermia. He makes the salutary comment that the treatment should not be worse than the disease.

For the time being the primary management of choice in localized cancer is surgery or radiotherapy or a combination of both. Intra-arterial chemotherapy may prove to be a worthwhile adjunct in certain instances where the orthodox weapons offer small hope of control. If so it should usually constitute the initial attack, since the operation and ionizing radiation each in its own way damages the vascular bed of the tumour. Any possible advantage in terms of control of the disease must be weighed against the very real dangers associated with the method. The indications for this treatment are broader in those parts of the world where radiotherapy is not available.

In the control or palliation of localized malignant disease recurring after operation or irradiation intra-arterial therapy has proved to be largely disappointing, disturbingly hazardous,

¹ Klopp, C. T., Alford, T. C., Bateman, J., Berry, G. N., and Winship, T., *Ann. Surg.*, 1950, **132**, 811.

² Creech, O., jun., Kremenitz, E. T., Ryan, R. F., and Winblad, J. N., *ibid.*, 1958, **148**, 616.

³ Sullivan, R. D., Miller, E., and Sykes, M. P., *Cancer (Philad.)*, 1959, **12**, 1248.

⁴ Creech, O., jun., and Kremenitz, E. T., *J. Amer. med. Ass.*, 1964, **188**, 855.

⁵ Stehlin, J. S., jun., and Clark, R. L., *Amer. J. Surg.*, 1965, **110**, 366.

⁶ Moore, M. R. R., and Newton, K. A., *Cancer Chemother. Rep.*, 1964, **41**, 19.

⁷ Sullivan, R. D., and Zurek, W. Z., *J. Amer. med. Ass.*, 1965, **194**, 481.

⁸ Westbury, G., Newton, K. A., Humble, J. G., Ford, H. T., Pegg, D. E., and White, W. F., *Brit. med. J.*, 1962, **1**, 1238.

⁹ Espiner, H. J., Vowles, K. D. J., and Walker, R. M., *Lancet*, 1962, **1**, 177.

¹⁰ Helman, P., Sealy, R., Malherbe, E., and Anderson, J., *ibid.*, 1965, **1**, 128.

¹¹ Tindel, S., *J. Amer. med. Ass.*, 1967, **200**, 913.

¹² Harrison, D. F. N., *J. Laryng.*, 1967, **81**, 173.

and burdensome to patient and doctor. If indicated at all, it should certainly be conducted by an experienced team and not by the occasional practitioner.

Clinical Lessons from Developmental Neurology

The Mental Health Research Fund lecture for 1967 was given by a developmental neurologist, Professor H. F. R. Prechtl (p. 763 of this week's *B.M.J.*), on the sequelae of prenatal and perinatal complications. Some people might think the choice of speaker and subject rather remote from the field of mental health. This is not the case, however, for it reflects an increasing awareness of the fact that neurological, behavioural, educational, and psychiatric problems in childhood and later years may all have their origins and first manifestations in the early months of life. The statistical data and carefully reasoned discussion of Prechtl's presentation contain important lessons about the mechanisms of neurological disturbances and the techniques of neurological examination in infancy.

Many consider that a newborn baby is either completely normal or patently the reverse. Linked with this view is the notion that if a baby does not come to notice as a result of the presence of obvious symptoms and signs then all is well and further examination is unnecessary. This may be true of the immediate future, but it is the more distant outlook that counts. The aim is that the child should have every chance of growing into a mentally and physically healthy adult. H. Knobloch and her colleagues¹ have challenged the correctness of the "all or none" concept. These workers suggested that there was a "continuum of neurological damage," ranging from gross defects to initial minor damage with later sequelae, and this hypothesis is strengthened by Prechtl's findings. If their view is correct then detailed neurological examination of neonates is necessary to detect those with less obvious lesions who may later develop other more serious defects. To do this we need to be sure that our diagnostic tools are sufficiently precise for the task.

Prechtl's observations show that our present clinical techniques are unsatisfactory. Comparing the results of his methods of examination with those obtained by classical neurological techniques, he found that, though all the babies considered abnormal by the classical methods also scored poorly in his examination, many babies who appeared to be normal on the classical type of examination had low scores in his examination and also developed later sequelae. Prechtl's technique² consists of a battery of quantitative observations made under strictly controlled conditions. This is time-consuming work which is not easily adapted to clinical practice. Nevertheless, it should be studied so that the routine neurological methods used in diagnosis may be improved.

Important applications arise from this work concerning the rearing of young babies. Some of the difficulties which commonly occur in the rearing of young babies are attributed to the inexperience or fault of the mother. Possibly there is a

neurological basis for them which a Prechtl type of examination might reveal. Moreover, these minor neurological disturbances may be sufficient to affect the early behaviour of the infant and impair the mother-child interaction. This important period of emotional development is already being studied extensively, and everyone concerned should take note of Prechtl's work.

The concept of the "at risk" infant, which was introduced by Sheridan³ to stimulate the early detection of handicaps, has been criticized because of the unsatisfactory criteria of risk.⁴ Those concerned with finding satisfactory criteria might consider Prechtl's work. He points out that adverse obstetric factors rarely occur singly and has assessed the influence of clusters of adverse factors, using a "risk score" in his analyses.

Prechtl's work also has several implications in research. In particular, he has shown the importance of carefully standardized quantitative methods in developmental neurological examinations and their use as a research tool. It is reassuring that in Britain these methods are already being studied and taught in our more progressive departments of child health.

Miliary Crohn's Disease

The diagnosis of Crohn's disease can on occasion be puzzling. Recently K. W. Heaton, C. F. McCarthy, R. E. Horton, J. S. Cornes, and A. E. Read¹ have drawn attention to a form of it which may give rise to difficulties. They describe three patients in whom at laparotomy the conspicuous finding was the presence of many tiny pale nodules on the serosal surface of the bowel. Tuberculosis was initially diagnosed in two of the patients and they were started on antituberculous therapy.

The distinction between Crohn's disease and abdominal tuberculosis is a matter of some practical importance, for corticosteroids might prove disastrous in tuberculosis inadvertently diagnosed as Crohn's disease. The great majority of the granulomatous lesions in the ileo-caecal region are due to Crohn's disease,² and it seems likely that many patients suffering from it were diagnosed in the past as having hyperplastic tuberculosis. Nevertheless, some modern physicians have described the occurrence of tuberculosis of the ileo-caecal region,^{3,4} so that the possibility of this disease being present cannot be excluded without full investigation.

Histologically, the serosal nodules of Crohn's disease consist of non-caseating granulomata with giant cells of Langhans's type present. Caseation is exceptional in Crohn's disease, whereas it is one of the characteristic features of tuberculous nodules. The granulomata of Crohn's disease are bacteriologically sterile, while those of tuberculosis usually yield tubercle bacilli on culture or guinea-pig inoculation.

One of the patients described by Heaton and his colleagues is of particular interest because the serosal nodules were numerous, though the intestinal wall was barely affected. The authors were then led to postulate that the granulomata are the dominant lesions in early subacute Crohn's disease, and the fact that they follow the lines of lymphatics supports the view that the first pathological changes occur in the

¹ Knobloch, H., Rider, R., Harper, P., and Pasamanick, B., *J. Amer. med. Ass.*, 1956, **161**, 581.

² Prechtl, H. F. R., and Beintema, D., *The Neurological Examination of the Full-term Newborn Infant*. Little Club Clinics in Developmental Medicine, 1964, No. 12, London.

³ Sheridan, M. D., *Mon. Bull. Min. Hlth Lab. Serv.*, 1962, **21**, 238.

⁴ Richards, I. D. G., and Roberts, C. J., *Lancet*, 1967, **2**, 711.

¹ Heaton, K. W., McCarthy, C. F., Horton, R. E., Cornes, J. S., and Read, A. E., *Gut*, 1967, **8**, 4.

² Lee, F. D., and Roy, A. D., *ibid.*, 1964, **5**, 517.

³ Howell, J. S., and Knapton, P. J., *ibid.*, 1964, **5**, 524.

⁴ Anscombe, A. R., Keddie, N. C., and Schofield, P. F., *ibid.*, 1967, **8**, 337.

lymphatics. Moreover, they were hopeful that patients treated at this stage with corticosteroids might do well and the bowel wall escape any major damage. The particular patient was doing well on prednisone therapy at the time they wrote their article, but unfortunately in an addendum they have to report that widespread radiological changes of Crohn's disease appeared in the small and large intestine, though the patient remained symptomatically well.

Cerebral Angiomas

Once discovered, cerebral angiomas are much less likely to cause death from haemorrhage than are the commoner berry aneurysms of the circle of Willis and its branches. This is evident from the recent account by W. R. Henderson and R. de R. L. Gomez¹ of the natural history of these malformations, and they confirm the findings of earlier workers, notably H. J. Svien and J. A. McRae.² Indeed, J. M. Potter³ has drawn attention to a number of patients who lived for many years at relative peace with their lesions and often with little or no disability, particularly after receiving the sort of radiotherapy that was given 30 to 40 years ago. This did not, of course, prove that radiation was necessarily effective—most authors think that it is not—but it did show that it would have been unnecessary to have submitted those patients to operations carrying the mortality and morbidity prevalent in those days.

Any major operation of uncertain prophylactic value needs to be examined critically. Present techniques for the precise localization of these angiomas and the definition of their feeding and draining vessels (they nearly all have arteriovenous fistulae), together with modern neurosurgical and anaesthetic methods, enable the surgeon to operate on apparently formidable lesions in the expectation of a relatively low mortality. However, some degree of disability—hemiparesis, hemianopia, or dysphasia if the dominant cerebral hemisphere is affected—is still an ever-present and unpredictable risk unless the malformation is well clear of the related cortical areas. Nevertheless, many neurosurgeons prefer to operate if it appears at all feasible to do so, and the indications for excision may therefore be briefly reviewed.

Many of these patients have some form of epilepsy as their sole symptom, and, while it is true that seizures may be modified or abolished at least for a time after operation, surgical treatment is unreliable. Indeed, the resulting brain scar may itself produce fits in some patients who did not have them before operation. Only if the epilepsy is frequent, disabling, and uncontrolled by anticonvulsant drugs does surgery appear to be indicated.

Some believe that the removal of a cerebral angioma is prophylaxis against the insidious development of mental and physical deterioration that these patients sometimes suffer, but firm proof of this is lacking, and any penalty from the operation itself may be unwelcome. Rarely (in only two patients in the series of Henderson and Gomez), the lesion itself gives rise to increased intracranial pressure, for which some kind of decompressive procedure appears mandatory. More often the cause is a sizable haematoma that requires

evacuation, and it is then often possible to remove the angioma at the same time.

Apart from these indications, it seems proper, as Henderson and Gomez suggest, to operate only on those malformations that are likely to be removable without risk of producing serious neurological damage. Estimates of this risk will differ. Thus the proportion of cases submitted to operation, and whether there is resulting neurological damage or not, will depend on the individual surgeon's judgement. But even when the operation has apparently been completely successful statistics cannot ever tell us whether it was necessary in that particular case. If an operation is undertaken, the whole lesion must be removed to ensure prophylaxis, for if any abnormal vessels are left behind the risk of further haemorrhage remains. An ingenious method of treatment remains to be mentioned, that of artificial embolization of the arteriovenous fistulae by means of plastic spheres,⁴ but this may be said to be still in the experimental stage.

Spontaneous intracranial haemorrhage occurring in patients without evidence of cardiovascular disease, and particularly in younger people, always raises anxiety about treatment, so that there is much to be said for knowing early on what is its cause and to be sure that there is not, for example, a small, easily removable angioma situated in a silent area of the brain. Consequently, some workers may consider that cerebral angiography should be undertaken more readily than Henderson and Gomez suggest. However, their important paper indicates that, in the light of present knowledge, conservative treatment may be appropriate for the majority of these patients, and that an angioma need not be removed simply because it is there.

B.M.A. Awards

This week notices appear at the end of the *Supplement* inviting members of the B.M.A. to apply for grants to help their research. Awards of this kind, together with substantial monetary prizes, are a prominent part of the Association's endeavours to "promote the medical and allied sciences," which is the first of its stated objects. If the *B.M.J.* may be forgiven for regarding the publication of this journal and its associated periodicals (15 specialist and two abstracting journals) as pre-eminent in the Association's fulfilment of its primary aim, the numerous scholarships and prizes nevertheless make a large contribution in offering both encouragement and acknowledgement to many doctors keen to advance medicine. In addition, a number are also available to medical students and nurses.

The Chairman of Council, Dr. Ronald Gibson, suggested at a recent meeting of the Committee on Medical Science, Education, and Research (reported at *Supplement* page 92) that maintaining "the interests of the profession," another of the B.M.A.'s declared objects, had somewhat overshadowed its other aims, at least in the public eye. Certainly political conflict is apt to excite attention to an extent unlikely to be rivalled by the uncontentious stimulus to research afforded by grants and prizes. But in a remarkable number of cases a B.M.A. fellowship has been the starting-point for a long and fruitful career in research.

Most of the awards go up to about £300, but now a new whole-time research fellowship of £1,500 is being offered. It is tenable for a year, normally renewable for a second year, and is offered to assist research into any subject relating to the causation, prevention, or treatment of disease.

¹ Henderson, W. R., and Gomez, R. de R. L., *Brit. med. J.*, 1967, 4, 571.

² Svien, H. J., and McRae, J. A., *J. Neurosurg.*, 1965, 23, 23.

³ Potter, J. M., *Ann. roy. Coll. Surg. Engl.*, 1955, 16, 227.

⁴ Lucassenhop, A. J., Kachmann, R., Shevlin, W., and Ferrero, A. A., *J. Neurosurg.*, 1965, 23, 400.

Papers and Originals

Neurological Sequelae of Prenatal and Perinatal Complications*

H. F. R. PRECHTL,** PH.D.

Brit. med. J., 1967, 4, 763-767

In recent years several attempts have been made to assess the hazards of prenatal and perinatal complications. There is little doubt that obstetric complications carry an increased mortality (De Haas-Posthuma, 1962; Butler and Bonham, 1963). Moreover, where several obstetric complications are present in combination it would be expected, *a priori*, that the risks will be additive. While the exact causes of death in any case may be diverse, one major factor is fatal damage to the central nervous system. Post-mortem examination of the brains of babies who would have died after obstetric complications or unfavourable events during the neonatal period has clearly shown the possibility of these factors producing lesions in the nervous system (Debré *et al.*, 1955; Norman, 1956; Malamud, 1959; Clark and Anderson, 1961; Morf and Bretscher, 1966). Studies in monkeys (Ranck and Windle, 1959; Windle, 1960; Windle *et al.*, 1961) have provided evidence of the harmful consequences of experimentally induced perinatal complications.

While studies of mortality rate have a strict criterion available—death of the foetus within a given period of time—the assessment of damage to the surviving infant is much more difficult. Signs have to be found which indicate the baby's condition, and these signs must have both high interobserver reliability and long-term prognostic value. Apgar's technique has merits but is restricted to the first few minutes after birth and deliberately covers only general aspects of physiological status (Apgar, 1966; Drage and Berendes, 1966). A quite different approach has been used by Graham (1956), Graham *et al.* (1956), and Graham *et al.* (1957), who measured behaviour patterns of babies a few days old.

In my own department a detailed neurological examination has been developed for the assessment of babies (Precht and Beintema, 1964). This examination has good interobserver reliability and high prognostic value (Precht and Dijkstra, 1960; Precht, 1965). In a sample of 102 neonates without neurological signs 86% were found to be neurologically normal at follow-up between two and four years later. Of 150 neonates with abnormal neurological signs, 73% still showed abnormal signs at follow-up during a similar period.¹ Certain constellations of neonatal abnormal signs, which we designated hyperexcitable syndrome, apathetic syndrome, and hemisyndrome respectively, were prognostic of continuing neurological abnormality in 67%, 59%, and 73% of cases respectively, when the latter were examined at 2-4 years (Precht, 1965). Preliminary findings from our follow-up studies at 8 years show a similar picture to that found at 2-4 years. This method of examination may thus be regarded as a highly sensitive indicator of long-term neurological functioning. The identification of

factors which contribute to neurological abnormality in the newborn is therefore a problem of crucial importance.

The aim of the present paper is to examine some interrelationships between obstetric complications and the results of this examination. Our hypothesis is that obstetric complications carry a high risk of neurological damage to the surviving infant. The data on which the present study is based have been collected over a period of 12 years. This paper is restricted to presentation of a number of global findings. Full data will be published elsewhere.

Method

The Sample.—A neurological examination was carried out on 1,515 infants born in the Department of Obstetrics of the Groningen University Hospital. In the Netherlands about 70% of all infants are born at home. The 30% delivered in hospital are therefore primarily cases with a risk of obstetric complications, though a minority go to hospital for social reasons, such as poor housing. From this total the following were eliminated: (1) babies of women who did not regularly attend the outpatient unit of the obstetric department during pregnancy; (2) babies whose birth weight was less than 2,500 g.; (3) babies with gross malformations; (4) babies whose mothers were in a poor nutritional state, suffered from psychiatric disease, epilepsy, diabetes, or heart disease, or whose basal metabolism was low; and (5) babies whose mothers had suffered prolonged sterility. Both categories 4 and 5 occurred rarely in our material. Babies whose condition was poor or dangerous in the first week were not subjected to full neurological examination. The sample remaining after exclusion of the above cases consisted of 1,378 babies.

Neurological Examination.—The standard neurological examination technique has been previously described (Precht and Beintema, 1964). All infants were examined once, two to three hours after a feed. All examinations were carried out between the second and fourteenth days, 91% of them being between the third and tenth days. The babies were picked at random from the obstetric department and were examined without knowledge of the obstetric history.

Data Processing.—The obstetric and neurological data were entered on precoded forms and later transferred to IBM punched cards. Seventy-six items were related to the mother, the course of pregnancy and delivery, and the general aspects of the infant, and 142 items to the neurological examination. All computations were carried out on a general purpose computer (TR4) at the Computer Centre of the University.

Incidence of Obstetric Complications

An obstetric complication may be defined as any factor or group of factors in the prenatal or perinatal environment which

* Mental Health Research Fund Lecture delivered at the Middlesex Hospital Medical School, London, on 22 February 1967.

** Department of Developmental Neurology, University of Groningen, The Netherlands.

¹ The correlation between neonatal findings and the presence or absence of abnormal neurological signs on follow-up gave a value of $\phi=0.583$ ($P<0.0001$).

increases the risk of foetal mortality. These will be symptoms of maternal disease during pregnancy, signs of foetal distress, and mechanical intervention in the delivery. Few of these factors are independent of each other and many are causally related. For example, maternal toxæmia may lead to perinatal foetal distress, which in turn will lead to instrumental extraction.

In order therefore to give a more precise meaning to the rather loosely used term "complication," the following procedure was adopted. For every case 42 variables of the obstetric history were analysed and a count was made of the number of variables which departed from optimal conditions, according to generally accepted criteria. The largest number of such non-optimal conditions was 15, while in 6.2% of our sample all 42 variables were in the optimal condition. Table I shows some of the most frequently occurring non-optimal conditions.

The data were next divided into six subgroups: those with 0, 1-2, 3-4, 5-6, 7-9, and 10 or more non-optimal conditions. The percentage of cases in each subgroup is given for boys and girls separately in Fig. 1.

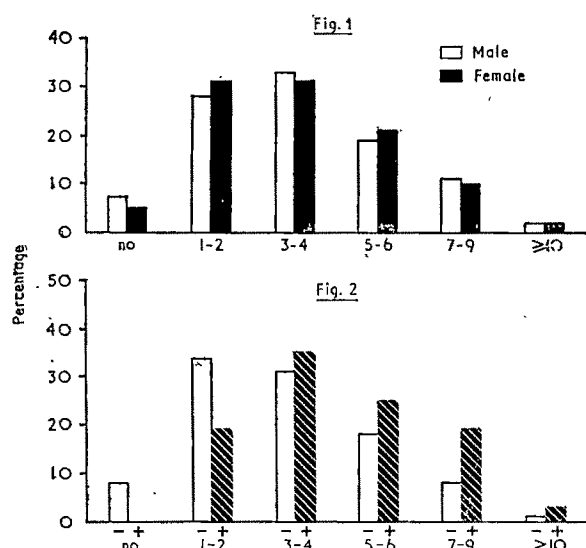


Fig. 1.—Incidence of non-optimal conditions in boys and girls. Fig. 2.—Percentage of the non-toxaemic (—) and moderate and severe toxæmic cases (+) (N=370) in each subgroup of non-optimal conditions. The difference is significant.

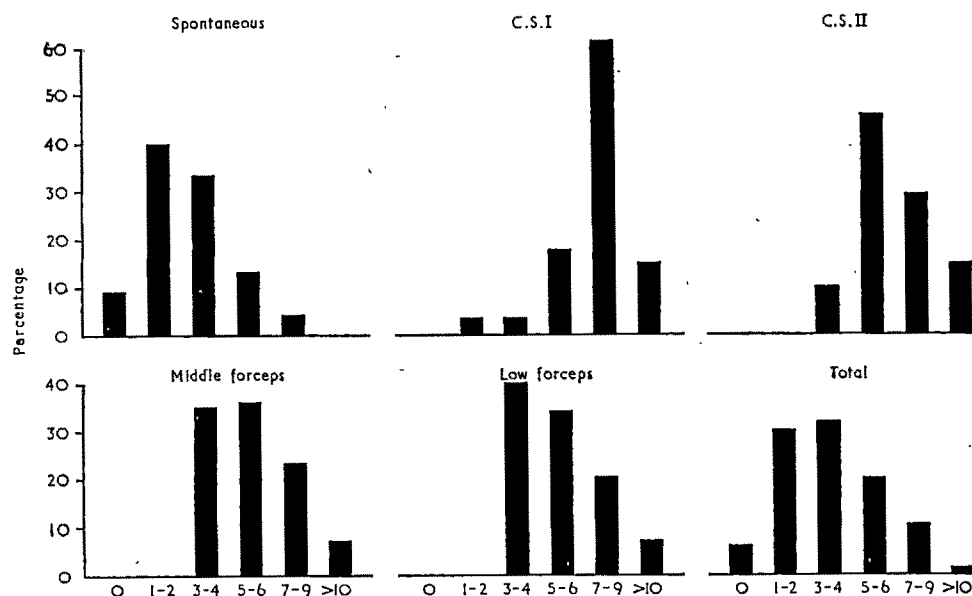


Fig. 3.—Type of delivery and obstetric subgroup. Spontaneous delivery, elective caesarean sections C.S. I (N=33), non-elective C.S. II (N=48), middle forceps (N=85), and low forceps (N=133) are presented separately.

There were no statistically significant sex differences with respect to occurrence of non-optimal obstetric conditions. In the subsequent analysis the data for boys and girls are combined.

TABLE I

Condition	No.	%
Maternal age above 30 years	342	25.0
Moderate toxæmia	250	18.1
Severe toxæmia	108	8.5
Other than vertex presentations	235	17.2
Non-spontaneous delivery	427	31.0
Caesarean sections	81	5.9
Middle forceps	75	5.4
Low forceps	133	9.7
Prolonged labour ≥24 hours	170	12.3
Second stage longer than two hours	96	7.0
Tight cord around the neck	101	7.3
Foetal bradycardia <100/min.	188	13.6
Post-partum apnoea >1 min.	224	16.3

Interrelationships between Non-optimal Obstetric Conditions

It is of interest to examine which conditions occur in combination with others and which do not. This summary is confined to three examples only, illustrating complications of pregnancy, delivery, and foetal state respectively.

Toxaemia.—If all cases with moderate or severe toxæmia (characterized by blood pressure $\geq 140/95$ and by albuminuria and oedema respectively) are compared against the rest with respect to the distribution of non-optimal conditions it will be seen that there is a marked tendency for the toxæmia cases to occur in association with a large number of other non-optimal conditions (Fig. 2).

Delivery.—A similar picture emerges, as might be expected, for instrumental as compared with spontaneous deliveries (Fig. 3).

Foetal Heart Rate and Apnoea.—Signs of foetal distress, such as tachycardia or bradycardia during the second stage (Fig. 4) and post-partum apnoea longer than one minute (Fig. 5), behave similarly to the complications above.

Non-optimal Obstetric Conditions and Neurological Symptoms

Most of the items of the neurological examination are assessed on an ordinal scale with three or four points. For instance, the palmar grasp reflex is recorded as being absent (—), being weak or just discernible (+), giving a good sustained response for 10 seconds (++) , or giving an exaggerated forceful grasp (+++). The rooting response is recorded as being absent (—), showing only a weak turn toward the stimulated side (+), giving a full turn and a grasp with the lips (++), and consisting of a very vigorous turn with grasping (+++). The intensity of the Moro reflex is recorded as low, middle, or high. In the case of the palmar grasp reflex and rooting response the ++ category may be regarded as the optimal response, whereas for the Moro reflex the optimal response would be that of intermediate intensity and threshold.

If we assume that for each item of the neurological examination there is an optimal response we may examine the frequency with which cases with varying numbers of obstetric complications fall into the optimal and non-optimal categories.

For the purpose of this analysis the data were divided on the

basis of the obstetric complications into three subgroups: (1) a "low risk" group (N=264; 19.2%) with no or only one non-optimal condition; (2) a "middle risk" group (N=943; 68.4%) with two to six non-optimal conditions; and (3) a "high risk" group (N=171; 12.4%) with seven or more non-optimal conditions. The word "risk" is used to denote a raised probability of mortality during the delivery and the first two weeks of life. It involves no assumptions about the possible outcome of the neurological examination.

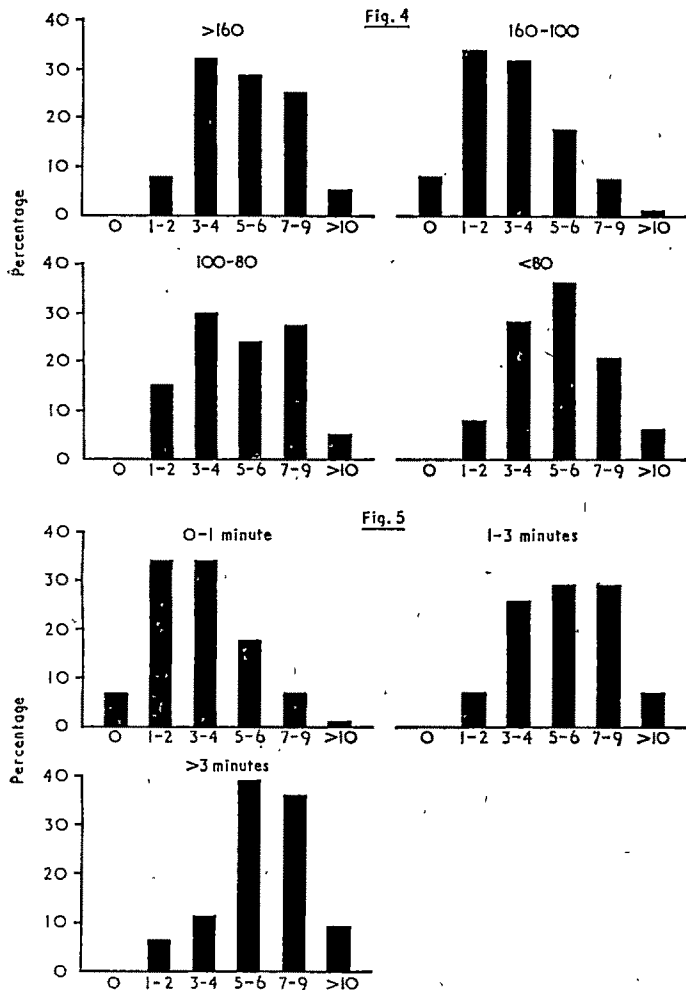


FIG. 4.—Foetal heart rate and non-optimal conditions. The tachycardia group with a heart rate >160/min. (N=59) and the two groups of bradycardia 100-80/min. (N=101) and <80/min. (N=89) are all significantly different from the group with normal heart rate (160-100). FIG. 5.—Onset of respiration and incidence of non-optimal conditions. The longer the apnoea the more other non-optimal conditions are present. The difference is highly significant at 1-3 min. (N=187) and >3 min. (N=37).

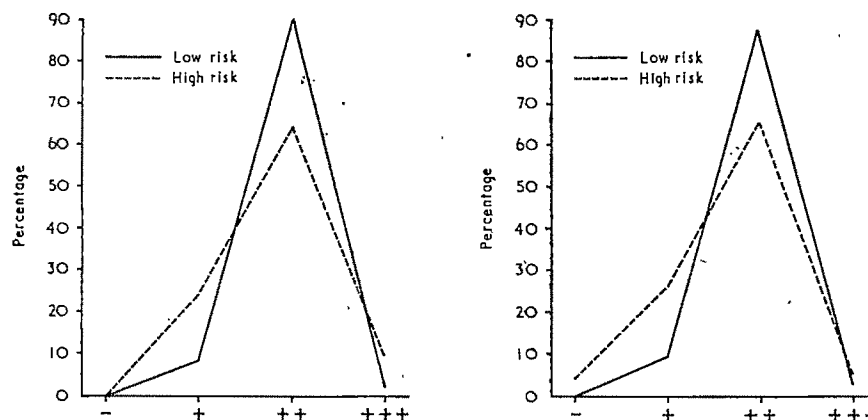


FIG. 6.—Distributions of response intensities of the palmar grasp reflex in the low and high risk groups. The difference is significant ($\chi^2=60.9$; $P<0.001$). FIG. 7.—Distributions of response intensities of the rooting response in the low and high risk group. The difference is significant ($\chi^2=22.2$; $P=0.001$).

For illustration the distributions of response intensities of the palmar grasp reflex and the rooting response are shown for the low and high risk groups (Figs. 6 and 7).

Fifty-eight neurological items were selected which, as above, could be assigned a position on a four-point ordinal scale. Contingency tables were constructed showing the frequency with which patients from the three risk groups fell into different positions on each scale. In 42 of the tests the differences between expected and observed frequencies as measured by χ^2 tests were significant at least at the 1% level of confidence. The low risk group predominantly showed those responses described as "optimal," whereas the high risk group showed relatively few optimal responses. In all 42 items the middle-risk group was intermediate between the other two with respect to the number of optimal responses. In other words, there is a highly significant association between the number of non-optimal obstetric conditions and neurological abnormalities in the newborn.

The relation between non-optimal obstetric conditions and neurological abnormality is seen even more clearly if we carry out the following transformation. For each ordinal item of the neurological examination a score of "1" was given if the baby's response was in the optimal category. It was thus possible to obtain a "neurological score"—the number of items of the neurological examination in which the baby gave an optimal response. For all babies on whom the full neurological examination was carried out (N=1,378) the neurological scores were plotted against the corresponding number of non-optimal conditions. It was found that the mean neurological score decreased as the number of obstetric complications increased.

The neurological scores were next separated into three main groups, taking the following cut-off points: scores equal to 47 or less, scores 48 to 52, and scores 53 to 58. The babies in each of these three groups were then allocated, on the basis of

TABLE II

Neurological Scores	Risk Group			Totals
	Low	Middle	High	
≤47	73 (101.7)	375 (363.4)	83 (65.9)	531
48-52	84 (87.9)	316 (314.1)	59 (57)	459
53-58	107 (74.3)	252 (265.5)	29 (48.1)	388
	264	943	171	1,378

Figures in parentheses are expected frequencies.

their mother's obstetric score, to the high, middle, and low risk groups. The relation between the neurological and obstetric findings is shown in Table II. There was a very highly significant difference between the observed and expected frequencies with which the three neurological subgroups were represented in the three risk groups ($\chi^2=38.5$, d.f.=4, $P<0.001$). It is clear, therefore, that there is a high association between obstetric complications as measured by the obstetric scores—and the occurrence of neonatal neurological abnormalities.

Obstetric Risks and Neurological Syndromes

If a group of symptoms occur repeatedly in combination they may be said to constitute a syndrome. We have previously described a combination of low intensity of general motor activity and of sucking, rooting, hand- and foot-grasping, head-lifting in prone position, recoil of forearms, and the labyrinthine reflex—the *apathy syndrome* (Prechtl and Dijkstra, 1960). Similarly, babies showing lowered resistance to passive movements of the neck, trunk, shoulder, elbow, hand, hip, and knee and ankle joints have been described as hypo-

tonic. Significantly more babies showing the apathy syndrome and hypotonia were found in the high risk group than in either the middle or the low risk group. Babies with asymmetries of posture, tendon reflexes, and skin reflexes* (which we have previously described as the *hemisindrome*) were equally distributed among the three risk groups. Interestingly, however, babies with the hemisindrome and those with facial palsies had a significantly raised incidence of occurrence after forceps delivery and version-extraction. Babies who are what we have called *hyperexcitable* were significantly overrepresented in the middle risk group. Hyperexcitability occurred significantly more among the boys.

Neurological Scores and Classical Neurological Signs

I have so far argued that there is a high positive correlation between non-optimal obstetric conditions and neurological abnormality as measured by our standardized procedure. Because neonatal abnormalities with this technique are predictive of continuing abnormality and future behavioural disturbance (Prechtl, 1965) we believe it is essential that full neurological examination is carried out on all babies who are obstetrically at higher risks. It might be argued, however, that since the full examination is a time-consuming and expensive procedure it is sufficient to record the presence of obvious neurological signs which any well-trained obstetrician or paediatrician could not fail to see. In fact, 25 of our babies showed one or more "obvious" neurological signs: facial palsies; bulging fontanelles; deviation of eye position; absence of sucking, Moro, or palmar grasp reflexes; severe floppiness; or marked asymmetry.

It is of interest to examine the distribution of the neurological scores of these babies relative to that of the remainder. No baby with an obvious neurologically abnormal condition ever obtains fewer than four non-optimal subtest items—that is, the baby is never misclassified as normal by our examination. On the other hand, a very large number of babies with no classical neurological signs obtain the same neurological scores as those with such classical signs. It is clear, therefore, that examination merely for gross pathological signs will result in the omission of a considerable amount of neurological abnormality which is prognostically ominous. Thus the presence of "classical neurological signs" is not exclusive evidence of neurological abnormality. Moreover, we have shown that neurological abnormality, as measured by the full standardized procedure, increases in relation to the number of non optimal obstetric conditions. It therefore follows that the urgency for full neurological examination of the newborn increases also as a function of the number of non-optimal obstetric conditions present.

Discussion

The identification of what constitute obstetric hazards remains still an urgent clinical problem. An approach to this question through studies of mortality rate has great merits, but the answers must remain incomplete, since the majority of infants survive obstetric complications. Among these babies, however, may be many who suffer major or minor impairment of brain function. The early recognition of nervous dysfunction is of great importance both with respect to the possibility of early treatment and in relation to handling difficulties arising during the development of the mother-infant relationship. Many studies seem to indicate that, besides handicaps such as cerebral palsy due to prenatal and perinatal brain damage, minor brain dysfunctions, undramatic from the clinical neurological point of view, may lead to severe problems in the life of children and their parents. Though well-controlled studies are still scarce the available data are alarming.

In the context of these aspects the need for early indicators of risks is evident. The attempt to design risk registers which would select those babies from the population who are at special risk of brain damage is a major task. If only for the purpose of practical management, criteria are needed which do not select for special attention half or even more of all newborn babies. In the light of our study, one possible approach is through the obstetric score. It will be remembered that obstetric scores were highly correlated with neurological findings which were themselves predictive of continuing abnormality. In practice this would mean filling in a check-list of non-optimal conditions that results in a risk score. This is obviously a more reliable strategy than to look only for the presence of particular dangerous obstetric conditions in the baby's history.

As a further result of our study new criteria are suggested for the interpretation of the quantitative results of our neurological test items. Though it was possible previously to indicate the optimal intensity of responses, it was still questionable, for many responses, at which points of the scale one should speak of an abnormal response, a fact we have indicated in our manual for the neurological examination of the full-term newborn infant (Prechtl and Beintema, 1964). Differences found between the neurological item scores of the obstetrically high risk group and those of the low risk group are very suggestive of a more valid demarcation of neurological abnormality. For example, with respect to the rooting response, the differences between the two risk groups are apparent in the scores — and +, but the incidence of +++ is no higher in the high risk group than in the low risk group. This offers a possible operational definition of "abnormal" as being the — and + responses only, in contrast to the normal responses ++ and +++. In the case of the palmar grasp response, on the other hand, the +++ response would still be regarded as abnormal.

This new information is valid for many test items of the neurological examination. There remain certain neurological signs which are undoubtedly abnormal, such as the absence of sucking or of the Moro response, persistent deviation of the eyes. Our study has shown, however, that application of these generally accepted criteria of abnormality alone would leave many neurologically abnormal babies unrecognized. The French technique as advocated by Dargassies (1962) uses only such qualitative signs. The quantitative assessment of neurological signs is not, however, a mere academic refinement of neurological examinations, but a clinical necessity.

Summary

A group of 1,378 full-term newborn infants born in the Obstetric Department of the University of Groningen were subjected to a standardized quantitative neurological examination in their first 10 days of life. Data on pregnancy, delivery, and condition of the infant at birth were available.

Since previous correlation analysis of neurological results with obstetric complications failed to give instructive results a new approach was carried out. Forty-two variables of the prenatal and perinatal history were analysed and counted if they deviated from optimal condition, giving an obstetric risk score for each baby. The distributions of response intensities of many neurological items were shown to be different in the low, middle, and high risk groups. This held true also for some syndromes. The number of optimal neurological responses was negatively correlated with the number of non-optimal obstetric conditions.

It was shown that non-optimal conditions tended to occur in association with each other. The more a condition deviated from the norm, the greater the number of other non-optimal conditions associated with it. A simple count of the number of such non-optimal conditions present offers promise as a means of identifying those babies at risk of neurological damage.

It is suggested that the criteria for assessing what is an abnormal neurological response may be refined by reference to the responses of our low and high risk groups.

My thanks are due to Professor L. A. Joosse and Professor B. S. ten Berge, of the Department of Obstetrics, University of Groningen, for their interest and co-operation over the many years of this study. I am also indebted to my co-workers, Drs. J. D. Beintema, J. Dijkstra, A. v.d. Gaag, W. Lawant, and B. C. L. Touwen, for their part in collecting the data. Without the great assistance of Dr. D. Smits, director of the Computer Centre of the university, and Dr. R. Wippler and Mrs. J. H. van Dijk-v.d. Horst the data-processing would have been impossible. I want to express my warm appreciation for the help of Dr. S. J. Hutt in the preparation of the manuscript. This study was supported by a grant from the Association for the Aid of Crippled Children, New York.

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Concentration of Methoxyflurane for Obstetric Analgesia by Self-administered Intermittent Inhalation

VALERIE MAJOR,*† F.F.A.R.C.S.; MICHAEL ROSEN,* F.F.A.R.C.S.
 WILLIAM W. MUSHIN,* F.R.C.S., F.F.A.R.C.S.

Brit. med. J., 1967, **4**, 767-770

Methoxyflurane has been shown to possess advantages over trichloroethylene as an obstetric analgesic (Major, Rosen, and Mushin, 1966). In that initial study we varied the concentration of both vapours continuously, with the aim of giving each patient the best possible analgesia without undesirable side-effects. The design of the trial made it possible (by analysing the continuous recordings of the inhaled concentrations of methoxyflurane) to deduce that for intermittent use a single fixed concentration of the drug would prove adequate and that this would be 0.35%. The present trial tests the validity of these predictions.

Method

Two concentrations of methoxyflurane in air (0.35% and 0.25%) were compared. These were chosen because observations in our first trial indicated that patients tended to become unacceptably drowsy at concentrations higher than 0.35%. This decision has been confirmed by observations of some patients in this trial who were studied at a higher concentration (0.45%).

Methoxyflurane was given from identical Penlon P.D.V. vaporizers, as these were the most accurate "draw-over" vaporizers available to us for this drug. Each was modified so that only one predetermined concentration could be given. The vaporizers were calibrated by us with a katharometer, using a Beaver ventilator as a dummy patient, and the concentrations were checked frequently throughout the trial. Before being used by a patient each vaporizer was flushed with oxygen for at least three minutes to clear the "dead" space.

* Department of Anaesthetics, Welsh National School of Medicine, Cardiff.

† Abbott Research Fellow.

The day on which each concentration was used was previously randomized. Though an anaesthetist was present as an assessor throughout the inhalation, the conduct of analgesia was left to the midwife, so that the conditions were as near "normal" as possible. Inhalation was therefore started at the midwife's discretion, usually towards the end of the first stage of labour. A record was kept of the dose and time of administration of other drugs given during labour; no direction or restriction was made regarding their use. Assessments were made separately by an anaesthetist, by the midwife, and by the mother.

The same anaesthetist was present for all cases and made continuous assessments. For the full details of the method of assessment readers are referred to our previous paper (Major *et al.*, 1966). In brief, assessments are made of the mother's response to contractions, her level of consciousness, and any restlessness between contractions. The anaesthetist's observations are plotted to show the proportion of time during the whole period of observation for which each of the three factors is deemed "satisfactory." The periods for which all factors are satisfactory are calculated and expressed as a percentage of the total duration of inhalation.

As in the previous trial, the midwife, for whom the trial was blind, gave her assessment just after delivery with respect to the degree of analgesia, the drowsiness of the patient, and the restlessness of the patient. The mother was questioned twice—15 minutes after delivery and then 36 to 48 hours later. The questions at 15 minutes were slightly modified in this trial. She was asked: "Do you consider that what you had to breathe helped you?" "Do you feel drowsy?" "Did you drift off at all?" and "Could you do what we asked?" At the second visit other questions were asked regarding nausea, vomiting, memory, and smell.

Measurements of ventilation were made in some mothers by means of a Wright respirometer and a stop-watch. The baby was assessed by the Apgar score at one minute, and by noting the time to the onset of regular respiration.

Results

Forty-three patients were given inhalational analgesia. Twenty-three had 0.35% methoxyflurane (11 primigravidae, 12 multigravidae—19 spontaneous vertex deliveries) and 20 had 0.25% methoxyflurane (10 primigravidae, 10 multigravidae—18 spontaneous vertex deliveries).

Duration of Inhalation

The shortest period of inhalation was 16 minutes and the longest 6 hours 30 minutes. The mean duration for 0.35% methoxyflurane (0.35 group) was 1 hour 30 minutes, and for 0.25% methoxyflurane (0.25 group) 1 hour 26 minutes ($P > 0.70$). The groups appear similar in this respect.

Observations by Anaesthetist

All Factors Satisfactory (Table I).—The percentage of time of inhalation for all factors satisfactory was determined for each patient. The mean for each group was calculated. The 0.35 group was satisfactory for significantly longer (72.7%) than the 0.25 group (55.5%).

TABLE I.—Percentage of Duration of Inhalation Regarded as Satisfactory

Factor Studied	Mean Percentage of Time Satisfactory		Significance (t test)
	0.35% Methoxyflurane (23 patients)	0.25% Methoxyflurane (20 patients)	
All factors satisfactory	72.7	55.5	$P < 0.05$
Reaction to contraction satisfactory	72.8	55.5	$P < 0.05$
Level of consciousness satisfactory	100	100	
Restlessness satisfactory	98.9	94.6	$P < 0.10$

Reaction to Contraction (Table I).—The 0.35 group was significantly better in this respect (72.8%) than the 0.25 group (55.5%).

Level of Consciousness (Table I).—All the patients were satisfactory.

Restlessness between Contractions (Table I).—Only six mothers showed any restlessness—two received 0.35% and four received 0.25% methoxyflurane. The 0.35 group was satisfactory for slightly longer than the 0.25 group.

Effect of Duration of Inhalation on All Factors Satisfactory (Table II).—The effect of the duration of inhalation was studied by dividing each labour into consecutive half-hour periods starting five minutes after the beginning of inhalation. The mean time for the 0.35 group was higher for each half-hour period, and the difference between the two groups is significant in the first half-hour.

Effect of Progress of Labour on All Factors Satisfactory (Table II).—The effect that the progress of labour had on

all factors satisfactory was examined for the half-hour period immediately preceding delivery: the mean time for the 0.35 group was significantly higher.

TABLE II.—Effects of Duration of Inhalation and Progress of Labour on All Factors Satisfactory

Group	Mean Percentage of Time All Factors Satisfactory			
	Half-hour Period of Inhalation			Half-hour Preceding Delivery
	1st	2nd	3rd	
0.35	80.3	76.5	71.4	79.5
0.25	59.4	55.3	46.6	53.2
Significance (t test)	$P < 0.05$	$P < 0.20$	$P > 0.20$	$P < 0.02$

Effect of Pethidine on All Factors Satisfactory (Table III).—Nearly the same proportion of patients in each group received pethidine during the four hours immediately preceding the start of inhalation (13 out of 23 patients in the 0.35 group and 12 out of 20 in the 0.25 group). The difference in the assessment between the two groups does not appear to be due to the administration of pethidine.

TABLE III.—Effect of Pethidine on All Factors Satisfactory

Group	Mean Percentage of Time All Factors Satisfactory		Significance (t test)
	Pethidine during 4 hours Preceding Inhalation	No Pethidine during 4 hours Preceding Inhalation	
0.35	74.1	71.0	$P > 0.70$
0.25	54.1	58.0	$P > 0.70$

Opinion of Midwife

The midwives thought the analgesia "complete" in 31% of the mothers in the 0.35 group and in 5% of the mothers in the 0.25 group. This difference is significant (Table IV).

TABLE IV.—Midwives' Opinion of Analgesia

Group	Complete	Considerable	Slight	None	Significance	
					Complete v. All Other Replies	Complete and Considerable v. All Other Replies
0.35	7 (31%)	15 (65%)	1 (4%)	0 (0%)	} $P = 0.037$	} $P < 0.20$
0.25	1 (5%)	15 (75%)	4 (20%)	0 (0%)		

One patient (4%) of the 0.35 group was graded as restless, and four (20%) of the 0.25 group. The restless mother in the 0.35 group was graded as having "considerable" pain relief, whereas the four in the 0.25 group were also graded as having "slight" analgesia.

No mother in either group was thought by the midwives to be "too drowsy."

Opinion of Mother

Assessment of Pain Relief at 15 Minutes after Delivery (Table V).—Pain relief was thought to be "complete" in 43% of the 0.35 group and in 15% of the 0.25 group. This

TABLE V.—Mothers' Opinion of Pain Relief

Mothers' Assessment after Delivery	Group	Complete	Considerable	Slight	None	Significance	
						Complete v. All Other Replies	Complete and Considerable v. All Other Replies
At 15 min.	0.35	10 (43%)	13 (57%)	0 (0%)	0 (0%)	} $P = 0.044$	} $P = 0.21$
	0.25	3 (15%)	15 (75%)	1 (5%)	1 (5%)		
At 36-48 hours	0.35	8 (35%)	15 (65%)	0 (0%)	0 (0%)	} $P = 0.21$	} $P = 0.039$
	0.25	3 (15%)	13 (65%)	3 (15%)	1 (5%)		

difference is significant. No mother having 0.35% methoxyflurane gave a grading lower than "considerable." In the 0.25 group the inhalation was stopped in one case after an hour because the mother complained of getting no pain relief.

Assessment of Pain Relief at 36–48 Hours after Delivery (Table V).—Four mothers of the 0.35 group changed their previous opinion—three from "complete" to "considerable" and one from "considerable" to "complete" pain relief. In the 0.25 group two mothers changed from "considerable" to "slight" pain relief. In this later assessment those replying "complete" or "considerable" are significantly more in the 0.35 group.

One patient in each group had to be excluded from some of the more detailed questions owing to language difficulties.

Other Questions at 15 Minutes after Delivery.—Drowsiness: Nine out of 22 (43%) mothers in the 0.35 group and 7 out of 19 (37%) in the 0.25 group said they felt drowsy. **Sleep:** Only one patient (0.35 group) felt herself "drifting off." **Ability to Obey Commands:** All patients felt able to do all that was asked of them during labour.

Other Questions at 36–48 Hours after Delivery.—Memory of Labour and Delivery (Table VI): There was little difference between the two concentrations with regard to memory for labour and delivery. **Smell:** 13 (57%) of the mothers in the 0.35 group and 12 (60%) in the 0.25 group noticed the smell; only one (0.25 group) thought the smell unpleasant. **Nausea and Vomiting:** In the 0.35 group three mothers (13%) felt nauseated during delivery and another three in the next 24 hours; one of them (4%) vomited. Altogether six (26%) in the 0.35 group were affected. Only one patient in the 0.25 group felt sick, and that was during delivery; none vomited. The difference between the two groups is nearly significant ($P=0.07$).

TABLE VI.—Mothers' Memory of Labour and Delivery

	Group	Mothers' Memory		
		Clear	Hazy	None
Labour	0.35	17 (77%)	5 (23%)	0 (0%)
	0.25	13 (68%)	6 (32%)	0 (0%)
Delivery	0.35	19 (86%)	2 (9%)	1 (5%)
	0.25*	16 (88%)	2 (12%)	0 (0%)

* One patient excluded (caesarean section).

Other Criteria

Condition of Babies.—Of the babies in the 0.35 group 92% had an Apgar score at one minute of 8 or over; and 89% in the 0.25 group. The onset to regular respiration was within one minute in 84% of the 0.35 group and 88% of the 0.25 group. The differences are not significant. No baby required artificial ventilation.

Blood Loss.—The mean blood loss, assessed by the midwife, was 5 oz. (142 ml.) in the 0.35 group and 8 oz. (227 ml.) in the 0.25 group. There was one postpartum haemorrhage of 40 oz. (1,134 ml.) in the 0.25 group after a vacuum extraction.

Inhaled Concentrations. Vaporizer.—We intended the mothers to inhale a constant concentration of methoxyflurane. However, the wide variations in ventilation which occur during

TABLE VII.—Concentration of Methoxyflurane Delivered at Various Minute Volume Ventilations

Ventilation		Concentrations Delivered by Vaporizer			
Minute Ventilation (l./min.)	Tidal Volume (ml.)	0.25% Setting		0.35% Setting	
		3 min.	30 min.	3 min.	30 min.
5	250			0.35%	0.35%
10	500	0.25%	0.25%	0.35%	0.35%
15	750	0.25%	0.25%	0.33%	0.33%
20	750	0.24%	0.24%	0.33%	0.33%
25	930			0.31%	0.31%
30	1,100	0.21%	0.21%	0.29%	0.29%

labour make this technically difficult to attain with any "draw-over" vaporizer. We chose for the trial the vaporizer which gave us the most constant concentrations under simulated clinical conditions in the laboratory. The variations in concentration with these vaporizers at different minute ventilations are shown in Table VII. The uptake of methoxyflurane by the rubber hose was also investigated. The results show that a standard length of rubber breathing-tube has only a negligible effect on the inhaled concentration (S. C. Khataniar, personal communication, 1967).

Inhaled Concentrations. Ventilation.—Serial measurements of ventilation were made during contractions in 12 out of 23 in the 0.35 group and in 10 out of 20 in the 0.25 group. The ventilation during each contraction in the half-hour immediately preceding full dilatation was selected for study, since minute volume is greatest at the end of the first stage of labour (Reid, 1966). The ventilatory volumes in Table VIII were calculated from measurements made in the first 30 seconds of the contraction, since the majority of our patients stopped inhaling within 50 seconds of the onset of the contraction. None inhaled for less than 30 seconds. The mean and standard deviation for each patient and each group are shown in Table VIII. The distribution of all these measurements of ventilation is shown in Table IX.

TABLE VIII.—Mean Ventilation Per Minute Measured for 30 Seconds of Each Contraction in the Half-hour Preceding Full Dilatation

Patients' Code	Methoxyflurane 0.35%		Patients' Code	Methoxyflurane 0.25%	
	l./min.	Standard Deviation		l./min.	Standard Deviation
A	7.5	0.40	R	8.7	1.23
H	7.7	1.78	B	9.7	1.04
N	8.1	1.11	Q	11.5	1.02
O	8.2	1.65	P	12.8	2.11
C	11.7	1.64	D	18.6	5.76
S	15.7	2.09	E	20.4	5.24
F	16.4	2.02	V	25.3	6.54
G	17.0	1.56	M	26.2	5.92
T	17.5	1.31	J	27.1	4.32
K	20.3	3.97	L	28.6	5.17
U	20.9	2.94			
I	25.0	3.90			
Mean	14.7 ± 6.03		Mean	18.9 ± 7.72	

t test between two groups, $P < 0.20$.

TABLE IX.—Number of Measurements of Ventilation During Half-hour Preceding Full Dilatation

Group	No. of Measurements of Ventilation												Total No.
	0→ 1./min.		10→ 1./min.		15→ 1./min.		20→ 1./min.		25→ 1./min.		30→ 1./min.		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
0.35	39	30	14	11	52	39	15	11	12	9	0		132
0.25	13	13	20	19	14	14	26	25	15	15	14	14	102
Total	52		34		66		41		27		14		234

χ^2 test, $P < 0.01$.

The difference seen between the two groups indicated that higher ventilations accompany the less satisfactory pain relief of 0.25%. This difference is significant. This increase in ventilation is probably due to a mixture of a heightened respiratory response to pain and an attempt on the part of the patient to compensate for inadequate analgesia.

Rejection of 0.45% Methoxyflurane

Eight patients were given 0.45% methoxyflurane (mean duration of inhalation 1 hour 10 minutes; range 30 minutes to 2 hours). Five of the eight mothers (who had all received pethidine) were assessed as "very drowsy" by the anaesthetist. The mean percentage of time of inhalation during which the level of consciousness was deemed unsatisfactory in these eight patients was 17. We could not accept this high liability to drowsiness. Our opinion was confirmed by the midwives, who scored two of these patients as "too drowsy." Pain relief as

assessed by the mothers was no better with this concentration than with 0.35%. It became clear to us that a concentration of 0.45% methoxyflurane introduced no obvious benefit and was too strong for general use unless restrictions were to be placed on the duration of inhalation and perhaps on the use of pethidine.

Discussion

The mothers', the midwives', and the anaesthetist's assessments all demonstrated that 0.35% methoxyflurane is a better concentration than 0.25%.

In our previous trial (Major *et al.*, 1966) our aim was to vary the inhaled concentration for each mother until either there was no reaction to a contraction or she became too drowsy or restless. Therefore on theoretical grounds, because the inhaled concentration was carefully and continuously adapted for the needs of each patient (and must have been optimal), no improvement can be expected on the score recorded then for reaction to contraction. On the other hand, since in our first trial the methoxyflurane had to be "pushed" so as to assay its full potential value, there was inevitably a small incidence of side-effects. This must have reduced somewhat the best possible score for "all factors satisfactory." Our present trial of 0.35% methoxyflurane has equalled the original trial with regard to the score for reaction to contractions (72.8 and 71.8%), and has exceeded it for all factors satisfactory (72.7 and 60.3%). Since the percentage of time "satisfactory" for reaction to contractions with 0.35% methoxyflurane is the same as that achieved in our previous trial, and both a lower and a higher concentration proved less satisfactory, 0.35% must clearly be the optimum concentration. The mothers' and midwives' opinions of the 0.35% support the anaesthetist's assessments. In fact, they show a slight improvement on the results in the original trial.

Our conclusion about the optimum concentration is based on the administration of fixed known inhaled concentrations. We realized, however, that even the best temperature-compensated "draw-over" vaporizer would not give an absolutely fixed concentration, owing to the high ventilation which commonly occurs during contractions. However, the effects of any ventilatory changes are small with the vaporizer used in this trial. The maximum ventilation measured in our patients was about 30 l./min.—that is, a change of about 100% from the mean ventilation. At this the inhaled concentration fell by only 17%—from 0.35 to 0.29% (Table VII). Even at the extreme of ventilation measured in our patients this slight fall in inhaled concentration has a relatively small effect on the alveolar concentration, because of the large increase in the coincidental and causative minute volume (Mushin and Galloon, 1960).

Our recommended concentration of 0.35% methoxyflurane is less than that reported by other workers. Bodley *et al.* (1966), using a reputed 0.5% methoxyflurane from a Cyprane A.E. vaporizer, found that 82.2% of mothers thought the pain relief complete or adequate. However, 12.7% were unco-operative as judged by the anaesthetist-observer. Johnstone (1963), using an uncompensated vaporizer with "0.5%," found the analgesia inadequate, but 4 out of 25 (16%) of his patients were too sleepy to co-operate in the second stage. Canadian and American workers (Romagnoli and Korman, 1962; Savel *et al.*, 1967) also used an uncompensated inhaler—the Cyprane—at the setting recommended by Messrs. Abbott in their literature. Holl and Shnider (1967) have shown that the Cyprane vaporizer gives an initial concentration of 1%, falling in a few minutes to between 0.4 and 0.5%, and that general anaesthesia may develop. It is important to stress that our own results were achieved with a virtually constant inhaled concentration from a vaporizer well compensated for temperature and over a wide range of ventilation. It is clear from our

trial that a change in inhaled concentration of 0.1%, which may appear small, does in fact make a great difference to the results.

Our ultimate aim is to determine whether methoxyflurane is suitable for administration by unsupervised midwives. We therefore observed strict criteria in seeking for a concentration which would not only give a degree of analgesia at least as good as that commonly attained with trichloroethylene, but in addition would ensure full co-operation of the mother during delivery—not always a feature of existing methods. The value of methoxyflurane depends on whether this is possible: the results of our studies indicate that it is. Furthermore, the quality of the pain relief appears to be quite different from that seen with either trichloroethylene or nitrous oxide. The mother lies quietly, looking well sedated but quite able to co-operate. Many mothers comment spontaneously that they feel detached from the process of labour and that any pain seems remote.

The only side-effects of note were nausea and vomiting, well known to occur in association with labour. The incidence of these in our trial (0.35 group), bearing in mind that our inquiries extended for 24 hours after delivery, was comparable to that observed in connexion not only with methoxyflurane but with other analgesics as well (Johnstone, 1963; McAneny and Doughty, 1963; Bodley *et al.*, 1966; Ransom, 1966).

Our initial experimental study was concerned with developing a screening method to ascertain the value of methoxyflurane as a self-administered obstetric analgesic. The method has clearly proved able to produce reliable predictions about the intermittent use of methoxyflurane and of the concentration required. In addition, it has done so with remarkable economy of patients. Now that we have established that methoxyflurane has attractive qualities as an obstetric analgesic we believe that it should be given a wide field trial. This we propose to do.

Summary

The present investigation has confirmed the value of our previously published method for screening obstetric analgesics from which we predicted that 0.35% methoxyflurane would prove suitable for intermittent self-administration during labour.

Fixed inhaled concentrations of 0.35% and 0.25% methoxyflurane in air, from carefully calibrated thermo-compensated vaporizers, were compared. The results were assessed by an anaesthetist, by the mother, and by the midwife. All these assessments indicate that 0.35% is significantly better than 0.25% methoxyflurane. A higher concentration introduces an unacceptable degree of drowsiness. A field trial is now in progress.

We wish to thank our obstetric colleagues and the midwives at the Maternity Unit, St. David's Hospital, Cardiff, for their enthusiastic help and collaboration during this trial. We would also like to acknowledge the useful comments and criticisms of W. W. Mapleson, Ph.D., and of many other colleagues. This work was partially supported by a grant from Abbott Laboratories Ltd. The vaporizers were kindly presented by Longworth Scientific Ltd. (Penlon).

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Improving the Acceptability of Oral Continuous Progestogens in Microdosage for Fertility Control

JUAN ZAÑARTU,* M.D.

Brit. med. J., 1967, **4**, 771-772

The use of continuous microdoses of progestogens is a new concept in fertility control, and a major improvement of oral contraception. Introduced by Martinez-Manautou, Cortez-Gallegos, and Rudel in 1964, it has aroused an increasing interest in the medical profession because of its simplicity, excellent tolerance, and effectiveness. These advantages explain its present popularity (Martinez-Manautou *et al.*, 1966a, 1966b, 1967a, 1967b, 1967c; Martinez-Manautou and Rudel, 1967).

Our own experience with oral continuous chlormadinone acetate 500 µg. in 390 young fertile women observed during 3,400 months confirms the qualities recently reported by Martinez-Manautou *et al.* (1967a) in a much larger group of women followed during 13,202 cycles. However, we have had a slightly higher incidence of accidental pregnancies due to therapy failure (3.3 per 100 treated women) (Zañartu *et al.*, 1967a).

The method is particularly useful in women intolerant to conventional oral oestrogen/progestogen contraceptives. It requires a much lower dosage to inhibit fertility, without necessarily interfering with ovulation—another advantage particularly for young women wishing to plan their families (Rudel and Martinez-Manautou, 1966).

However, according to recent reports irregular uterine bleeding and menstrual cycles are significant side-effects in more than 35% of the users. In our observations, unfortunately, the incidence of irregular uterine bleeding, prolonged menstrual cycles, and amenorrhoea is high enough to be annoying. Indeed, it is a factor which causes women to discontinue therapy (Zañartu *et al.*, 1967a).

This paper reports a simple improvement in an attempt to correct such a side-effect.

Material and Methods

Fifty young fertile women who had previously taken oral contraceptives were selected from a large group. They used conventional "combined" or "sequential" oestrogens/progestogens, but because of poor tolerance this method was discontinued, and oral chlormadinone acetate (0.5 mg. daily) was given instead. While they were under oestrogen/progestogen therapy their menses were regular and acceptable. The subjects were from an educated and high socio-economic group; they had completed high school and many were professional women enjoying a comfortable life.

Once the new therapy was started menstrual records were carefully kept. Patients were seen at regular intervals of three to four months, and a complete clinical and gynaecological examination was performed at each control.

Clinical and laboratory findings on subjects under continuous chlormadinone therapy have been reported (Zañartu *et al.*, 1967a). This particular group of women were included in our study because while on oral continuous chlormadinone they presented irregular uterine bleeding (mainly hypermenorrhoea, spotting, and/or intermenstrual bleeding), prolonged cycles

(over 45 to 60 days), or amenorrhoea. The condition interfered with the acceptability of the method. In fact the fear of being pregnant arose when menses were delayed or because of amenorrhoea. This increased the incidence of office calls and consultations. Evidently they were annoyed by the disturbance in spite of the good tolerance of the method.

To correct uterine bleeding and regulate cycles, oral "accessory" oestrogens were given for five to seven days in each calendar month, or from the 21st to the 25th or the 19th to the 25th day of the menstrual cycle. In other words, one extra tablet of conjugated oestrogens (Premarin 2.5 to 5 mg. daily) was given during these days because of the good tolerance to it. However, 0.05 mg. of ethinyloestradiol was occasionally given in the same fashion when well tolerated.

The possibility that accessory oestrogens could reverse the cervical mucous changes induced by the progestogen, and nullify its contraceptive effect, was studied by post-coital Huhner-Sims tests performed at the expected ovulation time of the cycle.

Results

The effect of "accessory" oestrogen therapy in regulating menstrual cycles and making uterine bleeding more comparable with normal menses was evident, and it was satisfactory to all treated subjects. This effect was achieved without interference with the antifertility action of oral continuous contraceptive therapy with microdoses of chlormadinone acetate. In fact not a single accidental pregnancy occurred in this group during 650 months of observation.

The accessory therapy was added during five or seven days in each calendar month while the subject received one 0.5-mg. tablet of chlormadinone acetate daily. The effect of this additional therapy on uterine bleeding and cycles is summarized in the Table. It will be seen that the average duration of uterine bleeding and menstrual cycles is quite acceptable.

"Accessory" Oestrogen Therapy in 50 Women

No. of Cases	Oestrogen Therapy		Uterine Bleeding (Average) Duration Days	Menstrual Cycles (Average Duration) Days
	Daily Dose	No. Days*		
35	C.O. 2.5 mg.	5 or 7	4.7 (3 to 8)	29.7 (26 to 33)
12	C.O. 5.0 mg.	5	3.9 (3 to 7)	28.5 (27 to 32)
3	E.O. 0.05 mg.	5 or 7	3.5 (2 to 6)	26.9 (26 to 31)

C.O. = Conjugated oestrogens (Premarin).

E.O. = Ethinyloestradiol.

* Of each calendar month, or from 21st to 25th day or 19th to 25th day of the cycle.

During the study 45 tests were performed 4 to 12 hours after coitus at about the expected ovulation time of the corrected cycle. In 35 tests the anti-oestrogenic effect of chlormadinone was evident: the mucus was thick, tenacious, with low spinnbarkeit, was loaded with leucocytes and cells, and did not crystallize. However, this effect was minimal in 10 tests. The physical characteristics of mucus were similar to those observed at about the 14th or 15th day of normal non-treated

* Department of Fertility, University Maternity Hospital, University of Chile Medical School, Santiago, Chile.

ovulatory cycles with good sperm tolerance. The tests were performed from 10 to 18 days after the last additional oestrogen tablet was taken.

Discussion

The incidence of uterine bleeding and menstrual cycle modifications in women receiving oral continuous chlormadinone acetate in microdoses is significant. In our experience 153 (39.2%) out of 390 women presented some alterations in uterine bleeding while using this contraceptive method; amenorrhoea, for instance, was observed in 15% of our subjects. However, the modifications of menstrual cycles were slightly less frequent (in 147 (37.6%) out of 390 treated subjects). The most annoying symptoms indeed were amenorrhoea, prolonged cycles, and intermenstrual bleeding.

These alterations are apparently related to the anti-oestrogenic effect of the progestogen and are shown by those subjects more sensitive to such action. Furthermore, our macroscopic and microscopical observations on ovaries of subjects treated with 0.5 mg. of chlormadinone daily, who presented prolonged menstrual cycles or amenorrhoea, showed that ovulation was inhibited. A marked effect of the compound at the endometrium stroma and glands was also evident (Zañartu *et al.*, 1967b).

These findings help us to understand why additional oestrogen therapy given for a few days for bleeding and cycle regulation could eventually reverse the effect in cervical mucus of chlormadinone 0.5 mg. daily, and yet preserve the main contraceptive effect of the therapy at other levels of the reproductive system (endometrium, endosalpinx).

The gratifying action of the accessory oestrogens by correcting uterine bleeding and regulating cycles significantly helps to improve the acceptability of this valuable contraceptive method. It has also been valuable in improving the acceptability of other progestogens in microdoses.

Summary

Fifty women presenting alterations of uterine bleeding and menstrual cycles while using oral continuous 0.5-mg. chlormadinone tablets for fertility control were given additional oral oestrogens to correct the condition. Conjugated oestrogens 2.5- or 5-mg. tablets were given for five to seven days in each calendar month. Ethinyloestradiol 0.05 mg. was also used when well tolerated. The continuous oral administration of chlormadinone tablets was maintained.

Accessory oestrogens were useful in correcting the bleeding and cycle disturbances resulting from the anti-oestrogenic effect of microdoses of oral chlormadinone without interfering with the fertility inhibition effect. It is suggested that the addition of oral oestrogens is useful to improve acceptability of continuous chlormadinone in microdoses as a contraceptive while maintaining the outstanding properties of this therapy.

Chlormadinone acetate 0.5-mg. tablets were generously donated by Syntex International (Mexico) and E. Merck-Darmstadt (Germany). We are indebted to Ayerst Laboratories Inc. (New York) for the supply of conjugated oestrogens (Premarin).

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Transfer Factor (Diffusing Capacity) for the Lung in Simple Pneumoconiosis of Coal Workers

J. P. LYONS,* M.D.; W. G. CLARKE,† M.S.R., A.R.P.S.; A. M. HALL†; J. E. COTES,† D.M., M.R.C.P.

Brit. med. J., 1967, 4, 772-774

Established simple pneumoconiosis of coal workers is accompanied by a widening of the alveolar-arterial tension difference for oxygen (Brasseur, 1963) and a minimal reduction in the transfer factor (diffusing capacity) for the lung, measured by the steady state carbon monoxide method (Podlesch, Stevanovic, and Ulmer, 1966). These changes are probably due to uneven distribution of pulmonary ventilation and perfusion. The finding of a low transfer factor by this method is not necessarily evidence for a transfer defect; this is better assessed by the single-breath carbon monoxide method, which is less susceptible to the effects of uneven distribution. With this method a number of workers have found a proportion of men with simple pneumoconiosis to have a transfer defect (for references see Nicaise, Vereerstraten, and de Clercq, 1967); the change may be accompanied by an increase in the quantity of reticulum in the lung parenchyma (Gaensler, Hoffman, and

Elliott, 1960). A weak association with the punctate or pin-head type of radiological opacities has been suggested by Engle and De Coster (1965). The present observations on men attending a pneumoconiosis medical panel appear to confirm this finding, which is also supported by recent work from Belgium (L. Billiet, personal communication to J. E. C.).

Subjects and Methods

Over a period of 16 months men attending the Pneumoconiosis Medical Panel, Cardiff, who were thought to have simple pneumoconiosis of a pin-head type (punctiform opacities up to 1.5 mm. in diameter (International Labour Office, 1959)) together with some of a micronodular type (opacities of 1.5-3 mm. in diameter) were referred to the Pneumoconiosis Research Unit for assessment. Here the chest radiographs were read in duplicate by an independent observer (W. G. C.); respiratory symptoms were assessed by use of the M.R.C. Respiratory Questionary (Medical Research Council, 1960); and measurements were made of ventilatory capacity,

* Pneumoconiosis Medical Panel, Cardiff.

† Pneumoconiosis Research Unit of the Medical Research Council, Llandough Hospital, Penarth, Glamorgan.

Requests for reprints and for details of the physiological results should be addressed to Dr. Cotes.

lung volumes, and transfer factor (single breath for carbon monoxide), standard methods being used (Cotes, 1965; Meade *et al.*, 1965; International Labour Office, 1966). For each subject the findings on assessment of lung function were reported on at the time by one of us (J.E.C.) as being within the normal range or showing nonspecific changes, or as showing a ventilation defect of an obstructive type (low F.E.V., high R.V./T.L.C., and impaired mixing of inspired gas, but normal T.F. and T.L.C.), a transfer defect (low T.F. with normal or reduced T.L.C. and no evidence for airway obstruction), or possible emphysema (low F.E.V. and increased T.L.C. with or without a reduced transfer factor).

Results

Forty-seven subjects were thought to have simple pneumoconiosis involving all rib spaces in at least one lung (categories 2 and 3 of the International Labour Office classification). Of these men, on the basis of the first reading of the chest radiograph by W.G.C., 16 were thought to have only pin-head opacities, 11 only micronodular opacities, and 20 mixed opacities or additional lesions. The findings for the subjects classified in this way are summarized in Table I. The results of the lung function tests for the subjects who appeared to have simple pneumoconiosis of a pure pin-head or a pure micronodular type are reported in greater detail in Table II.

TABLE I.—Summary of Findings

	M	P	P+Mand/or Other Lesions
No. of subjects	11	16	20
Category of pneumoconiosis			
2 (No.)	1	3	—
3 (No.)	10	13	—
Grade of breathlessness			
1-2 (No.)	5	6	7
3-5 (No.)	6	10	13
Grade of bronchitis*			
0 (No.)	7	9	9
1-2 (No.)	4	7	11
Years of work underground	33.2	32.9	38.7
Normal or near normal lung function (No.)	9	4	5
Ventilation defect of obstructive type (No.)	2	1	5
Transfer defect (No.)	—	10	10
Possible emphysema (No.)	—	1	—

* Medical Research Council (1965).

M = Pure micronodular type. P = Pure pin-head type.

TABLE II.—Findings on Assessment of Lung Function (Mean Values)

	M	P
Number	11	16
Age (years)	50.4	51.6
Height (m.)	1.73	1.69
Weight (kg.)	71.9	65.8
Forced expiratory volume (F.E.V. ₁) (l.)	2.55	2.40
Forced vital capacity (F.V.C.) (l.)	3.75	3.71
(F.E.V. ₁ /F.V.C.) × 100 (%)	67.4	63.9
Total lung capacity (T.L.C.) (l.)	5.86	6.14
Residual volume (R.V.) (l.)	2.13	2.31
(R.V./T.L.C.) × 100 (%)	36.3	37.3
Transfer factor (T.F.) (ml./min./mm. Hg)	28.2	19.8*
Diffusing capacity of alveolar capillary membrane (Dm) (ml./min./mm. Hg)	49.4	31.4*
Volume of blood in alveolar capillaries (Vc) (ml.)	68.7	50.3†
Mixing index (VA/VA)	0.99	0.96

* P < 0.01. † P < 0.05.

This shows that the mean transfer factor for the men with the pin-head opacities is significantly less than that for the men with the micronodular opacities. The other findings are within the normal range.

In view of this result the x-ray films were re-read by W.G.C., who at no time had knowledge of the lung function findings. His readings differed from those on the first occasion only to the extent that two of the men initially graded as pure pin-head were now thought to have mixed pin-head and micronodular opacities. In both of these men the transfer factor was near to the average for their age and height. In addition the data were examined with respect to smoking habits, when it was found that the proportion of smokers among the men with the pin-head opacities (13/16) was higher than among those

with the micronodular opacities (3/11). The smokers had lower values for the transfer factor than the non-smokers and ex-smokers (mean difference associated with smoking 6.2 ml./min./mm. Hg, P < 0.05). However, the transfer factors for both the smokers and the non-smokers and ex-smokers were, on average, lower in the men with the pin-head opacities than in those with the micronodular opacities; the overall difference after adjusting for smoking was 5.4 ml./min./mm. Hg (P ≈ 0.07).

Discussion

The subjects for this study differ from the general population of coal miners in that they were referred after attendance at the Pneumoconiosis Medical Panel. The group may therefore be biased in two ways: (1) with respect to men having respiratory symptoms, because such men may be more likely to attend on their own initiative than men without symptoms; and (2) with respect to the extent of the radiological abnormality, because men with dense or progressive lesions are likely to be recalled to the Panel at more frequent intervals than those with less pronounced pneumoconiosis. However, that the former selective process was operating to a comparable extent for the men with both pin-head and micronodular opacities is suggested by the similarity of their average grades for both breathlessness and bronchitis (Table I). Therefore the finding for the transfer factor of a lower average value in the pin-head cases is unlikely to be biased on this account.

The cause for the low transfer factor is not known; it may be related to the dust in the lung or the reaction of the lung tissue. For example, it may be a result of more dust being present in the lung with the pin-head lesions than in one where the micronodular lesions predominate. Evidence on this aspect is so far incomplete (Rossiter *et al.*, 1967), but it is relevant that the average periods of work underground (Table I) and of work on the coal face do not differ to a material extent between the two groups of men. The nature of the reaction in the lung tissue in the pin-head cases is also unknown. The radiological appearance on a good-quality x-ray film is often an overall obscuration of the lung markings and of the "black" air spaces by the minute opacities, particularly at the lung bases. In addition there may be some linear opacities. These findings are suggestive of changes in the lung parenchyma, but the number of cases that were classified by their type of pneumoconiosis during life and have since come to necropsy is not yet large enough for a conclusion to be reached on this point.

Any morphological differences which may exist are unlikely to be related to diffuse infiltration of the rheumatoid type, since the serum titres for aggregated human gamma-globulin show little difference between the pin-head and the micronodular cases. In addition, the rate of progression to massive fibrosis, which may be dependent on this process (Wagner and McCormick, 1967), is if anything less for the pin-head cases. These points need to be clarified by a longitudinal study. In addition the apparent absence of a relation between the low transfer factor and breathlessness or other symptom requires examination by study of both these subjects in more detail, and other subjects selected by a process of random sampling from among men with simple pneumoconiosis.

Summary

Among men attending a pneumoconiosis medical panel a gas transfer defect of the lungs was observed in 10 out of 16 with simple pneumoconiosis whose opacities were of a pure pin-head type, but in none of 11 men whose opacities were of the micronodular type.

We are indebted to Dr. J. Watkins-Pitchford, Chief Medical Officer, Ministry of Social Security, and to members of the

Pneumoconiosis Medical Panel, Cardiff, for referral of cases; to Messrs. P. D. Oldham and G. Berry for statistical advice; and to Miss E. Dawkins for technical assistance.

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Outbreak of E.C.H.O. Virus Type 30 in a General Practice

D. H. IRVINE,* M.D.; A. B. H. IRVINE,* M.B., CH.B.; P. S. GARDNER,† M.D., DIP.BACT.

Brit. med. J., 1967, 4, 774-776

For many years E.C.H.O. viruses have been known aetiological agents in human disease, particularly aseptic meningitis; examples include type 4 (Chin *et al.*, 1957), type 6 (Kibrick *et al.*, 1957), and type 9 (Tyrrell and Snell, 1956). One of the latest to be linked with aseptic meningitis is type 30, described in Scotland originally as the "Frater virus" (Duncan, 1960). A virus now known to be identical was described in the United States as the "Bastianni virus" (Plager and Decher, 1963).

E.C.H.O. virus type 30 was first incriminated in illness in this country in 1950-60 and has been encountered only occasionally between 1960 and 1964 (Grist and Bell, 1967). Current information on symptomatology is based on isolated cases seen in hospital practice. In this communication we describe an outbreak of a febrile illness observed in a general practice for which there is evidence that the causal agent may have been E.C.H.O. virus type 30.

Present Investigation

The practice has two principals and a list of approximately 5,140 patients. Though the majority of patients are resident in Ashington, a colliery town with a population of 28,000 people, a considerable number live either in the adjacent urban

area of Stakeford, which lies on the opposite bank of the River Wansbeck, or in one of five near-by villages. The practice boundary is within a 3-mile (5-km.) radius from the centre of Ashington (see Fig.).

The outbreak began in mid-June 1966, when two children presented within a day or two of each other a clinical picture suggestive of aseptic meningitis. Faeces were sent for laboratory examination, but before the results became available two further cases were seen, though the illness was less severe. As it was now evident that an unusual illness was prevalent in the practice, arrangements were made to widen the field of study. It was agreed to observe any new patients presenting with a febrile complaint in whom it was impossible initially to make a definite diagnosis or who had symptoms similar to those seen in the earlier cases. This system of screening was thought desirable since no pathogen had been identified at that stage. It was anticipated that in some cases an alternative diagnosis would emerge; in the event these cases, with one exception, were grouped together before individual laboratory results became available (group C below).

Laboratory Methods.—Specimens of stool were taken from all suspected cases. On arrival in the laboratory these specimens were emulsified in a 10% suspension and centrifuged. Then 0.2 and 0.1 ml. respectively were inoculated into two monkey-kidney and two Hep. 2 tissue culture tubes. Tissue culture tubes were examined daily; suspected virus agents were passaged into fresh tubes and identified by neutralization against specific antisera. Details of the laboratory procedures used have been described (Gardner *et al.*, 1961; Gardner and Cooper, 1964).

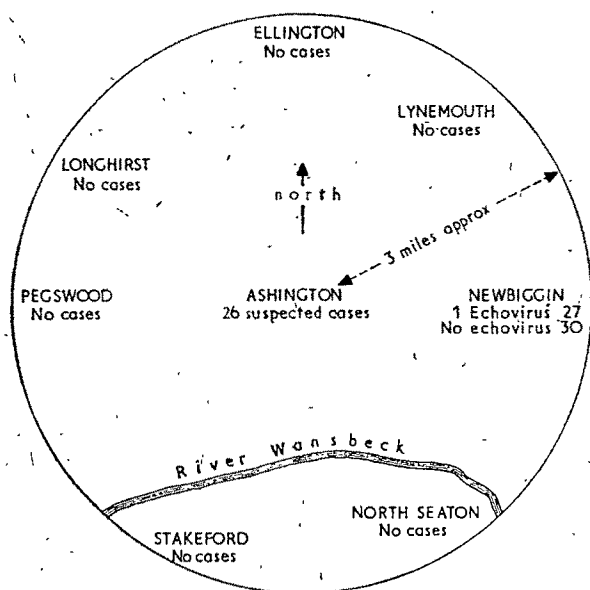
Results

Altogether 46 patients were examined in the period from 10 June to 22 August. It has been found convenient to classify them into three groups as follows:

Group A: Twenty-two patients (9 female, 13 male) with a symptom pattern peculiar to the outbreak in whom E.C.H.O. virus 30 was isolated from faeces.

Group B: Four patients (all female) with similar clinical features as group A in whom no virus was found in faeces.

Group C: Twenty patients (7 female, 13 male) presenting with a febrile malaise and later shown to be suffering from another condition. E.C.H.O. virus type 30 was not identified in their faeces.



Distribution of cases within practice boundary.

* General Practitioner, Ashington, Northumberland.

† Consultant Virologist, Royal Victoria Infirmary and University of Newcastle upon Tyne.

For further analysis groups A and B have been added together. Table I shows the relation of the outbreak to time; the apparently sudden onset was noted by other practitioners in the town. The end-point appears to have been reached as quickly, since no patients with a typical history were seen after 22 August. In Table II the age distribution of those with suspected E.C.H.O. virus 30 infection is compared with the overall practice population. The attack rates reported should be viewed with caution, as a numerically undetermined fraction of the total practice list is distributed in the outlying villages (see Fig.), where no cases were seen. Thus the attack rates given are probably an underestimate of the true rate in Ashington itself (Table II).

TABLE I.—*Relation of Outbreak to Time*

	20 June	10 July	30 July	20 Aug.
No. of cases in groups A and B	4	9	10	3

TABLE II.—*Age Distribution of Cases and Practice Population*

Age	No. of Patients		Attack Rate/1,000
	Total Practice	Suspected E.C.H.O. Virus 30 Infection	
0-9 years	711	14	19.70
10-19 "	703	5	7.11
20-29 "	618	3	4.85
30-39 "	634	3	4.73
40-49 "	666	1	1.50
50+ "	1,805	0	—

The geographical distribution of cases is interesting (see Fig.). Clearly the outbreak was extremely local, since no cases were reported in outlying areas of the practice despite the very short distances involved. In four instances two people in the same household were affected. Similarly, two patients in group B were on friendly terms and in social contact with two others in group A. They, in turn, were neighbours of two additional families in group A, which suggests that groups A and B may have a common causal agent.

Cases in group C were distributed randomly throughout all geographical areas of the practice.

It may be helpful to consider the main clinical groups in greater detail.

Groups A and B

Both in children and in adults the principal symptoms included headache, malaise, muscle pains, vomiting, and abdominal pain. The duration of complaint varied in individual patients from one to seven days, with an average of three days. Invariably the illness was of rapid onset—a period of two to three hours—and caused most distress in the first 24 hours.

Headache and muscle pains were experienced by all patients; indeed, headache was often severe, and it was the commonest presenting symptom. Vomiting (18 cases) was often limited to the first day. Colicky abdominal pain (11 cases) was not associated with a change in bowel habit but gave rise to concern in two patients when generalized abdominal tenderness and guarding were observed for several hours. Photophobia (eight cases) never persisted more than 18 hours.

Examination usually revealed only tenderness of muscle on palpation and a temperature rising above 100° F. (37.8° C.) (19 cases). Neck rigidity (four cases) was marked in the first two patients of the series, while a fleeting macular rash was seen once—otherwise the skin was not involved.

Illustrative case summaries from group A are given.

Case 1.—A boy aged 11 years gave a three-day history of increasingly severe headache, photophobia, and nausea. Examina-

tion at the first visit showed no abnormal signs except a pyrexia of 101.2° F. (38.4° C.); later that day he became sick, while the headache was unabated. Neck rigidity and Kernig's sign were then present. Thereafter the clinical course was one of rapid improvement to full recovery within two days.

Case 2.—A girl aged 7 years attended school one morning feeling perfectly well, but had to return home at lunch-time because she suddenly developed intense headache and was unable to focus on the blackboard properly. In the afternoon she began to vomit. Examination revealed a temperature of 101.8° F. (38.8° C.), raised pulse rate, and slight neck rigidity. By evening the headache was subsiding; the following morning the child had fully recovered.

Case 9.—A married woman aged 33 became ill suddenly one afternoon complaining of intense headache, malaise, nausea, and quite severe abdominal pain. There was generalized muscle-aching. The following day she requested her doctor to visit because of intense pain in the right loin and right iliac fossa. Headache was still present, now with photophobia. Abdominal examination revealed marked tenderness and guarding in the right iliac fossa, and a diagnosis of appendicitis was considered. Next day a generalized macular rash was present for a few hours; the patient felt better, as both headache and abdominal pain were subsiding. Two days later, apart from slight weakness, recovery was complete.

Case 18.—A boy aged 9 years gave a four-day history of intermittent malaise, nausea, headache, and abdominal colic. On the day of consultation his headache had worsened and he said that light hurt his eyes. The only abnormal physical sign was a temperature of 98.6° F. (37° C.), though his mother had recorded a higher temperature earlier. He returned to normal health two days later.

Group C

This group comprises patients presenting with a nonspecific febrile illness, later, with four exceptions, to develop manifestations of other infections. Eight patients had upper respiratory infections or tonsillitis. Four with watery diarrhoea showed none of the other main clinical features described in groups A and B. A urinary infection in one child was confirmed by laboratory examination, and acute appendicitis was found at operation in an adult. The firm diagnosis of infection with E.C.H.O. virus 9 was made in another child and later supported by laboratory findings. E.C.H.O. virus 27 was isolated from a boy who later complained of headache; he lived in an outlying village thought to have escaped the outbreak of E.C.H.O. virus 30. Finally, there were the four patients in whom diagnosis was never made. All were young children, feverish one day and better the next, with no localizing symptoms or signs whatsoever.

Discussion

It is often tempting to suggest a cause-and-effect relationship when viruses are identified in patients presenting with an otherwise inexplicable febrile illness. However, there is evidence that the finding of E.C.H.O. virus 30 in this series is of aetiological significance. Thus the outbreak began at a time of year when overt infection with E.C.H.O. virus is known to be most common. Typically, children are principally affected, as we found. Furthermore, the cardinal symptoms described in suspected cases (groups A and B) differ little from those in illness caused by other E.C.H.O. viruses (Sanford and Sulkin, 1959) and contrast sharply with the diverse patterns in group C, with the exception of the boy excreting E.C.H.O. virus 27.

The precise geographical localization of the outbreak, the first to be described linked with E.C.H.O. virus 30 so far as we know, is reminiscent of another attributed to E.C.H.O. virus 9 which was confined to a new residential estate in North-east England (Wright *et al.*, 1961).

Our findings suggest that, though E.C.H.O. virus 30 has been found only sporadically over the last six years, it is not a new virus and adults have an immunity to it.

Summary

An outbreak of a febrile illness confined to a local geographical area within a general practice is described. E.C.H.O. virus 30 was isolated from faeces in a majority of cases. The illness was of rapid onset but lasted only a few days, and the principal symptoms included headache, muscle pains and malaise, vomiting, colicky abdominal pain, and photophobia. Evidence that E.C.H.O. virus 30 was of aetiological significance in the series is discussed. Although E.C.H.O. virus 30 has been found only sporadically over the last six years, the results suggest that it is not a new virus and that adults have an immunity to it.

We are indebted to the technical staff of the department of virology of the Royal Victoria Infirmary for their help.

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Calf Muscle Denervation for Intermittent Claudication*

N. V. ADDISON,† M.B., F.R.C.S.

Brit. med. J., 1967, **4**, 776-778

It is now a well-established fact that the ideal treatment for femoropopliteal occlusions which cause intermittent claudication in the calf is a bypass graft. An autogenous saphenous vein is undoubtedly the best type of graft to use with good and lasting results (Darling *et al.*, 1967). The indications for inserting a graft usually depend on the individual surgeon, who may operate for intermittent claudication which is not particularly disabling. Others may limit the procedure to those with severe claudication, rest pain, or impending gangrene (Shucksmith and Addison, 1962). The reversed saphenous vein bypass graft is usually taken from the common femoral to the distal popliteal artery behind or below the knee joint. The problem arises when the distal popliteal artery is grossly diseased or totally blocked. Under these circumstances it may be possible to take the graft to the posterior tibial or peroneal arteries if the saphenous vein is left in situ. If both distal popliteal and tibial vessels are unsuitable for grafting then only palliative treatment can be considered. Claudication can be relieved or the claudication distance increased by inactivation of the calf muscles where the pain develops. Two operations can be performed to effect this inactivation, one by Achilles tenotomy (Boyd and Bloor, 1960) and the other by denervation of the calf muscles.

If these muscles are paralysed the patient learns to use other muscles, including the hamstrings, when walking. Learmonth and Slessor (1952) describe this procedure of myoneurectomy and claim that patients obtain a walking distance some five times greater than preoperative distances.

If the distal vessels are blocked and there is severe rest pain in the foot or calf then an above-knee or Gritti-Stokes amputation may be necessary, though a lumbar sympathectomy is well worth trying, especially if pain is relieved by a medical sympathectomy (Martin, 1963). Obviously rest pain cannot be relieved by inactivation of the calf muscles, but if it is localized to a small area in the foot, treatment by a selective peroneal or anterior tibial neurectomy may help.

I have adopted the method of calf muscle denervation for patients with popliteal or tibial occlusions, and for some older patients with calf pain, as an alternative to a bypass graft. This

paper is based on the first 40 denervations carried out during the past four years.

Cause of Ischaemic Pain in Calf Muscles

The cause of intermittent claudication is a relative anoxia of the muscles, and the importance of this anoxia was shown by Pickering and Wayne (1934). They found that by exercising muscles of an anaemic subject with no evidence of arterial disease characteristic pain of intermittent claudication could be produced. The clinical experiments of Lewis (1932) indicate that the direct cause of the pain is not oxygen lack itself but the stimulation of sensory nerves by the metabolic products of muscular activity. When the blood supply is inadequate and oxygenation therefore deficient, metabolic products accumulate. Lewis referred to the pain stimulus as "factor P." The nature of the chemical pain factor is unknown but is probably acid, and ingestion of sodium bicarbonate was found to increase the amount of exercise required to cause pain.

Nerve Supply of Calf Muscles

In a so-called motor nerve supplying a limb muscle at least 30 to 40% of the fibres are sensory in function and have their cell bodies in the dorsal root ganglia of the segmental nerves.

The endings of the afferent fibres in striated muscle vary a great deal in structure. The simplest ones are very fine non-myelinated nerve fibres with no specific ending. Some run in perivascular plexuses, and others are found in connective tissue, and it has been suggested that these are pain fibres (Bowden, 1960).

The medial popliteal nerve, arising from the fourth and fifth lumbar nerves and the first, second, and third sacral nerves, supplies the two heads of the gastrocnemius and the soleus. In the popliteal fossa it is concealed at first by the semi-membranosus and other hamstring muscles. It passes superficial to the popliteal vessels from the lateral to the medial side, and is thereafter found deep to the popliteus muscle under cover of the gastrocnemius and plantaris. Two branches arise in the fossa, one for each head of the gastrocnemius, and usually enter these muscles at the borders of the popliteal fossa. A nerve for

* Based on a lecture given at the invitation of the Professor of Surgery, Jefferson Medical College, Philadelphia, U.S.A., on 25 April 1967.
 † Consultant Surgeon, Royal Infirmary, Bradford.

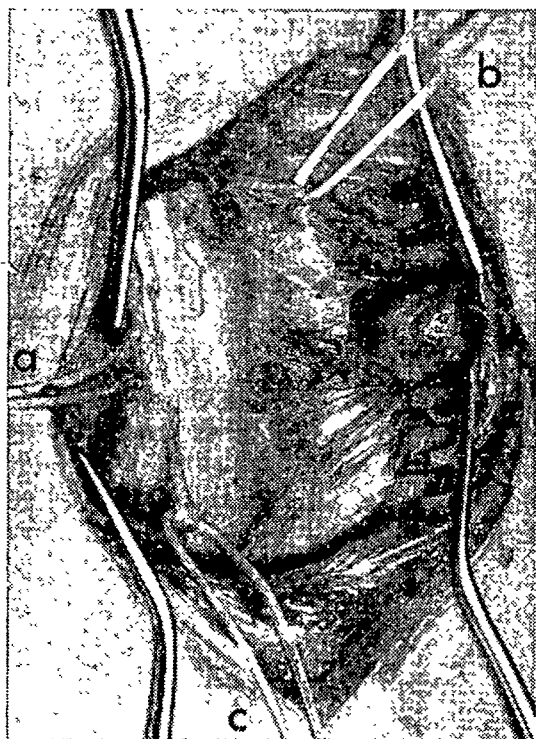
the soleus enters the superficial surface of the muscle near its proximal border and a branch from the posterior tibial nerve (which begins at the distal border of the popliteus) enters the soleus on its deep surface near the middle of the leg. The soleus can never be completely denervated unless this branch is divided. At the inferior angle of the popliteal fossa the medial popliteal nerve gives off the sural nerve, which leaves the fossa by passing downwards between the two heads of the gastrocnemius and continues down the posterior aspect of the calf with the short saphenous vein.

Operative Procedure

The patient lies in a prone position under general anaesthesia which must be light; under no circumstances must a long-acting muscle relaxant be used, because the nerves are identified by pinching them with artery forceps to stimulate immediate contraction of the muscles. If these are paralysed by long-acting relaxants, then the calf muscle nerves cannot be properly identified and there is the danger of dividing the wrong nerve. The sural nerve can be mistaken for a nerve to the calf muscles, and if this is divided then anaesthesia will result on the lateral side and back of the distal third of the leg, ankle, and heel and on the lateral border of the foot.

An incision about 2 in. (5 cm.) in length is made in the midline in the lower part of the popliteal fossa. The deep fascia is divided and the heads of the gastrocnemius are held apart with a self-retaining retractor. Care must be taken not to damage the sural nerve or popliteal veins that may lie superficial to the medial popliteal nerve, which is identified before dissecting out the nerves to the muscles.

There are usually three nerves to be divided and ligated with thread (see Fig.). Coagulation diathermy should be avoided and



Operation of calf muscle denervation showing silk tapes around the nerves to the lateral head of gastrocnemius (a), the medial head of gastrocnemius (b), and the superficial part of soleus (c).

haemostasis should be complete before suturing the deep fascia and skin. If a lumbar sympathectomy is to be carried out then the patient is turned over and this is proceeded with. The patient is got out of bed as soon as he becomes fully conscious, the following day he is encouraged to walk up and down the

ward, and he is discharged 48 hours after operation. It is most important to walk immediately, wearing a firm crêpe bandage to support the calf.

Selection of Cases for Operation

Any patient with disabling claudication whose arteriogram showed occluded distal popliteal or tibial arteries was considered for muscle denervation, provided that the symptoms had been present for at least one year, as about 50 to 60% of patients with untreated claudication improve spontaneously up to 12 months after the onset, owing to the development of a collateral circulation. The presence of calcification on a plain radiograph of the lower limb was also thought to be unsuitable for a vein graft, though some surgeons do not regard calcification as a serious hazard.

It is important to select only those patients with pain in the calf. If claudication occurs in the buttocks and thighs as well then surgery of the aortoiliac region is necessary to relieve the pain. Unilateral calf claudication was desirable for a good result as it was in Boyd and Bloor's (1960) selection of cases for Achilles tenotomy. It is useful to choose a fairly intelligent patient who will understand the nature and purpose of the operation.

If the foot was cold then a lumbar sympathectomy was carried out at the same time as the denervation of the calf muscles.

Results and Follow-up

In the present series 40 patients have undergone calf muscle denervation, and two of these were bilateral. Their ages varied from 45 to 70 years, the majority being 55 to 64 (Table I). There were four failures in the first six months, due to poor selection of cases, and two of these failures had bilateral denervations.

TABLE I.—Age of 40 Patients Undergoing Calf Muscle Denervation

Age	45-54	55-64	65-70
No. of patients	8	28	4

The remaining 36 patients have been followed up at regular intervals for a minimum of six months and a maximum of 44 months (Table II). There have so far been no deaths in the series.

TABLE II.—Follow-up of 36 Patients After Calf Muscle Denervation

Time (years)	Less than 1	1-2	2-3	Over 3
No. of patients	8	12	12	4

The claudication distance preoperatively was recorded and in 18 patients was 50 to 100 yards (45 to 90 metres), and in 22 patients 101 to 200 yards (91 to 180 metres) (Table III). After operation patients were seen at three-monthly intervals and asked how far they were able to walk on the flat before pain developed. The distances recorded were based on the patient's

TABLE III.—Claudication Distance Before and After Muscle Denervation

Distance		No. of Patients
Yards	Metres	
<i>Before muscle denervation</i>		
50-100	45-90	18
101-200	91-180	22
<i>After muscle denervation</i>		
No change		4 (10%) including 2 bilateral
0-300	0-275	6 (15%)
301-600	276-550	8 (20%)
601-2,000	551-1,830	12 (30%)
No limit		10 (25%)

subjective assessment, which is an inaccurate method of judging results, especially in estimating walking distances less than 500 yards (455 metres). When a patient stated that he could walk over half a mile (800 metres) or indefinitely without pain, the recording of results was made much easier. In the earlier cases an attempt was made to estimate improvement by recording pain when patients were asked to step up and down on to a box 1 ft. (30 cm.) high before and after operation, but the test was not helpful and was therefore abandoned.

Preoperative arteriography carried out in 38 patients showed that 32 had unilateral femoropopliteal blocks, the remaining six being occluded in both legs. In the bilateral occlusions there were four early failures and the other two were not very successful, as their increased walking distance was less than 300 yards (275 metres).

In 20 patients there was associated aortoiliac disease but not occlusions, but this did not appear to have any effect on the final results in 17. In the other three patients there was only slight improvement postoperatively.

Those patients with the most severe disease demonstrated radiologically and a preoperative claudication distance of less than 100 yards (90 metres) did not benefit from surgery as well as those with less severe disease and a longer claudication distance up to 200 yards (180 metres).

It is apparent that the early results are most encouraging, and that at least 70% are able to walk 500 yards (455 metres) or more without pain, and that the long-term results are satisfactory up to three years after operation (Table III).

Complications of Muscle Denervation

There were two cases of deep thrombophlebitis seen earlier on in the series and both responded rapidly to anticoagulant therapy. One case of deep thrombophlebitis in the calf was seen 18 months after operation, but the patient had been able to walk indefinitely without pain after operation until the onset of the attack, which resolved with rest and a firm supporting bandage. One case of pulmonary embolism was recorded in one of the patients suffering from deep thrombophlebitis.

In one case early on in the series a haematoma needed to be evacuated surgically, and in another patient the lateral popliteal nerve was accidentally crushed, but this recovered fully after almost a year. Complete haemostasis, a firm bandage, and immediate ambulation help to eliminate any complications that may arise.

Discussion

The results in this series would appear more favourable than those undergoing Achilles tenotomy reported by Boyd and Bloor (1960). In 72 patients they reported complete relief of pain in only 22%, temporary relief for one year in 21%, and immediate failure in 57%. Claudication developing elsewhere in the same leg or other leg accounted for 50% of their immediate failures. They suggested that their results could have been better with a more careful selection of cases for operation.

Disadvantages of Achilles tenotomy include early union by fibrous tissue of the ends of the divided tendon leading to a return of symptoms. Another disadvantage is the difficulty of walking immediately, as patients must learn to stand with confidence before trying to walk. After calf muscle denervation they can walk immediately, though they all have a slight limp and a few have needed to use a stick, but all regarded this as a small price to pay in return for relief of pain.

Muscle denervation has a more logical approach to the relief of pain than Achilles tenotomy, and its effective action may be due to three factors: (1) paralysis of the gastrocnemii and part of the soleus muscles with wasting; (2) division of somatic afferent pain fibres in the mixed motor nerves; and (3) division of sympathetic afferent pain fibres in the mixed motor nerves. It is possible that division of the motor nerves destroys sympathetic as well as somatic afferent fibres, and this relieves pain to some extent. Relief of intermittent claudication after a lumbar sympathectomy alone may be due to division of afferent pathways, since some patients claim that though their halting distance is unchanged the severity of the pain is diminished (Myers and Irvine, 1966). A lumbar sympathectomy was carried out simultaneously in 12 of the 40 denervations, and it was recorded that six of these patients could walk indefinitely without pain after operation.

In assessing the results of calf muscle denervation it is stressed that improvement was based entirely on the patient's subjective assessment of walking distance without pain. Twenty-two patients (55%) stated emphatically that they could walk about half a mile (800 metres), or indefinitely, and these were judged to be very successful. A further 8 (20%) claimed that their walking distance had increased up to three times their preoperative distance. In view of the difficulty of estimating short distances with any accuracy, these results were not judged as successful as those who could walk half a mile (800 metres) or indefinitely. On the other hand, these eight patients definitely benefited from surgery, compared with the remaining six who had only slight improvement of walking distance up to 300 yards (275 metres).

Summary

Patients with intermittent claudication in the calf caused by femoropopliteal occlusions are usually treated with bypass vein grafts, but this procedure is impracticable if the distal popliteal and tibial arteries are grossly diseased or blocked.

An alternative operation of calf muscle denervation is described in 40 patients who have been followed up for six months to over three years. There were four early failures due to poor selection of patients for this procedure.

Early results are encouraging, and 70% of patients are able to walk at least 500 yards (455 metres) and 25% are able to walk indefinitely without pain. The long-term results would appear to be satisfactory.

Calf muscle denervation is a simple operation with little morbidity, and is advised for inoperable femoropopliteal occlusions. The operation can be performed selectively in operable cases in the older age group.

I wish to thank Mr. P. Harrison for the illustration, and Mr. C. L. O. Macalister for his helpful advice.

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Gynaecomastia in Chronic Renal Failure

R. M. LINDSAY,* M.B.; J. D. BRIGGS,* M.B., M.R.C.P.; R. G. LUKE,* M.B., M.R.C.P.

I. T. BOYLE,* M.B., B.Sc., M.R.C.P.; A. C. KENNEDY,* M.D., F.R.C.P.

Brit. med. J., 1967, 4, 779-780

Gynaecomastia is associated with several clinical conditions, but so far as we can ascertain the only report of it occurring in chronic renal failure is that of Shaldon (1966). He mentions gynaecomastia in patients undergoing regular dialysis treatment, and attributes this to the refeeding of malnourished uraemic patients at the start of dialysis. It does not seem to have been observed in uncomplicated chronic renal failure without regular dialysis treatment.

The presence of gynaecomastia has been observed in all four of the male patients at present undergoing regular dialysis treatment in the renal unit of the Glasgow Royal Infirmary and in two other patients with chronic renal failure.

Case Reports

The clinical and biochemical data of the six patients are summarized in Tables I and II. The patients receiving regular dialysis treatment each had two 10-hour haemodialyses a week by means of a Kolff twin coil dialyser incorporating a 0.9-sq. m. cellophane coil (Chron-a-Coil, Baxter).

The existence of gynaecomastia was determined, and agreed on by two observers, by the presence of readily palpable concentric increase in the subareolar tissues. The features of the gynaecomastia in each patient are summarized in Table III.

No patient had any clinical evidence of hepatic or of other systemic disease unrelated to the renal failure. Standard liver-function tests, serum transaminases, and a B.S.P. (bromsulphalein) excretion test were carried out on each patient. These estimations were performed by routine methods in the biochemistry department of this hospital. In no patient was any abnormality of these tests detected.

Case 1.—A bachelor aged 21 had noticed better general health, a great increase in libido, and improvement in secondary sexual characteristics since he started regular dialysis treatment. One month after beginning regular dialysis treatment he complained of considerable tenderness in the areolar region. Examination

revealed bilateral tender gynaecomastia. This had diminished considerably but was still present.

Case 2.—A man married for 13 years, with no family, had from 1962 onwards experienced a decline in his general health and also in libido but without impotence. Since starting regular dialysis treatment there has been marked improvement in health but not in libido. At the time of writing he was impotent. Two months after his first dialysis he complained of tenderness in the nipple area, and examination revealed slight bilateral tender gynaecomastia. This had now almost disappeared.

TABLE III.—Characteristics and Duration of Gynaecomastia

Case No.	Features of Gynaecomastia
1	Bilateral and tender—appeared after 1 month of R.D.T.—lasted 9 months—now virtually absent
2	Bilateral and tender—appeared after 2 months of R.D.T.—lasted 9 months
3	Bilateral and tender—appeared after 1 month of R.D.T.—diminished but still present after 8 months
4	Unilateral and tender (left side)—appeared after 1 month of R.D.T.—lasted 3 months
5	Bilateral and tender—lasted 3 weeks—not on R.D.T.
6	Bilateral and non-tender—duration unknown—not on R.D.T.

Case 3.—A married man with two children, aged 5 and 7, had experienced a progressive decline in health from January 1966 in association with loss of libido and impotence. After one month of regular dialysis treatment libido and potency returned. At this time he also noticed tenderness in the nipple region. Examination revealed gynaecomastia, which, though considerably reduced, was still present after eight months (Figs. 1 and 2).

Case 4.—A married man with a child aged 6 experienced a decline in health plus loss of libido from July 1966. There was no impotence. He started regular dialysis treatment in January 1967, and thereafter he had a rapid increase in libido. One month after starting regular dialysis treatment unilateral slightly tender gynaecomastia was observed. This completely regressed after three months.

Case 5.—This patient was a bachelor aged 24. In July 1966, after a six months' decline in health, he was diagnosed as suffering from chronic renal failure. He improved with a 20-g. protein diet, but in December 1966, because of considerable proteinuria (11.8 g./24 hours), the dietary protein was increased to 30 g. a day.

* University Department of Medicine, Glasgow Royal Infirmary, Glasgow C.4.

TABLE I.—Clinical and Biochemical Data of Patients Receiving Regular Dialysis Treatment (R.D.T.)

Case No.	Age	Diagnosis	Duration of R.D.T. (months)	Average Pre- and Post-dialysis		Other Management	Comment
				Blood Urea (mg./100 ml.)	Serum Creatinine (mg./100 ml.)		
1	21	Renal hypoplasia	10	140→46	12.0→5.7	40-g. protein diet	Rehabilitated
2	38	Chronic G.N.	12	182→66	11.4→5.4	40-g. protein diet. Methyl dopa	Partially rehabilitated
3	36	Chronic G.N.	9	147→42	11.5→6.0	40-g. protein diet	Rehabilitated
4	28	Chronic G.N.	6	118→45	7.5→4.2	40-g. protein diet. Methyl dopa	Partially rehabilitated

G.N. = Glomerulonephritis.

TABLE II.—Clinical Data of Patients not Receiving Regular Dialysis Treatment

Case No.	Age	Diagnosis	Creatinine Clearance (ml./min.)	Blood Urea (mg./100 ml.)	Comment
5	24	Chronic G.N.	6.4	170	Hypertensive. Being prepared for R.D.T. On Glavanetti diet + methyl dopa
6	59	Pyelonephritis. Hydronephrosis. Urethral stricture	4.7	180	Hypertensive. Has perineal urethrostomy. On 40-g. protein diet + methyl dopa

Creatinine clearance at that time was 9.2 ml./min. In April 1967 he was feeling well but complained of nipple tenderness, and slight bilateral gynaecomastia was evident on examination. This disappeared after three weeks. By May he became unwell again with nausea and vomiting. His creatinine clearance had fallen to 6.4 ml./min. and his haemoglobin was 7.1 g./100 ml. He was transfused, and was started on a Giovanetti-type diet plus methionine supplements. This led to considerable improvement in his symptoms plus a recurrence of the nipple tenderness, which lasted for about 10 days and was uncomfortable, but there was no convincing gynaecomastia.

Case 6.—This patient, a married man with five children, had long-standing chronic pyelonephritis with hydronephrosis secondary

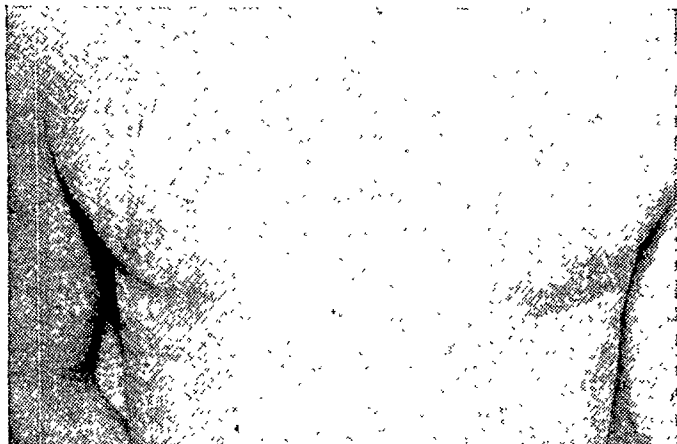


FIG. 1.—Anteroposterior view of gynaecomastia in Case 3 after eight months' regular dialysis treatment.

to a urethral stricture. The latter was of such a degree that six years ago a perineal urethra was fashioned for him. His renal disease was complicated by calculus formation. His general health was poor. His creatinine clearance was 4.7 ml./min. Therapy consisted of a 40-g. protein diet plus methyl dopa 250 mg. t.i.d. to control his hypertension. In April 1967 he was admitted for blood transfusion. During this admission gynaecomastia was noted to be present, but as the patient had not noticed this we are unaware of its duration.

Discussion

According to Paulsen (1962) the clinical conditions most commonly associated with gynaecomastia are: normal puberty, hypergonadotrophic hypogonadism (for example, Klinefelter's syndrome, functional prepubertal castrate); male pseudohermaphroditism, "refeeding gynaecomastia" (for example, recovery from generalized malnutrition, liver cirrhosis, digitalis therapy, pulmonary tuberculosis); testicular tumours (for example, choriocarcinoma, interstitial cell adenomas); spinal cord lesions; hyperthyroidism, hypothyroidism; Hodgkin's disease; and bronchogenic carcinoma.

Four of the six patients were on methyl dopa at the time the gynaecomastia was observed. We can find no reference that gynaecomastia may be caused by this drug, though breast enlargement and lactation has been reported as a rare side-effect in females (Pettinger *et al.*, 1963). No other drugs were being given to the patients during this time. We think it unlikely, therefore, that drugs could be implicated in the production of the gynaecomastia in these patients.

The gynaecomastia observed in Cases 1 to 4—that is, those receiving regular dialysis treatment—can probably most readily be explained on the basis of "refeeding" after the start of treatment. This is further suggested by the rapid increase in libido and potency. Presumably, as a consequence of chronic renal insufficiency plus a low protein intake, which are both likely to cause depression of pituitary gonadotrophins (Paulsen, 1962), testicular function is quiescent. With the beneficial



FIG. 2.—Lateral view of gynaecomastia in Case 3 after eight months' regular dialysis treatment.

effects of regular dialysis treatment, plus the increase in daily protein intake allowed by this regimen, a "second puberty" ensues, and this may often lead to a transient gynaecomastia.

The gynaecomastia in Cases 5 and 6, however, is without obvious explanation.

Conclusion

It would appear that transient gynaecomastia may occur not uncommonly in male patients with chronic renal failure during the early stages of regular dialysis treatment. It is also apparent that it may occur in similar patients not receiving this treatment. Further investigation into the incidence of its occurrence in chronic renal failure, and into its precise pathogenesis, is indicated.

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ABO Blood Groups and Infantile Hypertrophic Pyloric Stenosis

J. A. DODGE,* M.B., B.CH., M.R.C.P.ED., D.C.H.

Brit. med. J., 1967, 4, 781-782

An association between blood group A and cancer of the stomach was first reported by Aird, Bentall, and Fraser Roberts (1953). Further associations between blood groups and gastrointestinal disorders have since been described (Clarke, 1964a). This paper reports an investigation into the ABO blood group distribution and salivary secretor status of patients with infantile hypertrophic pyloric stenosis.

Material

The ABO groups of 303 patients with infantile hypertrophic pyloric stenosis were determined as part of a follow-up study. In all instances the diagnosis had been confirmed at operation, and all patients were resident in Belfast or its immediate environs at that time.

Information concerning the distribution of the ABO blood groups in Belfast was obtained from the Serological Population Genetics Laboratory (A. C. Kopeć, personal communication, 1967) and used for control purposes.

The salivary secretor status of 288 patients with infantile hypertrophic pyloric stenosis was investigated. Control data were obtained from 96 children admitted to hospital for tonsillectomy or adenoidectomy and from 435 children attending school dental clinics in Belfast.

Methods

Blood samples were obtained by venepuncture except in a small number of infants, when capillary blood obtained by heel stab was used. In all cases a full explanation was given to the parents, and in no instance was permission for blood sampling refused. ABO blood groups were determined by the tube method.

Samples of saliva were examined for the presence of ABH blood group substances. The children were asked to rinse their mouths with water before saliva was collected into plastic specimen jars and transferred to test-tubes. In the case of infants saliva was aspirated gently with a 2-ml. syringe. The tubes were partly immersed in a boiling water-bath for 10 to 20 minutes before being stoppered and stored in a refrigerator at 4° C. until testing, which was usually within 24 hours. Saliva specimens were tested for the presence of A, B, and H substances by the method of Dunsford and Bowley (1955). The anti-A and anti-B sera were provided by the N.I. Blood Transfusion Service, whose laboratories also prepared and extracted anti-H from the seeds of *Ulex europaeus*. Absence of inhibition of agglutination of O cells by anti-H serum diluted 1 in 8, in the presence of a 1 in 2 dilution of saliva, was accepted as a negative result. (This dilution was found to be the most satisfactory which could give a clear-cut result on microscopical examination.)

After the first 70 tests had been performed checking for A and B substances was omitted on most occasions because it was found that in all cases of secretion of A or B substances H sub-

stance could also be detected. Since the concentration of H substance in the saliva of group B secretors is often lower than in those of group O (Clarke, McConnell, and Sheppard, 1960), all non-secretors of known blood group B were reviewed a second time and their salivas examined for the presence of both B and H antigens; no trace of either could be detected in any instance.

Results

The distribution of ABO blood groups among 303 patients with infantile hypertrophic pyloric stenosis compared with controls is shown in Table I. It is evident that there were an unexpectedly large number of patients of blood group B in this series and a correspondingly small representation of patients of blood group A. These findings are statistically significant ($P=0.001$). Group O patients formed approximately the same proportion of the series as of the controls, and the slight excess of group AB patients was too small in actual numbers to justify further consideration. The relative incidence of pyloric stenosis in persons of groups O and B compared with group A is given in Table II. The χ^2 was calculated by the method of Woolf (1955) and is again statistically significant.

TABLE I.—Distribution of ABO Blood Groups in 303 Patients with Infantile Hypertrophic Pyloric Stenosis Compared with Distribution in Controls

Group	Patients		Controls	
	Total No.	Percentage	Total No.	Percentage
O	170	56.11	15,269	55.01
A	76	25.08	9,168	33.03
B	45	14.85	2,624	9.45
AB	12	3.96	696	2.51
Total	303	100	27,757	100

$\chi^2 = 18.228$. D.F. = 3. $P < 0.001$.

TABLE II.—Relative Incidence of Infantile Hypertrophic Pyloric Stenosis in Children of Groups O and B, Compared with Incidence of 1.0 in Persons of Group A

Group	Relative Incidence	χ^2	P
O	1.40	5.96	0.02 > P > 0.01
B	2.10	15.27	< 0.001

The incidence of salivary non-secretors was lower than expected, but this is not significant ($0.1 < P < 0.2$) (Table III). The secretor status of the blood group controls is not known, so Table IV gives a calculated expected incidence of each blood group and secretor type combination, compared with the observed incidence in infantile pyloric stenosis, but no claim is made that these results are statistically valid.

TABLE III.—Distribution of Secretor Status in 288 Patients with Infantile Hypertrophic Pyloric Stenosis Compared with 531 Controls

	Patients	Percentage	Controls	Percentage
Secretor ..	226	78.47	390	73.45
Non-secretor ..	62	21.53	141	26.55
Total ..	288	100	531	100

$\chi^2 = 2.52$. D.F. = 1. $0.1 < P < 0.2$.

* Department of Child Health, the Queen's University of Belfast, Northern Ireland.

TABLE IV.—Distribution of ABO Blood Groups and Secretor Status in 288 Patients with Infantile Hypertrophic Pyloric Stenosis Compared with Expected Incidence in the Control Population*

Blood Group and Secretor Type	Expected Percentage in Controls	Observed Percentage in I.H.P.S.
Group O secretor	40.40	42.71
Group O non-secretor	14.61	11.81
Group A secretor	24.26	21.88
Group A non-secretor	8.77	4.17
Group B secretor	6.94	10.76
Group B non-secretor	2.51	4.51
Group AB secretor	1.85	3.12
Group AB non-secretor	0.66	1.04

* Blood group data were obtained from the Serological Population Genetics Laboratory. As the secretor status of these donors was not known, the expected incidence of each blood group and secretor/non-secretor combination has been calculated by using the observed secretor/non-secretor ratio in the child controls referred to in Table III.

Discussion

It has been stated that infants with hypertrophic pyloric stenosis have a high incidence of peptic ulcer in later life (Bendix and Necheles, 1947; Belding and Kernohan, 1953; Hecker, Wenz, and Brückner, 1966), though control data are difficult to obtain. If this were so one might expect to find an increased incidence of blood group O among babies with pyloric stenosis, such as is seen in adult ulcer patients. Indeed, it is possible that the pyloric hypertrophy develops in association with a juxta-pyloric ulcer occurring in the neonatal period, for there is no apparent reason why newborn infants should not be equally subject to peptic ulcer as adults (Polacek and Ellison, 1966). Burge, Gill, and Lewis (1963) suggest that hypertrophic pyloric stenosis in adults is always related to ulceration in or near the pylorus, a view which was earlier put forward by Golden (1937).

The present series certainly demonstrates an excess of group O patients when compared with those of group A, of the same order as that seen in several series of duodenal ulcer patients (Clarke, 1964b). However, this apparent excess of group O patients is actually a reduced incidence of persons of group A, a deficiency which is largely compensated by the marked increase in the proportion of group B patients in the series. Thus group A may be regarded as in some way protecting against the development of infantile pyloric stenosis—or, alternatively, both group O and group B infants are at greater risk than those of group A (Table II). Though the group O babies would also have a theoretically greater chance of developing an ulcer, no association between group B and peptic ulcer has been reported.

Non-secretors of group O are particularly liable to develop peptic ulcers (Clarke, Price Evans, McConnell, and Sheppard, 1959). In this series secretor status appears to be unrelated to the occurrence of pyloric stenosis.

The blood group distribution seen in infantile hypertrophic pyloric stenosis may be compared with that found in relation to the production of alkaline phosphatase by the gut after a fatty meal. It has been shown that persons of groups O and B produce more of this type of alkaline phosphatase than those of groups AB and A (Arfors, Beckman, and Lundin, 1963a). Thus

individuals of groups O and B not only produce more intestinal alkaline phosphatase than those of group A but would also appear to have a greater susceptibility to infantile pyloric stenosis. It is known that secretors of ABH substances produce more intestinal alkaline phosphatase than non-secretors of the same blood group (Arfors, Beckman, and Lundin, 1963b). Thus secretors of groups O and B produce most alkaline phosphatase, followed by O and B non-secretors, with group A non-secretors producing least of all. Though not statistically significant, such evidence as this present study provides does suggest that (except in the case of group A) salivary ABH secretors are at greater risk of developing infantile pyloric stenosis than non-secretors. The series is too small to allow firm conclusions to be drawn in this respect, and no information is yet available about the secretion of alkaline phosphatase in pyloric stenosis.

Summary

Analysis of the ABO blood groups of 303 patients with infantile hypertrophic pyloric stenosis showed a significantly low incidence of group A compared with controls. The blood group distribution is discussed in relation to the quantitative differences in intestinal alkaline phosphatase found in persons of different ABO groups.

Investigation of salivary ABH secretor status showed no significant difference between patients with infantile pyloric stenosis and controls.

I thank the consultant paediatricians and surgeons of the Royal Belfast Hospital for Sick Children, Belfast City Hospital, and the Ulster Hospital for allowing me to review patients under their care; Professor I. J. Carré for his helpful advice and encouragement; Dr. M. C. Huth and Mr. T. Wilson for supplying anti-H serum; Dr. J. M. Bridges for laboratory facilities and assistance; Dr. J. D. Merrett for advice on statistical methods; and Dr. A. L. Walby, Schools Medical Officer, and the dental surgeons of the School Health Service, Belfast, for providing control specimens of saliva.

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Medical Memoranda

Neoplasia Complicating Uretero-sigmoidostomy

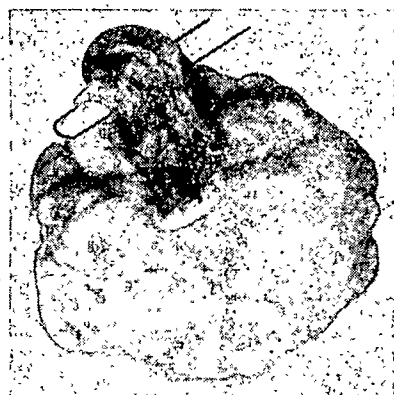
Brit. med. J., 1967, 4, 783-784

There are reports in the literature of 17 patients who developed neoplastic lesions at or close to the site of anastomosis after transplantation of the ureters to the sigmoid colon. Urdaneta *et al.* (1966) and Kozak *et al.* (1966) have published reviews and discussed the problems involved. Two further cases are here described.

CASE 1

A 26-year-old man had his ureters transplanted into the sigmoid colon in 1951, when aged 10 years, for incontinence secondary to an epispadias. Five years later he passed a small amount of blood per rectum. Sigmoidoscopy showed evidence of proctitis, and this was presumed to be the cause. He remained well until 1964, when once again he passed blood, this time from some small piles. The following year he was admitted to hospital as an emergency case with lower abdominal pain and discomfort in both loins. He was afebrile and mildly acidotic. Blood urea was 30 mg./100 ml. and haemoglobin 61%. A diagnosis of bilateral renal infection was made and he was treated with antibiotics. Intravenous pyelograms had been performed at regular intervals after his operation and remained normal until this admission, when both kidneys showed minimal dilatation of the pelvicaliceal systems consistent with the diagnosis of infection. Because of repeated severe attacks of infection, and while he was still passing blood occasionally per rectum, it was decided to convert his ureterosigmoidostomy to a ureteroileal conduit.

At operation a polypoid mass 5 by 5 by 3.5 cm. arising from colonic mucosa in the region of the left ureterocolic anastomosis was removed (see Fig.). Histologically the pedunculated cauliflower-shaped tumour showed irregular acini lined by pleomorphic hyperchromatic epithelium in both the polyp and its pedicle. The features were consistent with a diagnosis of adenocarcinoma.



Polypoid mass removed from Case 1. Diameter 5 cm. The probe has been passed through the ureterocolic anastomosis and marks the position of the ureteric "orifice."

CASE 2

This 19-year-old boy had his ureters transplanted into the sigmoid colon in 1951, at the age of 4 years, for incontinence secondary to an epispadias. He remained well until 1966, when he was

admitted to hospital as an emergency case with a large polyp prolapsing through the anus. This was reduced under a general anaesthetic. Subsequent sigmoidoscopy and a barium enema showed the tumour situated in the sigmoid colon 25 cm. from the anus. A series of intravenous pyelograms up to 1963 had demonstrated a normal upper renal tract; now, however, a pyelogram showed a hypertrophied right kidney, without evidence of obstruction, and a small left kidney with dilated calices and little function. He was mildly acidotic with a hyperchloraemia of 112 mEq/litre and blood urea of 40 mg./100 ml. The tumour was removed through a trans-abdominal colotomy from the region of the ureterocolic anastomosis. Histological examination of the cystic mucous polyp (diameter 5 cm.) showed areas where cell nuclei were hyperchromatic and displaced from their normal basal position. The possibility of malignancy could not be ruled out.

DISCUSSION

No aetiological agent has been clearly implicated in the development of these neoplasms. The chance occurrence of a spontaneous growth of the colon is unlikely because of the close proximity of all but two of the lesions reported in the literature to the transplanted ureteric "orifices," and the relative youth of the patients. Histologically two of these tumours were similar to those for which the operation was performed—namely, transitional-celled carcinomas of the bladder. The remainder consisted of 12 adenocarcinomas, three mucous-secreting adenomatous polyps, one transitional-celled carcinoma, and one scirrhous carcinoma. Twelve patients who developed a tumour in the colon after operation for some benign disorder such as bladder extrophy did so 10, 15, 15, 15, 15, 16, 17, 17, 30, 30, and 31 years later. Five patients whose ureters had been transplanted because of bladder malignancy developed growths of a different nature to the primary cancer 5, 7, 8, 9, and 9 years after the operation.

With improvements in the surgical technique of uretero-sigmoidostomy and in postoperative care these patients may anticipate a reasonably normal life-span. It would seem that a long-term survival brings with it the dangers of a complicating colonic carcinoma, and it is notable that 8 of the 19 patients were dead at the time their histories were reported in the literature. A review of case reports indicates certain warning symptoms and signs that were present in 15 of the 17 histories available for study. Upper urinary tract disease suggesting ureteric obstruction or reflux was detectable in 10. Large-bowel disorders were present in 11—chiefly alterations in bowel habit with evidence of obstruction in five and diarrhoea and tenesmus in others. Blood was passed per rectum in five.

These symptoms and signs are not especially remarkable in patients with a ureterosigmoid transplant, but their occurrence many years after the initial operation adds some significance. At this late stage most patients have a well-established routine of bowel action, and any change is quickly noted. Similarly, an unexpected alteration in the appearance of the kidneys on the routine follow-up intravenous pyelogram or the late development of a hydronephrosis must alert us to the need for radiographic examination of the large bowel and sigmoidoscopy. The presence of blood in the effluent should also be taken as an indication of possible neoplasia.

Urdaneta *et al.* (1966) have made a plea for routine follow-up proctoscopy and barium-enema examinations, but the practicality of performing these investigations regularly over many years is open to question. Clinical suspicion must remain the chief diagnostic weapon, followed by radiography, sigmoido-

scopy, and perhaps a willingness to convert these patients to ureteroileal conduit at the first sign of urinary tract trouble, when a carcinoma may be fortuitously discovered as in Case 1. Probably the ureteric stump and surrounding colonic mucosa should be removed at the time of this conversion, for Gillman (1964) described a case where an adenomatous polyp developed at the site of ureterocolic anastomosis seven years after the ureters had been transplanted into the colon, and six years after removal of the associated kidney.

We wish to thank Mr. R. K. Debenham, Mr. Victor S. Brookes, and Mr. G. H. Baines, under whose care these patients were

admitted, for permission to publish these reports, and Mr. Tom Dee for preparing the photograph.

JOHN N. KILLE, F.R.C.S.,
SELWYN GLICK, F.R.C.S.,
Senior Surgical Registrars, Department of Urology,
Queen Elizabeth Hospital, Birmingham 15.

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Nail-gun Fatality

Brit. med. J., 1967, 4, 784

The rising incidence of industrial accidents in 1966 was pointed out in a leading article in the *British Medical Journal* (1967) which commented on the Annual Reports of the Chief Inspector of Factories (1967). The accidental death described below must surely be one of the more unusual kinds of industrial hazard.

CASE REPORT

A foreman in charge of a local construction project gave a demonstration to his men on how to handle the explosive cartridge hammer or gun and showed that, provided the muzzle was not placed against a solid object, firing would not occur when the trigger was pulled. The function of the gun is to fire nails into building materials such as wood in order that a firm attachment can be made to masonry or metal. The motive force in this particular instance was supplied by the explosive charge of a 0.22 cartridge. A little later one of the employees held the muzzle of the loaded gun against a rigid support but left the end of the barrel exposed, intending to fire a nail through chipboard held 6 ft. (1.8 m.) away by a workmate. The nail penetrated the chipboard and ricocheted into a young electrician as he was ascending the stairs from the floor below. He was hit in the chest, stumbled backwards down a few steps, and died in a short time.

NECROPSY REPORT

The body was that of a well-built young man with pink froth at the lips and blood on the clothes, face, and hands. The clothing was removed after photographs had been taken, and in the mid-clavicular line on the anterior chest wall just beneath the first left rib was a discoloured area 2 by 1 cm., in the centre of which was a circular hole 0.5 cm. in diameter. There was severe haemorrhage into the tissues of the root of the neck and also from the intercostal vessels of the first rib space. The neck bleeding originated from tributaries of the left innominate vein; the missile had also penetrated the innominate artery and then embedded into the parenchyma of the right upper lobe.

The missile was a nail 5.2 cm. long with a head 0.5 cm. in diameter. The direction of the nail's path was across the chest

from left to right with a posterior and slightly downwards tilt; the pointed end of the nail was the leading edge.

The pericardium was not involved; the heart valves were within normal limits and the coronary arteries were normal. There was 1 pint (570 ml.) of blood in the right pleural cavity and half this volume in the left sac. Bruising and local bleeding into lung tissue, particularly into the right upper lobe, were prominent features and vesicular emphysema was widespread. The trachea and the bronchi of the right lung contained blood and froth; the nail had cut into large pulmonary vessels and several bronchi. The stomach contained some swallowed blood, but the small and large intestines showed nothing of note; the liver and spleen were smaller than normal, but the adrenals, pancreas, kidneys, ureters, and bladder were within normal limits. There was no evidence of cerebral haemorrhage. Death was due to haemorrhage and mechanical obstruction to respiration.

COMMENT

The use of this relatively new tool is widespread in the building industry and will almost certainly increase; it is thus of vital importance to know how to handle it in absolute safety. At the inquest on this case there was a rider brought in which deplored the fact that the instructions issued by the manufacturers of the hammer had not been followed, and it was requested that the accident prevention officer should instruct all contractors using such mechanical devices to warn all their employees of its potential danger.

The workers involved in this incident were young men, and the Chief Inspector of Factories drew attention to the high accident rate in this group. Certainly the increase in fatal accidents by 12% in 1966 over the preceding year is of serious significance. There might even be a case for licensing the tool and limiting its use to workers specially trained in its operation.

I wish to thank the Bailiff of Jersey and H.M. Viscount, Mr. H. V. Benest, for permission to publish this case.

JOHN CRAGG, M.D., B.Sc.; D.P.H., DIP.BACT., M.C.PATH.,
Consultant Pathologist, General Hospital, Jersey.

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Brit. med. J., 1967, 3, 507.

Clinicopathological Conference

A Case of Congenital Heart Disease in Mother and Child

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL

Clinical History

Dr. J. A. DAVIS: The patient (Case No. 298928, P.M. No. 11116) we are about to discuss was a male infant born on 30 December 1964. He was the child of the third pregnancy of a 25-year-old woman with a proved Fallot's tetralogy. The first pregnancy had ended in an abortion at 3 months; the second yielded a live infant who weighed only 1,420 g. at 37 weeks' gestation and died at the age of 30 hours following a hypoglycaemic fit. This pregnancy was uncomplicated but the mother was admitted to hospital for the last three months for rest. One month before delivery, at 33 weeks' gestation, an x-ray showed the baby to be the size of a normal 28-week foetus, and thereafter growth appeared to cease. At 37 weeks' gestation an elective Caesarean section was performed and the mother was delivered of a male infant weighing only 1,160 g. The placenta was also very small; the cord was shrivelled, and the baby had the appearance of an underweight-for-dates infant, the head being relatively large (H.C. 29 cm., H.C./B.W. ratio 25) though as regards central nervous system development he was assessed as of 32-34 weeks' gestational age. At 2 hours of age a glucose tolerance test was performed via umbilical vessel catheters. The fasting blood sugar was below 10 mg./100 ml. and returned rapidly to this level after rising to 63. The plasma growth hormone level at the depth of the hypoglycaemia was 50 μ mg./ml.

An injection of glucagon resulted in a small and brief rise of the blood sugar to 19 mg./100 ml. A solution of 7½% dextrose and 33½% fructose was given by infusion via a scalp vein at a rate of 2 ml./hour for 24 hours, and thereafter the blood glucose level was well maintained. The baby was asymptomatic and the E.E.G. pattern was normal for a baby of 32-34 weeks' gestation. During the performance of the glucose tolerance test it was noted that the blood in the umbilical artery was at low pressure (25 mm. Hg) and dark in colour (P_{O_2} 35 mm. in air; pH 7.28; no rise in P_{O_2} on increasing ambient oxygen).

On the second day a loud systolic murmur was heard down the left sternal edge and P_2 was noted to be very loud. Phonocardiography showed, in addition, an ejection click and a 4th sound. An electrocardiogram revealed excessive right ventricular hypertrophy; and there was clinical and x-ray evidence of cardiac enlargement though not of failure. Angiography was planned, but when the baby was 60 hours old the feet became white and pulseless and the arterial catheter had to be removed. The pulses in the feet then returned but the baby's condition steadily deteriorated and he died at 67 hours.

Clinical Diagnosis

- (1) Intrauterine malnutrition.
- (2) Neonatal hypoglycaemia.
- (3) Congenital heart disease (probably infantile coarctation).

Post-mortem Findings

Dr. M. J. R. DAWKINS*: The body was that of a male infant weighing 1,127 g. with a disproportionately large head for its size. Very little subcutaneous fat was present.

The main abnormalities were located in the *cardiovascular system*. A persistent left superior vena cava joining the coronary sinus was present. The aortic valve and the ascending aorta (circumference 8.5 mm.) were much smaller than the pulmonary valve and trunk (circumference 15 mm.). The ductus arteriosus was patent (Fig. 1) but showed intimal wrinkling and narrowing at the point of junction with the aorta. The isthmus of the aorta just above the entrance of the ductus showed a coarctation (circumference 3 mm.) (Fig. 1). The right atrium and tricuspid valve ring were widely dilated and there was a small defect (2 mm. diameter) (Fig. 2) high up on the interventricular septum underneath the septal cusp of the tricuspid valve, which was a little oedematous. The right ventricle was larger than normal (Fig. 3) and its wall was a little thickened (3 mm.). The interatrial septum and foramen ovale were normal and the left atrium appeared of normal size. The mitral valve and left ventricle were rather smaller than normal (left ventricle 1.5 mm.). Histologically the myocardium appeared normal.

The *lungs* showed areas of blotchy haemorrhage, and histological examination revealed focal intra-alveolar haemorrhage (Fig. 4) and generalized oedema. The intestines appeared normal and the *liver* (36 g.) was much smaller than normal, but histologically had the usual amount of extramedullary haemopoiesis. The ductus venosus was still patent. The *spleen* (3 g.) was normal, but the *thymus* (0.5 g.) was grossly atrophic and histological examination showed complete loss of the usual lymphoid cortex and only occasional Hassall's corpuscles (Figs. 5 and 6).

The *kidneys* (5 g. each) appeared normal (Fig. 7) and with no zone of glomerulogenesis, which suggests a gestation of at least 36 weeks. The glomeruli did not show the changes associated with cyanotic heart disease. The endocrine glands were normal apart from lipid depletion of the adrenal cortex. The *brain* (236 g.) was considerably larger than might be expected for the body weight and showed a mature convoluted pattern, consistent with the gestation of 37 weeks. Histological examination (basal ganglia, four areas of cortex and white matter, medulla and cerebellum) showed no abnormality and no evidence of the characteristic Purkinje cell changes associated with hypoglycaemia.

The *placenta* (270 g.) was much smaller than normal, and on the foetal surface the chorionic plate did not reach the placental edge (placenta extrachorialis). Outside the chorionic plate was a thick band of fibrin (Fig. 8), which in places appeared as laminated blood clot. Histological examination revealed normal villi in the underlying placenta with no evidence of dead villi in the ring of fibrin. Placental bed biopsies taken at the time of caesarean section and processed by Dr. Brosens

* Dr. Dawkins died on 27 June 1965.

showed diffuse infiltration of decidual stromal cells and giant cells with lipid. This type of infiltration has been found previously in association with prolonged pregnancy and hypertension and is attributed to local hypoxia.

Pathological Diagnosis

- (1) Congenital heart disease:
 - (a) Hypoplasia of ascending aorta and arch, with pre-ductal coarctation.
 - (b) Ventricular septal defect.
 - (c) Patent ductus arteriosus (closing).
 - (d) Persistent left superior vena cava.
- (2) Pulmonary oedema and haemorrhage.
- (3) Intrauterine growth retardation.
- (4) Placenta extrachorialis with fibrin deposition.

Discussion

Dr. DAVIS: There are a number of points worth drawing attention to here. First, Fig. 9 shows the relationship of birth weight to gestational age in babies born to mothers with cyanotic congenital heart disease.¹⁻¹² The line shows the relation of mean birth weight to gestational age for English children. Every single baby born to a mother with Fallot's tetralogy is below the expected weight line and most far below it. Some of these women in fact were subjected to operation before pregnancy; others fell pregnant with the uncorrected condition.

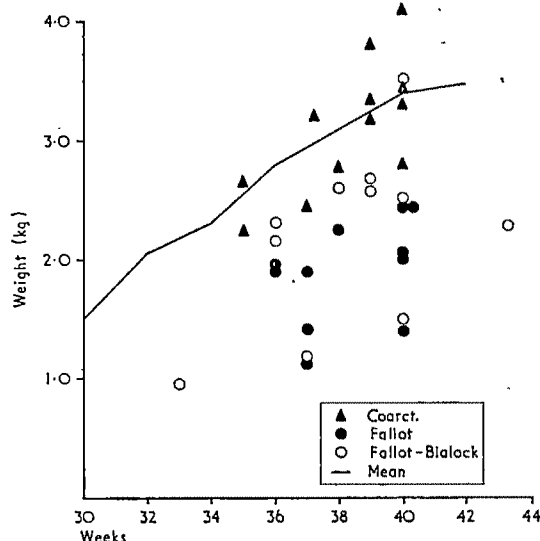


FIG. 9.—Birth weight plotted against gestational age in babies born to mothers with cyanotic congenital heart disease, with the mean for British babies. Figures from the literature; mean from perinatal mortality survey.

If one compares these figures with the birth weights of babies born to mothers with other forms of heart disease there is a very great contrast. Coarctation is shown in the Figure just as an example, but indeed in every other form of heart disease except cyanotic congenital heart disease the birth weights of the babies are normal for their gestational age. So there is something about the mother having cyanotic congenital heart disease which interferes with the growth of the baby in utero, whereas being in heart failure with some other condition apparently does not.

Hypoglycaemia

Then just a comment on our treatment of hypoglycaemia. We were in fact able to measure certain hormone levels in this

baby at the nadir of his hypoglycaemia. His growth hormone level was 50 $\mu\text{mg./ml.}$, which is about a normal level for a baby of that age but not a very spectacular response to a considerable degree of hypoglycaemia where levels as high as 250 $\mu\text{mg./ml.}$ have been described.¹³ His blood cortisol levels were also high, between 83 and 64 $\mu\text{g./100 ml.}$, but it is not yet clear what the response of a baby should be in these circumstances. Some time ago we successfully treated identical twins who were slightly hypoglycaemic; by giving prednisone to the more hypoglycaemic twin we were able to raise its blood glucose level, whereas in the other twin who was not given prednisone there was no such rise. The rise in blood glucose was associated with a rise in blood urea indicating that we had stimulated glucogenesis.

In the case under discussion we do not know whether it was feeding the baby—which does not usually have much influence on established hypoglycaemia—or the intravenous drip, or the administration of glucagon and prednisone which in fact rescued it from its hypoglycaemia. It is worth mentioning that the brain of the baby's sibling at death showed fairly gross lesions, which Dr. Sabina Strich has shown to be characteristic of hypoglycaemia, and that no such lesions were present in the brain of this baby. The normal level of blood glucose in healthy premature babies at this sort of birth weight varies over a wide range. They may have a low birth weight because they were born early or because they suffered from intrauterine malnutrition, and this is responsible for a wide scatter in the normal levels. Levels nearly as low as that found in this case are compatible with perfectly good health. Our experience has been that only when the level falls below 20 mg./100 ml. does the baby become symptomatic and that symptoms do not usually appear unless the level is below 10 mg./100 ml. There is some evidence that the brain can use other substrates as well as glucose for its metabolism in the first days of life.¹⁴ In this particular case we were able to predict the onset of hypoglycaemia and to treat it adequately, and it was sad then to find that the baby had severe congenital heart disease. There is, I believe, some unpublished evidence that the incidence of congenital heart disease is in fact very much higher in the children of mothers with Fallot's tetralogy or other forms of cyanotic congenital heart disease than it is in the general population. Of course, there is about a 3% incidence anyway in the children of women with congenital heart disease but the incidence when they have cyanotic congenital heart disease is considerably higher. So this baby's heart disease was probably environmentally determined; and this suggestion is supported by the fact that the baby had a different form of heart disease to its mother's. On the other hand, this baby's first cousin, born to a perfectly normal mother, died in the immediate neonatal period with a truncus arteriosus.

Effects of Heart Disease on Pregnancies

Professor J. F. GOODWIN: Dr. Oakley, I believe you have some views on cyanotic heart disease in pregnancy and the effects on the baby.

Dr. CELIA OAKLEY: A survey was carried out at Johns Hopkins Hospital by Dr. Catherine Neill on all patients who had attended the cardiac clinic with congenital heart disease and who had reached or passed the age of 18 when the survey was started.¹² Over 700 patients answered a questionnaire and 235 (159 families and 76 males) had had children. There had been 508 pregnancies with a 1.8% incidence of congenital heart disease in the children (roughly six times the expected). The outcome of pregnancy had been near to normal in the acyanotic patients and they didn't have a greatly abnormal incidence of miscarriages, other foetal abnormalities, or stillbirths compared with the general population. Dr. Neill found on the other hand that the outcome of pregnancy in the cyanotic mothers (but not in cyanotic fathers) was very different; they had an



FIG. 1

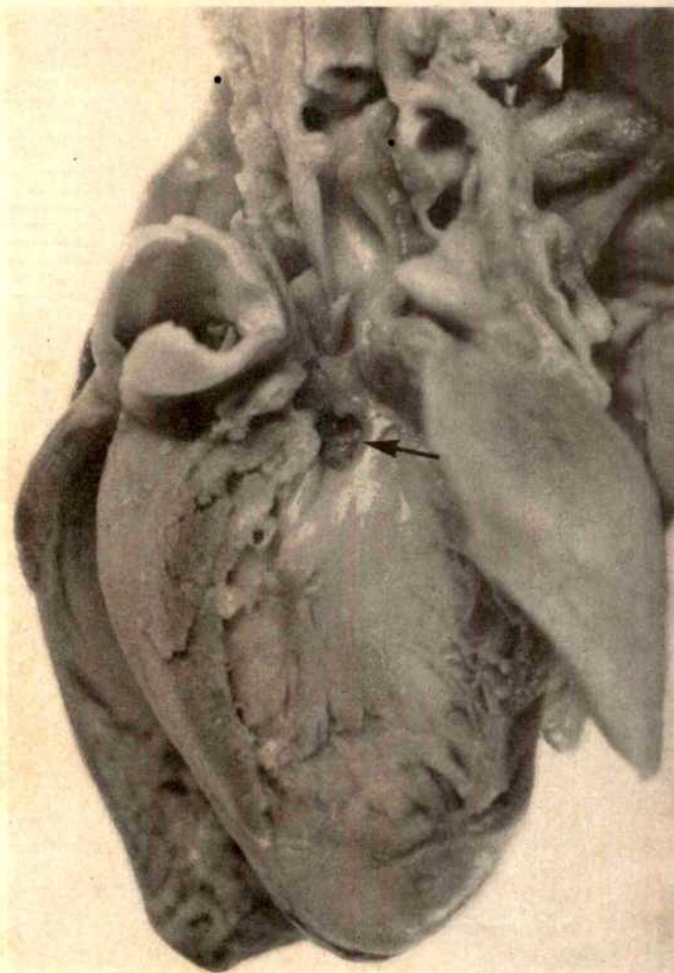


FIG. 2

FIG. 1.—Ductus arteriosus and aorta seen from the left.
A is ductus. B is site of coarctation.

FIG. 2.—View of ventricular septum from left ventricle. Arrow
indicates septal defect.

FIG. 3.—External view of heart showing the large right
ventricle.

FIG. 4.—Lung (H. and E. $\times 95$) showing intra-alveolar
haemorrhage to left of field and oedema on right.

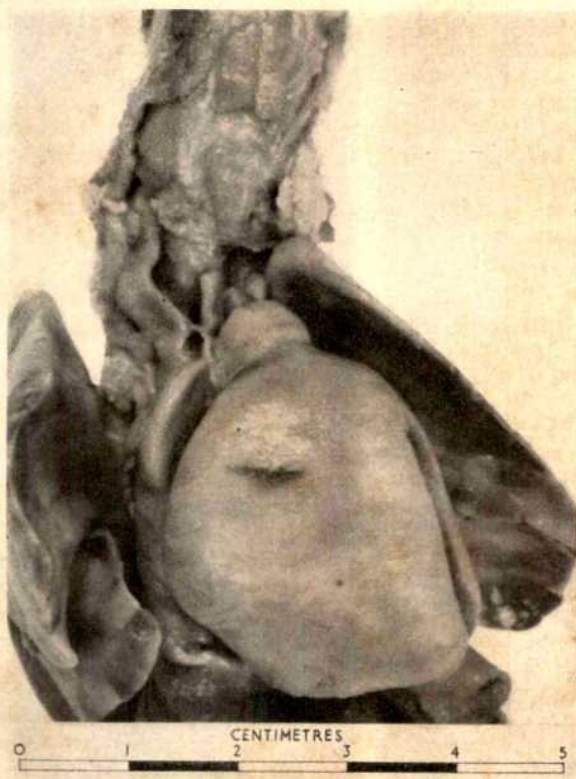


FIG. 3



FIG. 4

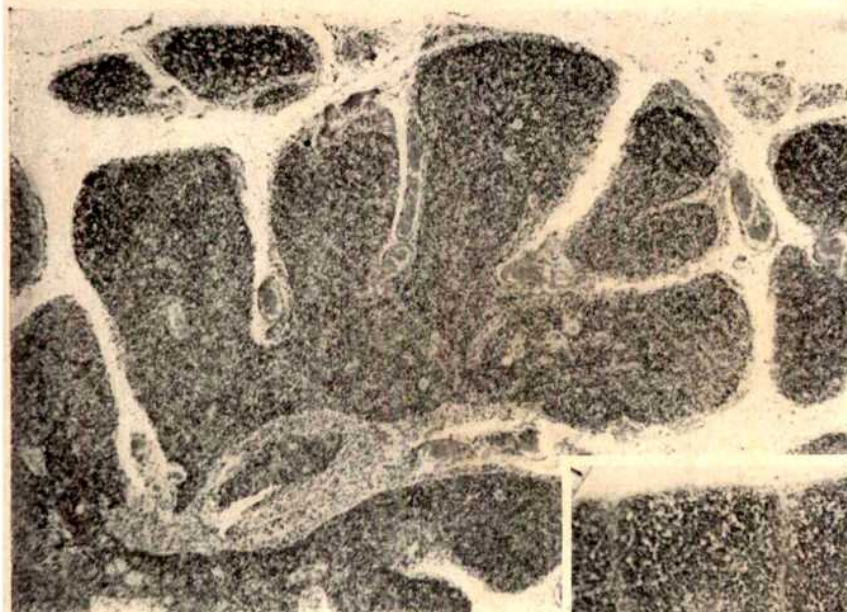


FIG. 5.—Thymus (H. and E. $\times 40$) showing loss of cortical lymphocytes and generalized atrophy.

FIG. 6.—Thymus from normal newborn infant. (H. and E. $\times 40$.) Note size of lobules and well-defined cortex and medulla.

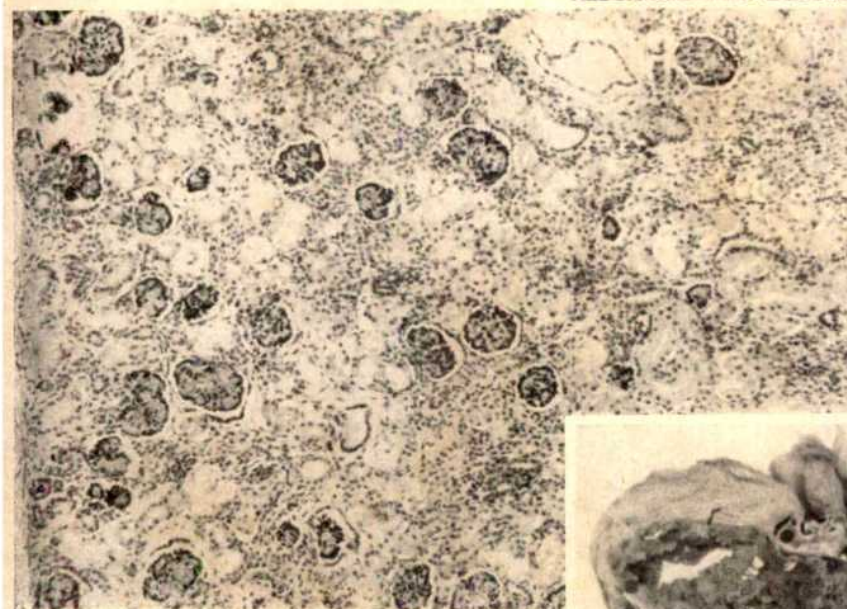
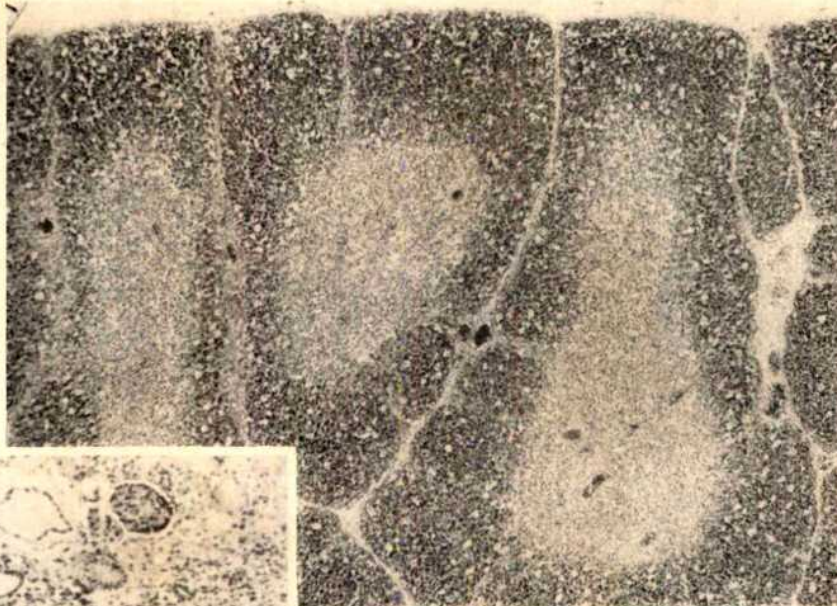
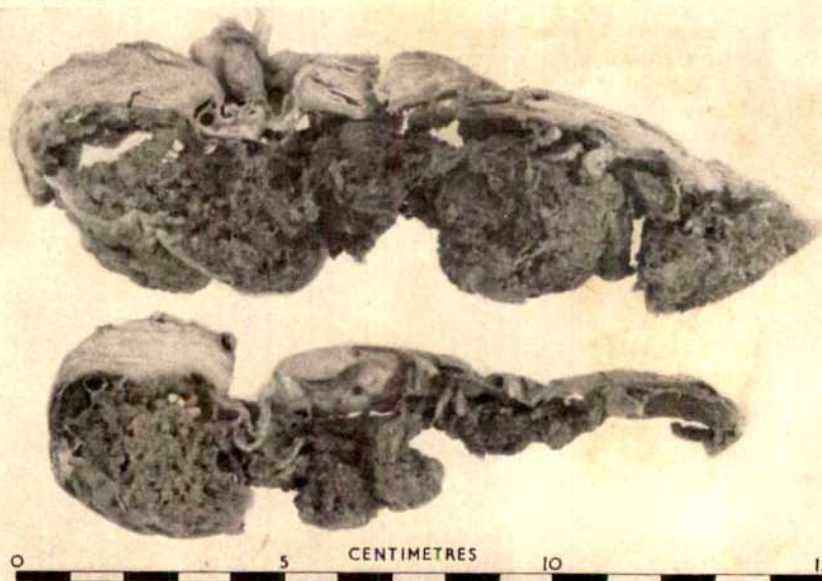


FIG. 7.—Kidney (H. and E. $\times 100$) showing mature glomerular structure.

FIG. 8.—Representative slices through placenta showing thick sub-chorionic fibrin deposits.



0 5 10 15
CENTIMETRES

exceedingly high rate of foetal loss. There were 110 pregnancies in 54 cyanotic mothers and Dr. Neill's figures which I will quote to you are based on these numbers. The rate of abortion was about six times the rate in the general population. This seemed to be so high that it was thought wise to try to break it down. The results were very interesting. In patients whose haematocrit was between 51 and 65% (moderate cyanosis) the miscarriage rate was over 60%. When the haematocrit was over 65% (severe cyanosis) the incidence of spontaneous miscarriage was over 80%. So that the cyanotic woman has a greatly reduced chance of bearing a live child.

The birth weights of these infants were low—they were low because the infants were born prematurely and the infants were also very small for their gestational age. The placentae on the whole were large and contained infarcts, but if infarction was extensive then the placental weight was low. These were children who had been subjected to hypoxia for a long time; a survey carried out in Peru at high altitude also showed that the average birth weights were low and the average placental weights were high. The average birth weights of infants born to the cyanotic mothers was only 5½ lb. (2.5 kg.). As it might be suggested that these low birth weights in the cyanotic adults were genetically determined, the children of cyanotic fathers married to normal mothers were used as controls, and the mean birth weight of the children born was found to be about 7½ lb. (3.4 kg.) (normal). The incidence of congenital heart disease in the children of cyanotic mothers and fathers (most of them had Fallot's tetralogy) was the same as the incidence of congenital heart disease in the infants born to parents with acyanotic conditions. So apparently the higher incidence of foetal death, stillbirth, and prematurity was due to an environmental rather than to a genetic cause. This of course is a generalization and there are some families who have high incidence of congenital heart disease in them where several siblings usually have a similar condition. This has a very important bearing on the mother of the child who is being discussed now. She is desperately anxious to have children and we want to know whether to advise her to have another try or to adopt children. Personally, I would advise her (if she survives the correction operation which she has just had) to have another pregnancy. Her chance, having become acyanotic, of having a healthy child should be very much better. The risk she will run of having a child with congenital heart disease is only about three times that of the general population, unless, as is somewhat suspect, she is one of those unfortunate cases in whom there is a definite genetic risk in the family.

Family History

Professor GOODWIN: It is worth enlarging on the mother's disease. We have known her for many years, for we first saw her as a child. She was investigated by Dr. Maurice McGregor and Dr. Mounsey in 1948-9. She had the tetralogy of Fallot with minimal cyanosis; and you will recall that the main factor which determines cyanosis in the tetralogy is the difference between the resistance to the blood flow offered by the right ventricular outflow tract and the systemic resistance. Thus patients with only moderate pulmonary stenosis may be almost acyanotic at rest but on exercise systemic resistance falls, peripheral vasodilatation occurs, the right ventricular inflow increases, and shunting of blood from the right ventricle to aorta occurs and cyanosis follows. Because she was only minimally cyanotic she was not offered a Blalock operation, which was current at that time, and indeed operation was advised against until such time as complete correction became available. Subsequent catheterization revealed an additional atrial communication and operation was advised. As Dr. Oakley says she has now had this operation.

This history does not bear on the present situation except that it is one further instance of a similar lesion in the child,

who had a patent foramen ovale as well as an atrial septal defect and ventricular septal defect. I suppose that acyanotic patients with the tetralogy are more likely to have a viable child than those who are frankly cyanosed. During pregnancy peripheral vasodilatation and cardiac output increase and they become more cyanosed. Reduced oxygen saturation in the blood supply to the foetus must play a part in affecting the foetus, and I think this must be the reason for the persistently low birth weights.

It is doubtful whether one should advise this patient to have another pregnancy. There have already been two disasters and there is a relative who had an infant with congenital heart disease. There are clearly two factors operating to compromise the baby's chance here.

Dr. OAKLEY: There was one cousin whose baby was abnormal, but it is not known whether this was due to a genetic cause and, therefore, relevant or whether it was environmental. I believe that the previous baby, who died of hypoglycaemia, had a normal heart. Advice should not be weighted too heavily just because of one cousin.

Bed Rest

Could I make one more comment? The mother of this baby was advised to spend a large part of her pregnancy in bed for a very good reason; it was not because of any concern for the mother herself, for we were fully confident that she would weather the pregnancy—she was a little blue and breathless without any undue trouble; but it was in an effort to keep the environment of the baby at as high an oxygen tension as possible. All these patients with Fallot's tetralogy change their arterial oxygen saturation very widely—they may be almost completely saturated at rest, but with a fall in systemic resistance on effort when the cardiac output goes up the oxygen saturation may fall by 30% or even further.

Professor J. P. M. TIZARD: Were any actual measurements made of arterial oxygen saturation in this patient during her pregnancy?

Professor GOODWIN: I don't think so.

Professor TIZARD: Was there a margin of safety, I wonder? In a normal woman the uterine arterial oxygen tension is about 90 mm. Hg, but by the time the oxygen reaches the foetus in the umbilical vein the tension is somewhere in the 40s (this is in normal pregnancy). This fall in tension has been shown recently by Geoffrey Dawes¹⁶ not to be due to any diffusion barrier but simply to what is used up in placenta tissue. If there is a marked drop in oxygen tension over a long period it is difficult to imagine how the foetus can survive.

Can I ask one question about the heart? The photograph of this baby showed that the lower half of his body was paler—why should the ductus close at all under these circumstances?

Effect on Ductus

Professor GOODWIN: I don't know. I agree that teleologically it ought to remain open. One might expect that in the severe tetralogy the ductus would be more likely to remain open, and there are situations—extreme forms of the tetralogy amounting to pulmonary atresia, where the patent ductus has remained patent as the major source of blood supply to the lungs. Most patients with the tetralogy don't have a patent ductus, however.

Professor TIZARD: But I would expect the oxygen tension in the blood reaching the ductus would be high enough to promote normal closure. I don't know whether Dr. Davis perhaps knows the limits of this.

Dr. DAVIS: I don't, but I suggest that we may have made this ductus close by putting this baby in higher than normal

environmental oxygen concentrations thinking that this action was therapeutic. We found a very low oxygen tension in the umbilical arterial blood—on the edge of a cliff as regards the dissociation curve—and we thought we had better try to raise it. This may be precisely what caused the final catastrophe.

Professor TIZARD: Successfully raising the venous blood tension?

Dr. DAVIS: Yes.

Professor GOODWIN: I wonder how likely it is that a low oxygen environment may be closely concerned with this type of developmental anomaly? In children born at high altitudes congenital heart disease is commoner than in those born at sea level; but it is usually patency of the ductus, though other forms do occur. Have you any views on the likelihood in this case of the congenital heart disease being related to the low oxygen tension?

Dr. DAWKINS: I have no views that I can support. Attempts have been made to investigate this problem in animals, but such experiments usually result in loss of the foetus or no particular damage. It depends on what might have happened over one day early on in the pregnancy.

Professor GOODWIN: It could have been very early in pregnancy.

Dr. DAWKINS: Before she was put to bed.

Professor GOODWIN: Also, perhaps, before she was really substantially cyanosed, unless she was taking a lot of exercise at the time.

Little is known with certainty about the causes of ventricular septal defect except that infection in the mother with rubella in early pregnancy is a cause. Chromosomal disorders may be associated with congenital heart disease. Otherwise there are merely suggestions such as consanguinity of parents and the difference between mother's age and father's age being greater than the average. These were factors in 180 cases of ventricular septal defect studied by Dr. M. Campbell and myself.¹⁶ There are some strange seasonal variations in the incidence of coarctation of the aorta and patent ductus which Polani and Campbell¹⁷ have described. Girls with patent ductus are born more frequently from August to October and less frequently from December to March. Boys with coarctation are born more frequently from December to July. This is even more odd because it doesn't even fit with the seasonal incidence of rubella.

Of course thalidomide and excessive irradiation are well known teratogenic poisons which may produce congenital defects.

Professor TIZARD: Genetic factors may play a partial and unimportant role in many forms of congenital disease but simple modes of inheritance are rare. Endocardial fibroelastosis is probably inherited as an autosomal recessive.

Professor GOODWIN: There is a possible suggestion that interference with the lymphatic flow is relevant. Endocardial fibrosis and subendocardial haemorrhage have been produced in animals by Miller and colleagues¹⁸ but whether this is related to human endocardial fibroelastosis I have no idea at all. Anoxia has also been put forward as a theory.

Obstetric Problems

Mr. G. DIXON: These patients with cyanotic heart disease, from our point of view, are rare examples of chronic placental insufficiency. We see a much more acute form in maternal hypertension and postmaturity and an intermediate form in the "small-for-dates" babies. Clinical assessment of insufficiency of the placenta is terribly difficult and the methods in use are still crude. Here, in an extreme form, one had a uterus which did just correspond in size to the gestational age for most of the pregnancy; but it is interesting that during the first half of pregnancy her uterus grew perfectly normally and

then apparently stopped. The methods we use are, as I say, terribly crude. The lady had put on 9 lb. (4 kg.) in weight during her pregnancy and this was indicative of the failure of the foetus to develop. We also measure the abdominal girth because while the girth is increasing we presume that the placenta is working well enough to allow the baby to grow; but there are many sources of error. There has been so much obstetrical erudition this morning that there is not much more to say, but I would like to add to Dr. Oakley's point about the oxygen saturation increasing when the patient rests by saying that presumably the intervillous blood flow increases, though we have as yet no real evidence of it.

Professor GOODWIN: The management of this mother was very difficult, and looking back we may possibly have made the wrong decision. She had been accepted for radical correction of the tetralogy and then became pregnant. This was her second child, she had lost the first, and one's impulse was to say, "Let us get on with the operation and hope the child survives; at least we shall have dealt with her heart lesion, corrected the cyanosis, and she can become pregnant again and all will be well."

Dr. Oakley and I had long discussions with the surgeons and obstetricians about what would be the best thing to do. We felt finally that we should not incur the risk to her and the baby of doing the operation during pregnancy. I don't know of any figures of pregnant patients operated on with cardio-pulmonary bypass, though there is plenty of information on pregnant patients operated on for mitral valvotomy and that as a rule does not disturb the foetus in the very least. But under cardio-pulmonary bypass things might be very different. Has anyone any information on this point?

Dr. DAVIS: Yes. Such operations have been done during pregnancy and I think one of the babies survived though the others were lost.

Professor GOODWIN: So the chances presumably would be against the survival of the baby. It is worth remembering that if you advise an abortion on the grounds of the mother's health you decide inevitably to sacrifice the baby, whereas if you advise an operation on the mother then you have a reasonable chance of saving both the baby and the mother. If we were faced with this situation again we should ask the cardiac surgeons to get on with the operation quickly. I think we would have lost the baby but we would have saved the mother a lot of distress—though the risk to her of operating during her pregnancy might have been greater.

Dr. DAVIS: I would like to stress that we needn't have lost the first baby, which died of a treatable condition, and that we expected this to be the only real problem in the second one.

Professor GOODWIN: We did not at that time know about the cousin. Dr. Mounsey, you have something to add?

Clinical Diagnosis

Dr. J. P. D. MOUNSEY: Initially there was some disagreement as to what the congenital lesion in this baby was likely to be. May I ask what the points were on which a correct diagnosis of coarctation with a ductus and a ventricular septal defect was made? I presume that the reason for diagnosing coarctation was the time of onset of deterioration of the baby, and the evidence of poor circulation to the lower part of the body, with reduced blood pressure and PaO_2 . The reason for the diagnosis of ventricular septal defect, I presume, was the presence of this systolic murmur, which was perhaps loud and harsh. I left out the E.C.G. There is more right heart hypertrophy than you would expect in a baby of this age.

Dr. DAVIS: What made us suspect coarctation was the low blood pressure in the umbilical artery. We had a direct reading of it and it was quite outside what we normally expect to find. This, associated with a very low oxygen tension, in a baby who

was plainly not in respiratory difficulties or in heart failure, very much suggested that the upper part of the body was being supplied with adequately oxygenated blood though we knew the lower part was not. Those two findings are not compatible with any other diagnosis. Why we rejected the diagnosis up to a point was that we thought the catheter may have been so placed as not to give us true blood pressure readings. The PO_2 did in fact rise during the period of observation. Thus there was every reason to believe that there was a coarctation, but the other findings could not be explained by that alone, and the murmur suggested that the baby had a ventricular septal defect—in fact, it was characteristic of that abnormality. That was the way we looked at it.

Professor GOODWIN: I thought it very likely that if there was any cardiac lesion it would be the same as the mother's. So I thought a ventricular septal defect was likely on those grounds. Now we know that a proportion of patients with the tetralogy of Fallot in childhood or later life may start with a ventricular septal defect only and then develop progressive infundibular hypertrophy to such a degree that the left-right shunt reverses, leading to the tetralogy. A ventricular septal defect would then be the sort of basic anomaly that one would expect the child to have if the mother had the tetralogy of Fallot or a ventricular septal defect without pulmonary stenosis. The cardiogram (I think one could have been a little cleverer about it) does show, as Dr. Davis pointed out, extreme right heart enlargement. This is the sort of tracing seen in babies born with pulmonary atresia and intact ventricular septum, or with, as this child had, the hypoplastic left heart syndrome with most of the work of the heart being done by the right side. The right ventricular hypertrophy is too great for ventricular septal defect alone, and perhaps too strong for an infant born with the tetralogy with established pulmonary stenosis. The loud second heart sound we thought might be the result of pulmonary hypertension.

Intrauterine Malnutrition

Professor TIZARD: Could I change the subject from the heart for a moment to say what an impressive lot of clinical, biochemical, and pathological evidence there is here in favour of the baby being a case of intrauterine malnutrition? Until a few years ago if a baby had been born at 37 weeks weighing 1,100 g. the conclusion would be drawn that the pregnancy was really very much shorter and that a mistake had been made about the date of gestation. Of course this is not only a matter of theoretical but also of great practical importance when it comes to looking after these babies, because the small ones born early present very different problems from the babies with normal gestation and intrauterine malnutrition. Could I just ask Dr. Dawkins a question with regard to this very small thymus? Is this a usual finding in intrauterine malnutrition and does this correlate with any immunological defect in the developing foetus?

Dr. DAWKINS: Certainly it is a usual finding in babies with intrauterine malnutrition. It is interesting that in this very

rare cause of intrauterine malnutrition you get the same effect on the foetus as with the more common causes of malnutrition like hypertension. There is no doubt that the small babies don't grow so well in the postnatal period and they have more infection in the first year of life, and there is some evidence that the immunological competence may be reduced in these babies. Of course it is well known that thymectomy in newborn animals produces failure of growth and this is shown to be due to recurrent infection.¹⁹ The thymus is responsible for the development of the lymphoid system throughout the body and removal of the thymus prevents the development of lymphoid follicles.

Dr. DAVIS: Could I make a last observation with regard to the blood chemistry in relation to the heart? With a PO_2 of that order I think you would expect high blood lactate levels, but they did not in fact rise until a few hours before death. This led us to believe that part of the body at least was being properly supplied with oxygen at normal tension. I would also like to point out that all those biochemical estimations were done on a total of 10 ml. of blood, which is quite a small proportion of the baby's total blood volume and a loss that babies can tolerate quite easily.

Professor GOODWIN: In conclusion, then, pregnancy in cyanotic heart disease is difficult and hazardous for mother and foetus, the chances of a successful pregnancy are small, and thus correction of the lesion is to be advised before pregnancy when possible.

We are grateful to Professor J. P. Shillingford and Dr. E. D. Williams for assistance in preparing this report, and to Mr. W. Brackenbury for the photomicrographs.

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Current Practice

DISEASE OF THE DIGESTIVE SYSTEM

Surgical Treatment of Upper Alimentary Bleeding

H. L. DUTHIE,* M.D., CH.M., F.R.C.S.

The place of surgery in the management of patients with bleeding into the stomach or duodenum is largely governed by two aspects of the haemorrhage: the total volume of blood lost and the rate of bleeding.

Other factors which are of importance are the cause of the bleeding and the age of the patient. Severe bleeding is one of the most demanding emergencies, and the decision may need to be made rapidly and the operation performed with dispatch. Fortunately most upper alimentary bleeding settles with conservative management and in only a minority of cases does immediate operation have to be considered. However, in all cases the question of surgery to prevent recurrence of the bleeding ought to be considered.

Co-operation

The approach to the diagnosis and treatment of upper gastrointestinal haemorrhage should be co-operative between physician and surgeon. In most centres such cases are admitted to medical units, but in the others to surgical units. The locus of the patient does not matter: the joint consultation is all-important. This joint action is too well established throughout Britain to need much emphasis; the surgeon benefits from seeing patients who do not require surgical treatment, the physician benefits from having earlier recourse to surgical assistance, and, best of all, the patient benefits by having the appropriate treatment at the appropriate time.

* Professor of Surgery, University of Sheffield.

Indications for Surgery

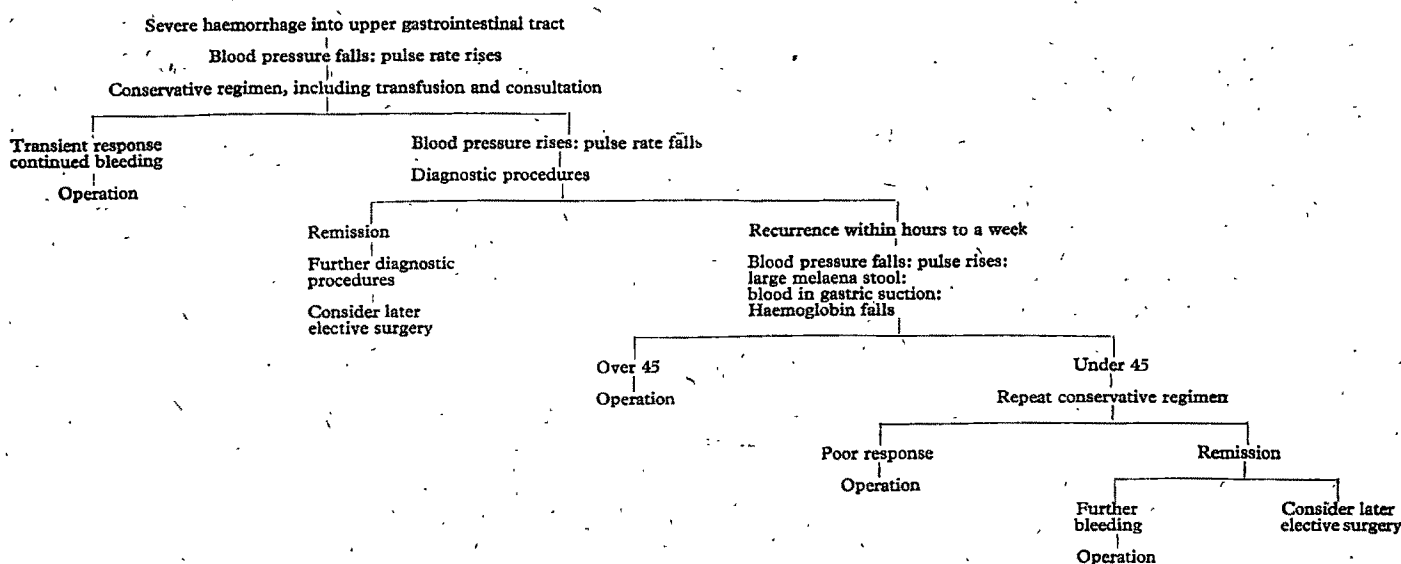
In the overall management of upper gastrointestinal bleeding the priorities may be stated as (1) life saving; (2) diagnosis; (3) definitive treatment. Surgical therapy may be called for in step one, when the endeavour is to accomplish all three objectives, or it may be left to stage three. Definitive treatment is to be preferred where it is compatible with the progress of the patient. The rapidity of the blood loss is the main factor indicating the correct time to operate (Table I).

Bleeding Threatening Life

When the bleeding threatens the life of the patient, despite adequate transfusion, operation must be done even though the diagnosis may not be known, provided that haemorrhagic disorders have been excluded. In some cases a preoperative diagnosis will have been established by a typical history of peptic ulcer, or of ingestion of aspirin, or of hepatic cirrhosis with portal hypertension, and in the last instance the physical examination will usually elicit signs of hepatic failure and the spleen will be palpable. A working diagnosis may be further buttressed by previous radiological findings. However, there may be no time to proceed to further diagnostic measures. Fortunately a bleed as demanding as this is uncommon and some time can usually be obtained for at least a radiographic study in the ward or for an endoscopic examination.

What does the surgeon do at operation? He first attempts to confirm or establish the source of the bleeding, then to stop

TABLE I.—Place of Surgical Treatment in the Management of Bleeding from the Gastrointestinal Tract



it, and finally to attempt to prevent its recurrence. Chronic duodenal ulceration is frequently detectable by inspection of the outside of the duodenum, but the duodenum may have to be opened to be quite sure of the presence of a small penetrating ulcer on the posterior wall. Gastric ulcers may be more difficult to detect and the stomach may have to be opened widely to locate the lesion, especially if it is an acute erosion. Another technique to assist in the location of the bleeding point at operation is to insert a sigmoidoscope through a small hole in the stomach. By inflating the stomach the mucosa may be examined, but the presence of blood and blood clot makes this difficult. I prefer opening the stomach and everting the lining, though blood clot may again make visualization tedious, and the mucosal folds must be carefully separated to make sure that a small lesion has not been overlooked. Portal hypertension is

indices of persistence of bleeding usually are the continued presence of occult blood in the stools and a consistently falling level of haemoglobin in the blood. The bleeding is then more an additional indication for surgery to treat the underlying cause rather than an absolute indication in itself.

Age

It is generally held that patients over the age of 45 to 50 should be considered more readily than younger patients for surgical treatment of bleeding, since vessels affected by the inevitable arteriosclerotic changes of age will be less likely to contract to assist in the arrest of the haemorrhage. However, in the case of the chronic duodenal ulcer this is hardly valid. No matter the age of the patient, the vessels in the base of the

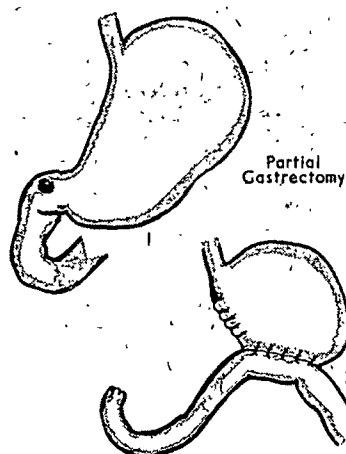


FIG. 1

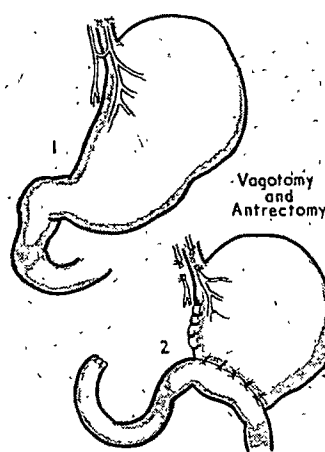


FIG. 2

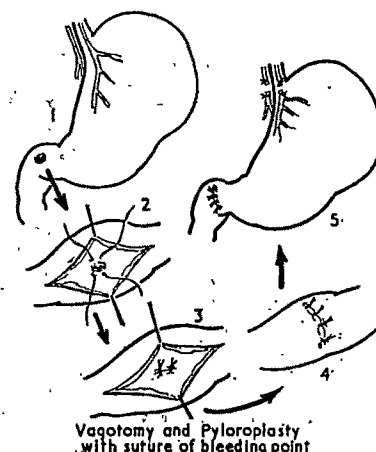


FIG. 3

usually diagnosed preoperatively, but, if not, the presence of venous collaterals in the abdominal wall is indicated by the excessive bleeding encountered when making the incision. Once the abdominal cavity has been opened the enlarged spleen can be felt and the cirrhotic liver can be seen together with the distended intra-abdominal veins.

When the source of bleeding has been found it must be stopped at once by direct pressure, by oversewing, or by applying a clamp, and the transfusion allowed to continue for a few minutes to improve the patient's general condition before proceeding with the operation. The choice of procedure will be discussed later.

Severe Bleeding—No Threat to Life with Transfusion

In this group the severity of the bleeding ranges from that in which the blood pressure can be maintained only with transfusion to the patient in whom the bleeding stops quickly and the transfusion replaces the lost volume. The value of time gained by transfusion is that the patient can get into a better condition to undergo surgery or to undergo investigation. History, physical examination, then immediate radiology, assessment of gastric acidity, and immediate gastroscopy combined can give a positive diagnosis in over four-fifths of patients. This is a great advantage to the surgeon, but no time must be lost attempting to make the diagnosis. If the patient's condition deteriorates, as seen by further fall in blood pressure, rise in pulse rate, and fresh blood in the gastric aspirate, immediate surgery is indicated. In this group recurrent haemorrhage is a frequent indication for operation, and usually after the diagnosis has been made.

Moderate Bleeding

When the amount of blood lost does not cause a decrease in blood pressure the problem is much less acute, and the

ulcer undergo periarteritis and become thickened. With this in mind, operation should not be postponed too long simply because the patient is in his twenties or thirties.

Cause of Bleeding

Both the indications for operation and the type of procedure will be influenced by the source of bleeding. The four most common causes in Britain are chronic peptic ulcer, acute ulceration, gastric cancer, and oesophageal varices.

Chronic Peptic Ulcer.—The bleeding is usually from a duodenal ulcer. Apart from the severity of the haemorrhage, the previous history of the patient will influence the decision to operate, especially if his symptoms are escaping from medical control. The general principle with this and any other cause of bleeding should be to treat surgically any patient who continues to bleed, either briskly—when an emergency procedure would be required—or more slowly over two or three days, when a more leisurely approach may be made. The other type of bleeding which leads to operation is recurrent bleeding—again the speed with which treatment is required depends upon the rate of the bleeding. This is assessed by the response of the pulse rate, which rises much earlier than blood pressure falls, the presence of fresh blood in the gastric aspirate (gastric intubation should be routine in these cases), and the clinical response to blood transfusion.

At this point it is well to mention another circumstance which occasionally has to be considered when the patient continues to bleed slowly but requires further transfusion of blood. If blood of the patient's group is in short supply, especially if of a rare group, a decision has to be made when three to four pints (units) are still available. If the bleeding seems to be stopped it may be safe to delay, but if any doubt exists this is a strong indication for operation while there is enough blood to cover it.

TABLE II.—Operations for Upper Gastrointestinal Bleeding

Procedure	Indications	Advantages	Drawbacks	Present Status
Partial gastrectomy	Duodenal ulcer. Gastric ulcer. Acute erosions. Gastric cancer	Removal of source of bleeding and reduced likelihood of re-bleed. Allows a larger gastric remnant	Severity of procedure. Still has some rebleeding. Small stomach symptoms	Most common procedure
Vagotomy with hemigastrectomy	Duodenal ulcer. Gastric ulcer. Acute erosions	More minor operation. No loss of gastric reservoir	As above except fewer symptoms from small remnant. Post-vagotomy diarrhoea	Gaining popularity as a compromise between 1 and 3
Vagotomy and pyloroplasty with oversewing lesion	Duodenal ulcer. Gastric ulcer. Acute erosions		Risk of rebleed. Post-vagotomy diarrhoea	Used when lesion is small (1 cm. or less) but still to find favour with majority

Thus in general a patient with a long history of proved peptic ulcer disease will come to surgery earlier than when the diagnosis is in doubt or when an acute ulcer is suspected.

Choice of Surgical Procedure.—The aim of the operation (Table II) is to stop the bleeding and to prevent its recurrence. Unfortunately none of the procedures available can guarantee to do both in all cases, but all achieve both aims in the majority of patients. The reasons for any choice of a particular operative technique are always multiple and are compounded of the risks involved to life and in terms of later morbidity, together with the efficacy in fulfilling the aims. In the surgical treatment of chronic peptic ulceration until 10–20 years ago the favoured operation was partial gastrectomy. This is now being displaced by vagotomy and a drainage procedure. A similar trend has occurred when treating bleeding ulcers, but it has been much less marked. Most surgeons still prefer to resect the ulcer, and so partial gastrectomy is the commonest operation (Fig. 1). Some surgeons who are more impressed by the reported incidence of undesirable side-effects of gastric resection prefer to resect less of the stomach (hemigastrectomy or antrectomy) and to combine this with a vagotomy to avoid recurrent ulceration (Fig. 2). My own preference is to control the bleeding by local excision of the ulcer if it is gastric or anterior duodenal or to oversew the bleeding point if the ulcer is about 1 cm. in diameter or less; then to attempt to prevent recurrence by performing a vagotomy and pyloroplasty (Fig. 3). It seems rational to denervate only the stomach and preserve the branches of the vagus to the liver, pancreas, and small bowel—a selective vagotomy. However, it takes longer to perform a selective vagotomy than to divide the main vagal trunks as they pass through the diaphragm, and in an emergency the latter procedure being more expeditious may on occasion be preferred.

Apart from the drawbacks of the "dumping" syndromes after gastrectomy and changes in bowel habit after vagotomy, the main untoward sequela of these operations when used in the treatment of haemorrhage is that they fail in 5% to 15% of cases—that is, bleeding recurs in these patients. The bleeding is usually more minor than the acute incident leading to the first operation. Opinions differ on the risks of this occurring with the various operations, but the general trend from the literature is shown in Table III. The further loss of blood

adopted. The aim should be to avoid surgery if this is at all reasonable, since the lesion in many cases is reversible. If the effects of the initial bleeding can be controlled until it stops the patient avoids an operation. In this group especially the use of gastric hypothermia seems to be most rational. The indications for operation are still persistent or recurrent bleeding, but the tendency is to postpone the operation longer than with the chronic ulcer patients. The choice of operation is the same as for chronic ulcer. There is a strong case for the use of vagotomy and a drainage procedure; this avoids the possibility of having to remove almost all the stomach if widespread lesions have all to be resected.

Gastric Cancer.—Gastric cancer is not very commonly the basis of a large haemorrhage, and usually the decision to operate can be made at relative leisure. The resection of the growth is the only practicable procedure: this may be a palliative excision only, but it will serve to arrest the haemorrhage.

Oesophageal Varices.—Massive bleeding often arises from oesophageal varices. This is another condition in which efforts are made to do without acute surgical intervention, particularly since the postoperative mortality and morbidity are high. The death rate from bleeding oesophageal varices is the highest of these four common causes of bleeding from the upper gastrointestinal tract. Management of the condition will be discussed in a separate article in this series.

Summary

The surgeon's role in the acute management of bleeding from the upper alimentary canal is to act when bleeding threatens life by its persistence or its recurrence. He may be called upon to make the diagnosis at operation and to proceed to control the bleeding. More usually the bleeding is less catastrophic and more time is available; the diagnosis has been made before operation and the control of the bleeding is the object of surgery. Partial gastrectomy is still the procedure most commonly performed for bleeding from gastric cancer or peptic ulceration, although direct control of the bleeding point along with vagotomy and pyloroplasty is also being used. Early joint consultation between physician and surgeon is the basis of sound management of upper gastrointestinal haemorrhage.

TABLE III.—Incidence of Further Bleeding After Partial Gastrectomy or Vagotomy and Pyloroplasty

Operation for Bleeding Ulcer	Number	Further Bleeding
Partial gastrectomy	167	12 (7.2%)
Vagotomy and pyloroplasty	142	9 (6.3%)

may be from the original ulcer if it was not removed, from the region of the stoma, from undetected lesions, or from recurrent ulceration. Though the surgeon succeeds in securing a definitive cure in the majority of patients, this worrying minority remains.

Acute Ulceration.—Whether the acute ulcer is peptic in the stomach or duodenum, or due to aspirin ingestion in the stomach, or is due to repeated vomiting tearing the mucosa at the cardia, a much more conservative approach should be

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ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Lithium in Schizophrenia

Q.—What, if any, is the effect of lithium salts in patients with schizophrenia, and have there been any trials of the use of lithium salts in the treatment of this disease?

A.—There is no unequivocal evidence that lithium salts have a beneficial effect in the treatment of schizophrenia, and a review of the literature does not indicate that any formal trial into the use of lithium salts in this disease has been carried out.

In a series of 28 papers recently reviewed concerning lithium therapy in other than affective disorders there is reference to schizophrenic patients within whole groups of patients suffering from other diseases, and for this reason it is difficult to interpret the claims made by some workers. Treatment responses even among these groups are classified by terms that have not been defined, making it even more problematical what the outcome has been.

The original work done by Rice¹ in Britain described the results of lithium therapy in 12 patients suffering from schizophrenia, and of these one improved but remained in hospital and one improved sufficiently to be discharged. Both of these patients exhibited aggressive behaviour in association with delusional thought content. In contrast with this group, nine patients who were suffering from a schizo-affective psychosis were also studied, and of these seven improved sufficiently to leave hospital. Annell² described a single adolescent patient with periodic catatonia in whom she found that lithium controlled the psychotic episodes.

Clinical impressions suggest that lithium can have a favourable effect in recurrent schizo-affective psychoses. Sir Aubrey Lewis³ has pointed out that it is in this type of psychosis (i.e., with affective symptoms) that the natural prognosis is more favourable, and for this reason it cannot be said that there is satisfactory evidence that lithium has been found to be of benefit in schizophrenia, though "blind trials" may yield further information.

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- ² Annell, J., personal communication, 1966. International Congress of Psychiatry, Madrid.
- ³ Lewis, A., in *Price's Textbook of the Practice of Medicine*, 10th ed., 1966, edited by R. Bodley Scott. London.

Intermittent Uniocular Diplopia

Q.—What might be the causes of intermittent diplopia in one eye in an otherwise healthy male aged 38?

A.—Uniocular diplopia is usually considered to be rare and caused only by such conditions as partial dislocation of the lens and retinal detachment. However, a type of uniocular diplopia can be demonstrated in a high proportion of otherwise normal subjects under certain conditions.^{1,2} It is best seen when viewing a horizontal white target against a dark background—for example, a fluorescent street lighting or neon signs at

night. The second image is displaced vertically by about 5 minutes of arc and is fainter than the primary image. The doubling is probably caused by the upper part of the lens acting as a weak prism, base down, the base of the prism crossing the upper part of the pupil.

Little attention has been paid to this phenomenon by ophthalmologists, and the symptom is dismissed as being due to astigmatism. Correction of any refractive error reduces the effect by improving the definition of the primary image. The second image is still present, however. Constriction of the pupil or viewing through a pinhole abolishes the diplopia but is not a practical solution. Explanation and reassurance are usually all that is required.

REFERENCES

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- ² Hales, R. H., *Amer. J. Ophthalm.*, 1967, 63, 459.

Wounds from Galvanized Wire

Q.—Is there any evidence to support the belief in the wire-rope industry that wounds caused by galvanized wire become infected more often than those caused by other types of wire?

A.—No direct evidence on this point is known. A similar belief was formerly held about injuries from copper, but when this was checked in a comparative study of "swarf" injuries due to different metals no extra incidence of sepsis was found.

Zinc is not very toxic when applied locally. A 1% solution of zinc sulphate, for instance, has been used in eye drops, and a 4% solution for treatment of skin lesions. Antiseptic properties are claimed for these preparations, so it seems unlikely that the zinc present on galvanized wire would itself increase the risk of sepsis. A recent study further claimed to show improved wound healing when zinc sulphate was given orally.¹

If enough comparable wounds caused by wire of different metals are seen a study of their relative sepsis rates would be of interest. It seems likely, however, that ancillary factors such as roughness of finish or extent of bacterial contamination might well be more important than the nature of the metal itself.

REFERENCE

- ¹ Pories, W. J., Henzel, J. H., Rob, C. G., and Strain, W. H., *Lancet*, 1967, 1, 121.

Turkey-meat and Tryptophan

Q.—May white chicken-meat be used as an alternative to white turkey-meat in a low tryptophan diet?

A.—Though the beneficial action against psoriasis of a diet containing turkey-meat has been attributed¹ to its low tryptophan content, the validity of this explanation is still doubtful. There is no satisfactory evidence that turkey-meat, either white or brown, is low in tryptophan. The absence of this essential amino-acid from any form of meat derived

from healthy musculature would seem surprising.

Without taking the question of colour into account, turkey and chicken meats have been found to contain about equal amounts of tryptophan. The good effects claimed for the turkey-meat diet can best be regarded as an empirical observation and not as a basis for theory. The substitution of chicken for turkey would not be expected to diminish the efficacy of the diet, but this point apparently has still to be investigated.

Psoriasis has long been believed to be aggravated by a diet rich in meat. Possibly some forms of meat are more harmful than others, with meats from birds less harmful than meats from mammals.

REFERENCE

- ¹ Spiera, H., and Lefkowitz, A. M., *Lancet*, 1967, 2, 137.

Alternating Hyperglycaemia and Hypoglycaemia

Q.—Is there a disorder of the carbohydrate-regulating mechanism in which bouts of hyperglycaemia are followed by bouts of hypoglycaemia sufficient to cause symptoms?

A.—The typical example of this is the lag type of glucose tolerance which occurs after operations on the gastrointestinal tract, such as partial gastrectomy. A similar response is sometimes found in apparently normal individuals, some of whom may eventually develop diabetes.

Alternating hyperglycaemia and hypoglycaemia occur in poorly controlled diabetics and in those with accompanying adrenal or pituitary insufficiency—for example, after hypophysectomy. Presumably, however, diabetes is not present in this patient, and there is no question of the surreptitious administration of insulin. Even though hyperglycaemia is said to be followed by hypoglycaemia, it would be wise to investigate the patient for other causes of hypoglycaemia.

Malar Flush

Q.—What is the explanation of the "malar flush" in patients with lobar pneumonia, and why do patients with apical pneumonia sometimes present with cerebral symptoms?

A.—The malar flush is due to cyanosis, and this is attributable to unoxygenated blood passing through areas of unaerated lung so that there is poor respiratory exchange. Pain may play a part in diminishing respiratory excursion, and of course in the worst cases cyanosis may accompany peripheral circulatory failure.

I have not heard of any satisfactory explanation for the confusion and delirium that commonly accompany apical pneumonia. Any patient with pneumonia may develop cerebral symptoms, presumably from factors such as toxæmia, anoxia, and retention of carbon dioxide. It is important to bear in mind in this context the occurrence of meningitis and cerebral abscess and the susceptibility of the alcoholic to pneumonia.

Book Reviews

Young Criminals

The Young Offender. By Dr. D. J. West. (Pp. 333, 35s.) London: Gerald Duckworth, 1967.

A review of the state of knowledge of the incidence of crime in young people is well-timed. The book includes a scholarly presentation of the literature of its aetiology and treatment. Dr. West casts doubt upon the reality of the recent increase of juvenile delinquency and calls attention to the trivial nature of much of it, comprising largely cases of larceny and breaking and entering (79% of all indictable offences in young people). There seems no increase of recidivism beyond that allowed for by the increase of population. Convictions for drunken behaviour, the use of prohibited drugs, vandalism, and assault have increased. The majority of young offenders seem not very different from groups of non-convicted, self-admitted delinquents.

Dishonest behaviour often seems more closely linked to the situation in which the juvenile finds himself than to any personality characteristic. The black-out in the north-east of the United States in 1965 led to a spate of looting. Experiments are referred to when the release of aggressive behaviour in normal subjects has been provoked by mild authoritative persuasion. Social pressures alone are not the determinant; multifactorial explanations seem more convincing. Poor education and health, broken homes and lack of adequate parental control, low salaries, and poor housing seem elements of a complex social handicap in

association with other personality and situational factors. The increased pressure towards conformity leads to greater strain upon the socially handicapped, and aspects of the English educational system are criticized for contributing to this.

The changing views on the influence of constitutional factors in juvenile delinquents are recounted. A strong case appears to have been made out for the existence of inherited factors in some serious and persistent criminals, but generally the influence of heredity seems small. A lack of verbal skills rather than poor intelligence is more characteristic of delinquents in general. The influence of minor physical handicaps, minor degrees of brain damage—sustained perhaps at childbirth—abnormal E.E.G., and the association of certain body types are comprehensively documented. Behaviourist theories are lucidly presented and related to psychoanalytic and sociological viewpoints. Adequate reference is made to the work of Piaget on moral development and maternal deprivation, the surveys of Douglas and Blomfield, the Cambridge-Somerville youth study, the important prediction tables of the Gluecks, and different attempts to classify delinquency.

Drug-taking and addiction and possible methods of their control are critically discussed. The incidence and types of sexual offence are competently dealt with. Such

offenders seem usually to have convictions for property offences also, but include many inhibited neurotic types quite different from the ordinary young delinquent. Reasons for the relative infrequency of female delinquency and an assessment of why wayward girls tend to be worse than delinquent boys are analysed. The expression of female maladjustment by promiscuous behaviour and the predominance of care and protection cases are adequately noted. The literature concerning pregnancy in the unmarried was presumably not thought appropriate to the author's task. A historical account of sentencing of young offenders includes nineteenth-century reforms, the development of approved schools and borstals. The innovations made in juvenile courts and the setting up of family councils is fully covered. In dealing with prevention the author argues for a failure of normal social control and efforts to strengthen these as having priority over measures for dealing with individual law-breakers. The treatment of delinquency in terms of reality and group therapy is discussed and an account of such methods as that of Aichhorn and other projects including behaviour therapy is given.

Throughout the book Dr. West uses the language of science in a field when speculative interpretation has often outweighed the facts of research. The book is carefully and logically arranged, is well written, excellently indexed, and is the most comprehensive account of its subject known to its reviewer.

JOHN S. BEARCROFT.

Obstetric Analgesia

Principles and Practice of Obstetric Analgesia and Anaesthesia. Vol. 1. *Fundamental Considerations.* By John J. Bonica, M.D. (Pp. 837+xvi; illustrated. £9 15s.) Oxford: Blackwell, 1967.

This is not armchair reading but a massive reference book to almost everything which can be conceivably connected with obstetric analgesia and anaesthesia. The present volume, which is the first of two, deals with the physiology of pregnancy and parturition and with the pharmacology and clinical effects of the various substances and methods used both for analgesia and for general and regional anaesthesia. The second volume, which is yet to come, will deal with the clinical side of analgesia and anaesthesia. The two volumes together look like containing something over 1,500 pages. By any standard this is a tome, but from the quality of the first volume an immensely important one.

It is essentially a comprehensive review of this field of medicine, and the documentation is therefore a particularly attractive feature. There is hardly a paragraph that does not

include a list of references; in some places every line has three or four. Bonica has already shown in his textbook on pain that he is capable of handling vast fields in a very detailed manner, and this book is further evidence of his capability.

However, even the best and biggest of books—and this surely falls into both these categories—tend to have a national or regional character, and this one is no exception. British readers must not be surprised, therefore, to find that in spite of the thoroughness of the rest of the book the common methods of analgesia used in Britain do not appear to be very important to the author. The self-administration of nitrous oxide is dealt with only in terms of mixtures with oxygen individually made up for each patient, and 75% nitrous oxide is advocated as a satisfactory concentration. Few anaesthetists in this country would be happy to leave a woman with this mixture. Nitrous oxide and air is dismissed in seven lines without any reference to the considerable experience which has accumulated here in 40 years of use, while premixed nitrous oxide and oxygen is not mentioned at all. Heroin is said to be still used in the British Isles, but the supporting

reference given is to a questionnaire sent out by the Association of Anaesthetists some 10 years ago to determine the use of heroin in general by anaesthetists. To this, only four out of 639 anaesthetists said they had ever used this drug in obstetrics.

Another curious feature, for a book which handles in such splendid fashion such a myriad of minutiae, is the juxtaposition of the abstruse and the obvious, the advanced and the elementary. Thus elaborate diagrams illustrate open drop ether, intubation of the larynx, and respiratory obstruction by the tongue. A massive reference book like this is hardly to be expected to offer somewhat elementary teaching material to junior residents and midwifery nurses.

These somewhat minor points caught the eye for obvious reasons. My overwhelming reaction to this volume is one of unstinted praise and recommendation for what must be the finest and most comprehensive book on obstetric anaesthesia and analgesia yet compiled. Everyone interested in the subject from houseman to advanced research worker or clinical teacher is bound to use this fine book sooner or later.

W. W. MUSHIN.

Microbial Disease

Recent Advances in Medical Microbiology. Edited by A. P. Waterson, M.D., M.R.C.P. (Pp. 355 + viii; illustrated. 65s.) London: J. & A. Churchill, 1967.

The forerunner of this new edition in the *Recent Advances* series, *Recent Advances in Bacteriology*, was published 12 years ago. Since then great progress has been made in the study of microbial disease, with major advances being made not so much in bacteriology but in the wider field of microbiology. The publication of this new edition under the title of *Recent Advances in Medical Microbiology* is to be welcomed for a number of reasons, not least because it may reflect a change in attitude towards the teaching of microbiology in medical schools.

It is natural that the number of subjects in a book such as this is limited, but they have been chosen with care to include those in which there have been major advances or in which a comprehensive review was needed. There are altogether nine chapters, five being devoted to various aspects of microbiology, one to the mycoplasmas, two to bacteriological subjects, and a final chapter on a protozoal infection, toxoplasmosis. All are complete in themselves and contain a useful set of references.

E. Norrby's chapter is straightforward and comprehensive, dealing in the main with the biological and antigenic properties of the virus and methods for measuring antibodies to measles, a subject to which the author has made important contributions. He discusses ways of achieving resistance against measles from which it is clear that he favours the use of killed measles vaccines. Whether he is justified in concluding that present evidence indicates that long-lasting immunity can be obtained with a killed vaccine is open to question, and for that matter there is as yet no evidence that a live vaccine will do so either. The next two chapters by D. M. McLean on aseptic meningitis and J. E. Banatvala on respiratory viruses bring the reader up to date with progress in these spheres which are of so much importance to the clinician. The chapter on diagnostic procedures by C. E. D. Taylor contains much information which will be useful to the clinician both on requesting tests for virological diagnosis and in interpretation of the results. The fourth chapter on a virological subject is by the late Alan P. Goffe on immunization against poliomyelitis. In it he gives an admirable account of the processes of immunity to poliomyelitis, and the story of the development of inactivated vaccines and later of attenuated vaccines is well told. This is an extremely well-balanced account of a complicated subject. It will be interesting to see whether Dr. Goffe's forecast that in the future vaccines will be prepared in human diploid cells will come to pass.

The discovery a few years ago that the Eaton agent, the causative agent of atypical pneumonia, was a mycoplasma has stimulated much interest in these organisms. As B. P. Marmion (his name is surprisingly misspelled in the first page of the chapter) records, much of the earlier work on these organisms in relation to veterinary bacteriology and studies on puerperal sepsis has been to some extent overshadowed by the discovery of the identity of the Eaton agent. This chapter describes in detail the general properties of these

organisms and methods for laboratory study. Their role as pathogens in man and animals is discussed in detail as well as the question of the possible association of these organisms with human leukaemia, certain solid tumours, and rheumatoid arthritis. The flag of bacteriology is kept flying in an article by R. Hare on the anaerobic cocci, and one on protein binding by G. N. Rolinson makes useful reading. The last chapter on toxoplasmosis by C. B. Beattie presents a fascinating account of the natural history and diagnosis of the disease caused by this parasite. It is an admirable choice of subject because in the past it has been largely ignored in textbooks, with too little detail on the clinical aspects in some and too much detail of the parasite in others. This lucid account will be of particular interest to pathologists and paediatricians.

This book is strongly recommended for pathologists, clinicians, and many others. At the present rate of progress a further edition will be required before another 12 years has elapsed.

J. A. DUDGEON.

Successful Surgery for Vesico-vaginal Fistula

The Vesico-Vaginal Fistula. 2nd edition. By J. Chassar Moir, C.B.E., M.D.(Edin.), M.A.(Oxon.), D.M.(Oxon.), F.R.C.S.(Edin.), F.R.C.O.G., Hon.L.L.D. Queen's University, Ontario, Hon.M.M.S.A. (Pp. 196 + ix; illustrated. 60s.) London: Baillière, Tindall & Cassell, 1967.

When this monograph first appeared in 1961 it was widely accepted as a gem among medical literature, and quite rightly. The second edition, in which the author's delightful personal style is preserved, is even better. It is a little larger because it contains new illustrations and additional sections which deal with the "circumferential" vesico-vaginal fistula, the construction of ileal and rectal bladders, and the treatment of ureteric injuries. The inclusion of the last (as well as of urethro-vaginal fistulas) is not inappropriate despite the title of the book, and serves to give the gynaecologist and urologist a complete picture of urinary fistulas in women.

The emphasis throughout this book is on the presentation of the technical details of operations (including instruments, suture material, and postoperative care) for the cure or circumvention of fistulas. Its object is to guide the surgeon who only occasionally deals with such problems and who is therefore likely to encounter difficulties and disappointments. In short, Professor Chassar Moir reveals the secrets which determine surgical success rather than failure. And no one is better qualified to do so since he has a unique clinical experience in this field, acquired in this country, in Africa, and in India. His record of achievement is remarkable. Of 350 patients suffering from fistulas of varied types and aetiology, two-thirds of whom had had 1 to 19 unsuccessful operations previously, only three were not treated surgically. And 255 vesico-vaginal and urethro-vaginal fistulas of traumatic origin were tackled with 100% anatomical success. No surgeon can afford to neglect the advice and tips given by one who can obtain results such as these.

T. N. A. JEFFCOATE.

Spalteholz in English

Atlas of Human Anatomy. Originally devised by Werner Spalteholz. 16th edition. Revised and re-edited by Rudolf Spanner. (Pp. 904 + xii; illustrated. £13.) London: Butterworth, 1967.

An English version of this atlas, well known to all anatomists since its first edition in 1895-1900, has been prepared in order to reach a wider public. This involved certain technical difficulties in that the plates, with their incorporated Latin terms, had already been printed. It was not possible to print both a running English text and lists of translated terms. The reader is therefore left with only a translation of Latin terms as far as possible picture by picture, although in some figures there are a few lines of useful commentary in English.

There is a wealth of anatomical information for the studious in these "pellucid images," even though the method of reproduction employed does not always succeed in giving the crispest of outlines. Colour is freely used, often to advantage and with clarification, but again in several figures achieves a certain haziness. Some of the neat diagrams in fact carry more conceptual information than the more spectacular contributions such as Fig. 754. This is labelled as a "composite diagram of the circulation," and is a masterpiece in its own right. Truly did Ruysch, the greatest of "injectionists," maintain that anatomy was blood vessels "variously arranged"; he would, even so, have hesitated before this phantasmagoria. Many of the radiographs, on the other hand, are quite excellent reproductions. The price of the atlas will, however, preclude any undergraduate buying it for himself. In this country it can only find a place in a dissecting room.

R. J. HARRISON.

Bile Pigments

Bilirubin Metabolism. Edited by Ian A. D. Bouchier, M.D., M.R.C.P., and Barbara H. Billing, Ph.D. (Pp. 294 + xii; illustrated. 63s.) Oxford: Blackwell, 1967.

This book gives a verbatim account of a conference held in the medical unit of the Royal Free Hospital in 1966. These international symposia have been held annually under Professor Sheila Sherlock's chairmanship for some years and now form an important contribution to medical literature. The present volume is edited by Drs. I. A. D. Bouchier and Barbara H. Billing, who are to be congratulated on the accuracy and completeness of the text.

The proceedings were divided into five main sections. The first on the origin of bile pigments was concerned with "early bilirubin" and includes important new information on this subject. The second section on the structure of bile pigments is mainly chemical. The hepatic transport of bile pigments was dealt with in the third section, and the last two were concerned with bilirubin metabolism in obstructive jaundice and with renal excretion of bile pigments.

With 50 contributors from 12 countries it is natural that many new experimental data were presented, and it is particularly valuable to have a complete record of the discussion

at the end of each section. It would be invidious to select any special article for comment, since the general standard is so high. The book seems to have appeared reasonably quickly after the conference, although the actual date is not mentioned. It can be strongly recommended both to clinicians and to laboratory workers interested in bilirubin metabolism.

N. F. MACLAGAN.

Cerebral and Spinal Disorders in the Young

Pädiatrische Neurochirurgie. Edited by Professor Joachim Gerlach *et al.* (Pp. 875 + xix; illustrated. DM. 287.) Stuttgart: Georg Thieme, 1967.

Paediatric neurosurgery is rapidly assuming an important position as a specialty in its own right, and a few surgeons in many countries are devoting their attention almost exclusively to the study and care of cerebral and spinal disorders in the young. There are numerous important differences in pathology, presentation, and prognosis between the surgical disorders of the nervous system in adults and in those in children and infants which demand special study and special modifications of treatment and management.

As a source of reference and information for the neurosurgeon and neurologist whose practice includes all age groups this new book, *Pädiatrische Neurochirurgie*, will prove invaluable. It will also, no doubt, be gratefully welcomed by paediatric neurosurgeons and their assistants as a detailed, comprehensive, and informed account of their specialty. The editors and most of the contributors are from the university clinics and hospitals of Würzburg and Vienna, but there are two contributors from Paris and one from the university of Groningen in Holland.

The work is in two parts. The first is a general section containing chapters on the anatomy, physiology, and embryology of the nervous system. Chapters follow on the examination of the central nervous system in infants and children, upon general clinical methods of examination, and special diagnostic procedures, referring separately, where appropriate, to the newborn, young children, and children of school age. Brief reviews of the bases of echoencephalography and

isotope scintillation scanning of the brain are included. There is also a useful section on anaesthesia and pre- and postoperative care.

In the second and larger part of the book the special pathology, diagnosis, and treatment of the various surgical disorders of the central nervous system in infancy and childhood are considered in methodical detail. Particularly valuable to the surgeon are chapters on some of the "medical" problems such as virus and parasitic infections and the demyelinating disorders of uncertain aetiology. This book is too detailed to be read from cover to cover by even the most assiduous student of neurosurgery, but it is a sound and orthodox work of reference. I am convinced that works of this calibre and scholarship dealing with a fairly small field should receive a wider readership by translation into other tongues.

There is an excellent general index, and a useful bibliography follows most of the chapters. The illustrations, x-rays, and diagrams are beautifully reproduced.

B. J. HARRIES.

Medical Society of New Jersey

The Healing Art. A History of the Medical Society of New Jersey. By Fred B. Rogers, M.D., and A. Reasoner Sayre. (Pp. 346 + ix; illustrated. \$10.) New Jersey: The Medical Society of New Jersey, 1966.

The Healing Art is an interesting account of the New Jersey Medical Society, which dates back farther than any other American or British medical society with the exception of the Royal Medical Society of Edinburgh. In the first chapter the authors give a brief account of early colonial medicine, which was very crude, as may be judged by the fact that John Wesley's *Primitive Physic* was much used. Throughout the whole book the stages of medical progress are described, and with just pride the authors point out how quickly the New Jersey Medical Society either took advantage of new discoveries or initiated reforms in the public health of the State.

The Society began on 27 June 1766, when fourteen physicians met together and signed the attendance book (still preserved) of this inaugural meeting. The first regular meeting of the Society took place a month later, but

for some years the Society met only twice a year, for difficulties of travel were great. The newly formed State Society recommended the physicians of each county to form a local medical society, and to elect delegates to the State Society. (By 1885 all 21 counties possessed a local medical society.)

During the War of Independence much fighting took place in New Jersey, and some members of the Society acted as medical officers in one or other army. Meetings of the Society were necessarily irregular during this period and for some time afterwards, for we learn that no meeting took place between 1795 and 1807. After that date the Society was re-established and has flourished ever since.

The Medical Society of New Jersey always had considerable political influence. As early as 1772 two members of the Society advised the two judges who granted licences to practise medicine in New Jersey, and for many years the Society possessed the right to grant an M.D. to suitable candidates. The Society often discussed the question of fees, and rightly so, because in 1849 it was stated that one-fourth of the members of the Society left their families destitute.

During the last hundred years many thousands of immigrants from Europe entered the State, so that in 1912, when the New Jersey Midwife Association was formed, it was necessary to provide lecturers in English, German, Italian, and Polish. The number of doctors increased along with the population, and in 1965 its membership reached 7,316 out of a total number of 8,734 doctors in the State. The Society always strongly opposed any undue encroachment of the State or Federal Government on the legitimate province of the general practitioner, and supported measures (such as the Blue Shield) that encouraged insurance for health by the individual.

Throughout the book there are numerous short biographies of physicians who have played an important part in the Society, and a timely tribute is paid to the many famous pharmaceutical firms whose centres of research are situated in the State of New Jersey. In 1928 a Women's Auxiliary to the New Jersey Medical Society was founded and since then has published a short history of its foundation, including an illustrated map of New Jersey. We commend its foresight, for this reviewer of *The Healing Art* had frequently to refer to an atlas.

ZACHARY COPE.

Books Received

Review is not precluded by notice here of books recently received.

The B.C.H. Vade-Mecum. 6th edition. Edited by B. S. B. Wood, D.M., F.R.C.P. (Loose-leaf in plastic binder 12s. 6d. Paper 7s.) Birmingham: Children's Hospital, 1967.

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Speech Pathology. Diagnosis: Theory and Practice. Report of the National Conference of the College of Speech Therapists in Glasgow, 1966. (Pp. 91. 30s.) Edinburgh and London: E. & S. Livingstone, 1967.

Il Metodo Sperimentale in Rapporto Alle Dottrine di B. Belesio E. F. Bacone. By G. P. Arcieri, M.D. (Pp. 159. \$5.00.) New York: Alcmæon, 1967.

Anaesthesia and Resuscitation. A Manual for Medical Students. Edited by R. A. Gordon. (Pp. 179. 24s.) London: Oxford University Press, 1967.

Coronary Heart Disease in Kristiansund. 1959-61. Incidence, Prevalence, and Mortality. By Per R. Gundersen. (Pp. 178. 45s.) Oslo: Universitetsforlaget, 1967.

Neurological Nursing. A Practical Guide. 2nd edition. By John Marshall, M.D., F.R.C.P. (Lond.), F.R.C.P.(Ed.), D.P.M., and Jean Mair, S.R.N. (Pp. 174 + x; illustrated. 25s.) Oxford: Blackwell, 1967.

The Influence of Perfusate Composition on Edema Development in Isolated Perfused Rabbit Lungs. By Per Knut M. Lunde. (Pp. 86. 45s.) Oslo: Universitetsforlaget, 1967.

Symposia Series in Immunobiological Standardization. Vol. 4. International Symposium on Immunological Methods of Biological Standardization. Edited by R. H. Regamey, H. Hennesen, D. Ikic, and J. Ungar. (Pp. 380 + xii; illustrated. £4 19s.) Basle and New York: S. Karger, London: Academic Press, 1967.

Physiology or Medicine. Nobel Lectures. 1901-1921. (Pp. 561 + xii; illustrated. £9.) Amsterdam: Elsevier, 1967.

The Experience of Childbirth. Revised edition. By Sheila Kitzinger. (Pp. 252; illustrated. 6s.) Harmondsworth, Middlesex: Penguin, 1967.

Middle Articles

GENERAL PRACTICE OBSERVED

Use of General Practitioners in the School Health Service

ALAN R. BUCHAN,* M.D., D.P.H.; A. PARRY JONES,† M.B., B.CH., D.P.H.

Brit. med. J., 1967, 4, 797-799

In recent years there has been increasing discussion on the use of general practitioners in the school health service. This has been motivated undoubtedly by the desire to secure better integration of the curative and preventive services, and to provide a more effective service for the schoolchild. Attempts to bring general practitioners into the school health service, however, raise administrative and organizational problems which are almost insurmountable, and so local education authorities have tended to employ selected general practitioners on a sessional basis in the neighbourhood of their practices but not solely on their practice patients (Chief Medical Officer, 1966a).

For some this is not acceptable, and a recent editorial in the *Practitioner* (1967) asks: "Has not the time come—indeed, been long overdue—when the care of our children be placed fairly and squarely upon the shoulders of family doctors. This would involve, among other things, routine medical examination of every child on first going to school. If any condition be found that should require special consideration, then the school authorities should be informed. The function of what would then be a much depleted school medical service would be the supervision of handicapped children—for example, the hard of hearing, the partially blind, the epileptic, the crippled. In this capacity they would act as paediatricians in conjunction with the local children's hospital."

In Somerset an attempt has been made to employ general practitioners in this more radical manner, and it is hoped that our experiences with a pilot scheme may be of interest.

Early in 1966 a full-time school medical officer retired unexpectedly. He had been solely responsible for the schools in a thinly populated and rural part of the county. The only towns in his area had populations of 3,000 to 4,000, and all of these were some miles apart. In the main, the general practitioners practised in groups from these towns, and each practice tended to have a distinct and local sphere of influence. Thus the majority of schoolchildren in each primary school in the area were patients of the local practice. Even in the secondary schools, which had wider catchment areas, circumstances were such that general practitioners could be employed to carry out school medical work on their own practice patients without causing chaos in the schools.

The Scheme

The scheme was confined to the Wincanton Rural District and covered 1,253 children at 15 primary schools and 821 children at three secondary schools, one of which had boarding facilities.

* Deputy Principal School Medical Officer, Somerset. Now Principal School Medical Officer, Leicestershire.

† Principal School Medical Officer, Somerset.

Eleven general practitioners in the selected area were approached and all agreed to participate. They were asked to undertake all the duties (as under) carried out by full-time school medical officers, with the following exceptions: examinations under S.34 of the Education Act, 1944 (to "ascertain" which children require special educational treatment); examinations under S.57 of the Mental Health Act, 1959 (to find those children thought to be unsuitable for education at school); and Heaf testing and B.C.G. vaccination for schoolchildren registered on their National Health Service list or that of the practice. For children from other practices different arrangements were made (see Results, below).

Duties Required of Practitioners.—(1) Basic routine medical inspections at school entry. (2) Selective examinations at school-leaving age and at an intermediate stage. (3) Special examinations as necessary after referral by heads of schools, educational psychologists, parents, etc. (4) Re-examination of children previously found to have defects. (5) Accident cover. (6) Completion of immunization and vaccination programmes (Modified Schedule P). (7) Annual hygiene inspection of school and report.

Routine screening tests were continued as for other parts of the county, as were the services of the school nurses, educational psychologists, peripatetic teachers of the partially hearing, and speech therapists.

Full-time county school medical officers were expected to deal with the ascertainment of physically and mentally handicapped children, problems associated with special educational treatment, B.C.G. vaccination, and with the children of those general practitioners outside the area who were not in the scheme.

Initially both parties had misgivings. The schools and our committee appreciated the value of having the services of family doctors who were on the spot, but had doubts about whether they would have sufficient time to devote to their new duties. Some felt that a full-time school medical officer wholly in county employ offered a second line of defence in the detection of defects in schoolchildren, and that a new pair of eyes could discover defects that previously had been missed.

In preliminary discussions all the general practitioners stated their preference for payment on a sessional basis, but were persuaded to accept an annual capitation fee despite long-standing antipathy towards this form of payment. However, it was thought likely that the general practitioners would not wish to devote a full two and a half hours one or more times a week to school work, but would develop a pattern of short though frequent visits to schools, thus providing closer linkage than could be given in this rural area by the existing full-time school health service. Remuneration by capitation fee obviated

the need for the general practitioners to keep records of the time that they worked, and it did away with the need to impose definitions of sessions and norms of work—for example, 15, 18, or 20 children per session. Though the doctors had reservations about "open-ended contracts" they agreed to accept them and to keep careful records of the time and effort involved for the duration of the trial.

Finally, it was agreed that fees from the local authority for vaccination and immunization record cards would continue until April 1967, and thereafter the practitioners would claim the revised fees for each procedure from the Somerset Executive Council.

Results

The scheme started in January 1967, and Table I gives the number of pupils on the register of each school and the number inspected during the spring and summer terms. Some 572 children were found to be on the lists of practitioners outside the prescribed area and for whom separate arrangements were made.

TABLE I.—*Number of Pupils on the Registers of the Maintained Primary and Secondary Schools in the Selected Area and the Number of Pupils Inspected by Practitioners*

School	No. of Pupils on Register	No. of Pupils Covered by G.P.s in Scheme	No. of Pupils Inspected by G.P.s		
			Arrears of Inspections	Current Inspections	Total
15 Primary schools ..	1,495	1,253	219	422	641
3 Secondary schools	1,151	821	231	44	275
Total	2,646	2,074	450	466	916

The spring term was devoted mainly to the examination of those children who had missed routine school inspections and re-examinations at the appropriate age owing to the illness of the now retired medical officer. In all, some 916 children were examined during the two terms, 608 of whom were seen for periodic inspections.

The number of pupils inspected at periodic inspections, together with the numbers found to require treatment (excluding dental disease and infestation with vermin), are given in Table II. Of the 159 pupils found to require treatment 50 were recorded as having visual defects.

TABLE II.—*Number of Pupils Medically Inspected at Periodic Medical Inspections, Together with the Number Found to Require Treatment (Excluding Dental Disease and Infestation with Vermin), During the Spring and Summer Terms 1967*

Age Group	No. of Pupils Inspected	Individual Pupils Found to Require Treatment	
		No.	%
5	53	16	30.2
6	162	35	21.6
7	91	39	42.9
8	39	7	18.0
9	25	7	28.0
10	23	9	39.1
11	85	14	16.5
12	34	7	20.6
13	20	3	15.0
14	12	5	41.7
15 and over	64	17	26.6
Total	608	159	26.2

The rate of defect finding (26.2% of children examined) compared favourably with that for the whole county, which averaged 18.3% over the previous five years, and the 15.8% for England and Wales (Chief Medical Officer, 1964, 1966b) over the four years 1962–5.

Seventy-one per cent. of the examinations carried out by general practitioners were attended by parents, compared with 64% for the remainder of the county area. The increase was

noticeable in the secondary school age group, where over a third of the children were accompanied by a parent.

Some 42 children were referred to appropriate specialists for further advice or treatment as follows:

Referred to orthopaedic clinic	20
Referred for ascertainment under S.34 of Education Act 1944	9
Referred to audiology clinic	6
Referred to child guidance clinic	4
Referred for speech therapy	3

The remaining 67 pupils were treated by the general practitioners. These defects fell broadly into three groups—namely, respiratory tract infections, skin disease, and minor emotional and behavioural disorders. By dealing satisfactorily with the behavioural disturbances, our impression is that the practitioners substantially reduced the number of referrals to the child guidance clinic.

These preliminary statistics appear to offer no support to the contention that general practitioners would find fewer defects than full-time school medical officers, and the system had the undoubted advantage that the doctor who found the defect was also responsible for its continuing treatment.

At the end of the summer term all the doctors and the schools were visited by one of us (A.R.B.) in order to assess the reactions of the participants. In general, the schools thought that the scheme offered considerable advantages to the children (and to the schools) over the traditional school health service, mainly because of closer contact with the doctor and ease of reference of problems at local level. The schools were also impressed that the new system had been well received by the parents concerned.

From the point of view of the school the scheme involved co-operation with more than one doctor, and necessitated coping with different techniques, and, more important, an increase in the frequency of visits. Most schools found that there was an additional work load placed in the school secretary, but part of this burden was occasioned by the backlog of children not examined, and by the newness of the system. One or two of the larger secondary schools were served by two and occasionally three practices. As might be expected, clerical difficulties increased when more doctors were involved with the school. In our view, and in that of the head teachers, these disruptions in the life of the school were more than outweighed by the advantages in having general practitioners doing the work. All are agreed, however, that a further increase in the number of doctors visiting a school would be undesirable. In urban areas the children at each school may have up to 20 different general practitioners. If the school health service is to be carried out in a school setting the number of general practitioners serving each urban school would make the administrative burden intolerable. In towns general practitioners could undertake school health work either on a sessional basis with one practitioner to each school or by conducting the examinations in their own surgeries. The latter solution would break the ties with the schools and in our opinion would be unacceptable to most teachers.

The general practitioners were, on the whole, well satisfied, and all agreed to continue the scheme. Several general practitioners appreciated the opportunity of acting as school doctor, and mentioned that there was no longer any likelihood of anxious parents presenting problems, previously discussed with their family doctor, to an unsuspecting school medical officer. We were impressed by the enthusiasm with which they carried out the work, and felt, like Didsbury (1964), that selective medical examinations were better carried out by doctors who already had a detailed knowledge of the child and its background and family. Referral for specialist advice and treatment had been simplified, and subsequent follow-up with the school had been improved.

Summary and Conclusion

An account is given of a trial project in Somerset employing general practitioners to undertake school health service duties for schoolchildren registered on their National Health Service list or that of the practice.

After the trial had lasted two terms everyone concerned wished to continue the scheme. Undoubtedly both parents and teachers appreciated having their own family doctors acting as school medical officers, and this advantage clearly outweighed the increased clerical work for the school. From the outset we

thought that these arrangements could only have a chance of working in a rural area. This view has been confirmed.

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MEDICAL HISTORY

A Letter from Sir Morell Mackenzie

MAXWELL ELLIS,* M.D., M.S., F.R.C.S.

Brit. med. J., 1967, 4, 799-800

A few months ago Sir Terence Cawthorne was moving house and was in the usual dilemma of what to take with him and what to leave behind or give away. Among the gifts was a fine mounted, framed, and signed Spy cartoon of Sir Morell Mackenzie, of which I was the fortunate recipient. I wanted

to hang it in my room at the Institute of Laryngology and Otology and decided that it should be reframed to match the other pictures. When the frame was removed the apparent signature "Yours truly, Morell Mackenzie" was found to be the ending of a letter which had been folded behind the picture,

exposing the signature to give the impression of an autographed portrait. The letter must have been in this position for a good many years, forgotten or unknown. The ink of the signature is greatly faded compared with the rest of the letter. The paper was dry and split at the folded edges, but the script is easily legible. Through the kindness of Dr. Noel Poynter at the Wellcome Institute the letter was carefully restored and mounted and is now in our historical museum at the Institute (see Figure).

Mackenzie was writing from Potsdam, the palace of Emperor Frederick III at Charlottenburg, and had been in almost constant attendance on the Emperor for four months, enduring the emotional professional complications which have been so exhaustively described by Mackenzie himself and many others. In Mackenzie's book *Frederick the Noble* he has a note on 10 April 1888 of the Emperor's remark about the patients in England almost identical with that in this letter of six weeks later, but the letter is unrecorded. It is of some additional historical interest as it is an uninhibited *cri de cœur* from the writer in a private communication to a friend. Mackenzie reveals how keenly he felt the anomalous position he was in and how he found it impossible to extricate himself. However, the Emperor's condition rapidly worsened and he died just over two weeks later, on 15 June.

By all standards this was a difficult case, the management of which was made more difficult by the blaze of publicity in which it was conducted and the personalities and jealousies of the numerous doctors concerned. Lionel Colledge held strongly

* Dean, Institute of Laryngology and Otology, London W.C.1.

Königsches Schloss
Charlottenburg
May 27 1888

My dear Cork

Thank much
for a small contribution
to the *Forbes*. A letter
from Lodge Place Harley
makes me feel very
much inclined to leave
this hole and retire to my
native river. I fancy
from the photographs I have
received that "The Little
House" has been
greatly improved since
I was at Wargrave.

My own idea is to when I have
be back in England
again. When I see a
time the Emperor seems
anxious for me to go, but
when the time comes for
my leaving he moves
suggests my departing
my departure for a little
time he does in the most
delightful way, saying
"I know your journey must
want for very much"
and "What can your
patients in England do
without you etc. But
all the same he seems
to think it quite
natural that I should
stay on! I don't like
to tell you I cannot
get away. This is most
disagreeable position but
I must in. I hope
Cork is well and
that the air there
is flourishing. It seems
as if you would send
him a letter before
I come back.

Yours truly
Morell Mackenzie

that the tumour from which the Emperor suffered probably arose below the vocal cords (subglottic), a condition which often presents diagnostic difficulties even nowadays. In 1887 the early diagnosis of such a lesion was virtually impos-

sible, and with the treatment available the outlook almost hopeless even if a diagnosis had been made. This illness must have been among the most fully recorded in medical history and one of the saddest from so many points of view.

CONFERENCES AND MEETINGS

Family Doctors Practising from Health Centres

[FROM A SPECIAL CORRESPONDENT]

A conference of family doctors practising from health centres was held at the Ministry of Health in London on 21 December. Opening the conference, the chairman, Sir GEORGE GODBER (Chief Medical Officer, Ministry of Health) said that it had been directly inspired by a letter to the *B.M.J.* by Dr. E. J. Lace and Dr. H. I. Howard, of Bristol (7 October, p. 49), which had suggested that the time had now come for a conference of general practitioners who actually worked in health centres to pool their views and iron out problems. It was not generally appreciated, Sir George said, how rapidly progress was occurring in developing health centres. Whereas only a few had been built from the beginning of the N.H.S. to 1965, since the latter year 23 had been built, 38 centres were under construction, and plans for a further 50 had been approved. For the 10 years before 1965 only £70,000 had been spent on health centres in every financial year; since then figures for the succeeding financial years were £340,000, £1 million, and £2 million, respectively—and in future he hoped that three times this last sum would be spent.

Why the Conference was Suggested

Giving his reasons for suggesting the conference, Dr. HOWARD said that several previous conferences had been held on the subject of health centres. Almost all of these had been devoted to contributions by well-intentioned theorists and paramedical workers. A number of articles had also been published on the subject by interested academics. Nevertheless, the views of the general practitioners working in the centres remained unknown, and what was wanted was an exchange of ideas. In his opinion the present-day family doctor working from a health centre had the opportunity of being a complete doctor, with co-operation from academic staffs and hospital consultants. It was almost 50 years since the Dawson Report had first defined a centre—but the authors of the report could never have envisaged the effects of such things as the population explosion and the brain drain.

The discussion on "The Health Centre and Hospital Service" was opened by Dr. M. A. SLEE (Witney, Oxon.). His centre, which had started two years ago, was situated 13 miles (21 km.) from the nearest district hospital at Oxford. It offered general-practitioner, local authority, and virtually full consultant services in the same building. Of the last, 28 sessions were held every month, though there were no sessions on otorhinolaryngology and children's and skin diseases. There were advantages for both patients and

doctor—the absence of travelling, and the ease of consulting with the specialist and obtaining a direct opinion. Diagnostic facilities at the centre included an x-ray department and a pathological laboratory, both of which were manned by part-time technicians, and even their own thermography unit. Doctors working there had established informal links with the teaching hospital at Oxford, with students undertaking attachment and attending outpatient sessions with the consultants.

Casualty services were restricted to minor injuries, and often these patients were seen by the nurse in the first instance. Concluding, Dr. SLEE emphasized that this centre had been founded by private capital and not by the Ministry of Health.

Dr. G. W. PAGE (Coventry) stressed the importance of geographic factors. It was not an economic proposition to have a casualty department and diagnostic facilities in a health centre when the hospital was just round the corner. He himself had a clinical assistantship in the orthopaedic and accident department in his local hospital, and he wondered whether, in collaboration with industry, it was not possible to develop peripheral casualty centres. These would not treat major injuries but would do much to relieve the load on the central hospital.

Speaking as the representative of a university teaching health centre, Dr. H. W. ASHWORTH (Manchester) said that it had been shown that it was uneconomic to provide diagnostic facilities in a health centre if there was open access to these in a local hospital. What was needed was really quick service. Dr. J. A. M. VASEY (Risca, Monmouthshire) spoke of difficulties in transporting specimens to the pathology laboratory, which was 5 miles (8 km.) away. In his view there was sometimes a strong need for a general-practice diagnostic unit, particularly when there were excessive delays; in his area it might take six weeks for a plain x-ray film, nine months for a barium meal, and ten months for a barium enema to be done.

Value of Consultant Services

Dr. G. G. WARD (Ottery St. Mary, Devon), who practised with two other doctors in a rural area with 8,000 patients, emphasized the value of consultant sessions in a health centre, for both the patient and the general practitioner. There was an excellent service for pathology tests from the laboratory of their local hospital. The family doctors had their own haemoglobinometer and electrocardiograph, and, armed with the results of tests done beforehand, they could present a "worked-up" patient to a visiting consultant.

Dr. D. H. KAY said that at Hythe (Hants) they had been fortunate in having a health centre built on to a pre-existing cottage hospital. A casualty service was provided by a rota of general practitioners, and they had a minor operating-theatre and an x-ray unit. Part of the success of their centre was due to the contact with the postgraduate medical centre at Southampton, 11 miles (18 km.) away. He thought that one of the most important things to have come out of the health centres so far was the increased mutual respect between consultants and general practitioners.

Dr. W. A. BROWN (Peterlee, Co. Durham), who said that their requests for consultant sessions had been rejected, called for residential accommodation to be provided for two medical students in every health centre. He and his colleagues at the centre were co-operating with the local technical college in the training of medical secretaries.

Dr. R. H. GLENDINNING (Bristol) asked what was the best size—for the health centre building, its staff, and the population served. He thought that the optimum size lay somewhere between the single-doctor centre, of which there was one in Devon, and the vast polyclinics found in Eastern Europe. Could the essential doctor-patient relationship be preserved with a large team which included laboratory technicians and visiting consultants? He had found after working in a centre for four years that his referrals to hospital consultants were now more specific—for example, he now referred an individual patient to a genito-urinary specialist rather than to a general surgeon.

Sir GEORGE GODBER asked whether it was a waste of doctors' time to do too many laboratory investigations themselves. Where should the main diagnostic services be situated? What was needed was a specialist service based on the hospitals, and a generalist service based on the health centres.

Size of Health Centres

Discussing the size of health centres, Dr. VASEY emphasized the need to plan for increases in the population served. Since their centre at Risca had been planned the population had risen from 10,000 to 14,500. The centre was now too small to serve these people properly and he was worried lest the good work already done should be wasted because of lack of space. Dr. S. DILLON (Rugely, Staffs) said that they had the same problem, with a continual rise in the number of patients served by the practice. Should the health centre be enlarged, or should it stay at its present size and develop satellite centres? Dr. BROWN said that at Peterlee they had resisted the temptation to build

satellites and had built more consulting suites at the main centre.

Dr. L. ROODYN (London) pointed out that it had been shown that a population of at least 60,000 was needed for x-ray and consultant services to be provided on an economic basis; hence they probably could not be provided in health centres. He thought that a third of all patients coming to the surgery did not need to see a doctor, but could see a nurse. The patients themselves would accept this approach, and the nurse should work on an appointments system.

Speaking of ancillary workers Dr. A. DUNNILL (Oxford), said they already used the district nurse to do simple treatments on patients at home. In their practice the midwives helped the general practitioner at the antenatal sessions and in the maternity unit, which was linked to the specialist unit and the teaching hospital.

Dr. D. A. MOORE (Buckfastleigh, Devon), who practised with a partner in a health centre serving a scattered rural population of 4,500, also spoke of delegating work. It was no use having high-powered equipment in a centre if there was no time for the doctor to use it. Recently he had concluded that only one out of eight patients seen on a visit needed to be seen by a doctor. They had recently abandoned a branch surgery to get one extra visiting day a week.

Dr. ASHWORTH said that if the nurses were to do visits and treat patients a change in the attitudes of both doctors themselves and of the Royal College of Nursing would be needed. Dr. A. J. BRAY (Ilfracombe) urged doctors not to lose sight of the personal element of general practice. Consultations should still be run on traditional lines, with the patient seeing his own doctor, and sufficient time would be gained by centralization and the introduction of an appointments system.

Role of Practice Nurse

Dr. R. N. CARTER (Peterlee, Co. Durham) spoke of their two months' experience with a practice nurse, who divided her time between district visits and work in the surgery. Some of these sessions were by appointment, and her other duties included taking the blood pressure of patients with hypertension and weighing obese patients. Future duties planned included taking smears for cervical cytology, visits to the chronic elderly sick, and follow-up visits to patients with minor illnesses.

Dr. H. E. BACH (Harlow, Essex) thought that some first visits could be done by nurses. He called for interchangeability of nurses' superannuation rights between hospital and general practice. Dr. R. H. GLENDINNING (Bristol) said that they were trying to abolish the boundary between what the general practitioner and what the local authority was expected to provide. Though in their own practice all the clinical work was done by doctors, many duties were delegated to the nurse—thus she did 200 venesections a week, for which the doctors took full responsibility. At the child welfare clinics the family doctor was in one room, and the health visitor in another.

There was also a geriatric clinic, based on the age-sex register compiled at the centre. A carefully worded letter was sent to patients on the practice list who were about to retire

asking them to come to the centre for a check-up. The health visitor visited the patients and inquired into the patients' social circumstances; a very full medical examination was done by a local authority medical officer; and the patient was referred back to his own general practitioner if treatment was needed. The number of visits required to the chronic sick patient had gone down considerably.

Dr. Page emphasized that the health team must be a permanent one, with nurses of high quality who received additional training in medicine as seen in general practice. A seven-year experience of working with a psychiatric social worker had convinced him of their value, particularly in dealing with emotional and marital problems and with patients of inadequate personality.

Miss A. M. LAMB (Deputy Chief Nursing Officer, Ministry of Health) pointed out that because of the general shortage of nurses it was essential for them to be used for the tasks for which they had been trained. Nevertheless, there was a place for all types of nurse in the community services. Job-satisfaction was of paramount importance for the health centre nurse, and in this communications were all-important; doctors and nurses must meet at least once a week. She emphasized that State-registered nurses working in the community had already been trained to the standard of ward sister, and they had usually had additional training in community services. These workers must be kept up to date with developments, from the nurses' point of view. Finally, Miss Lamb referred to the conditions of service, saying that the provision of cars, housing, adequate off-duty periods and holidays, and refresher courses were essential.

Dr. G. H. LEWIS (Harlow, Essex) regretted that in some health centres the nurses' first loyalty was to the M.O.H. and not the family doctors. He called for more flexibility by local authorities. Miss Lamb pointed out that this situation described a liaison scheme and not a true nursing attachment. Full consultation between doctors, nurses, and the local authority chief nursing officer was essential in planning attachment schemes, and an agreed local scheme took a minimum of three months to draw up.

Taking Patients to Doctors

Dr. VASEY described an experimental scheme for transporting patients to the health centre, which was sponsored by the Ministry of Health and was due to start on 1 January 1968. If the scheme was successful it might reduce the work load tremendously, and possibly 30% of patients who requested visits might be taken to the centre. Two minibuses had been bought, and an extra secretary engaged to deal with the scheme. Though extra consulting time would have to be provided, he thought that this would be an economic proposition.

Continuing, Dr. Vasey spoke of two fears. Firstly, that the scheme might be abused and used merely as a transport service. Secondly, if the scheme failed, that the visiting rate might rise rapidly and the doctors would be unable to cope.

demanded from doctors for maintenance costs attached to large health centres for transporting patients and specimens to the pathological laboratory. Dr. D. FARQUAR (Romford, Essex), referring to the high sums being

demanded for doctors for maintenance costs and ancillary help at health centres, said that caution was necessary with these grandiose schemes. Eventually the general practitioner might find himself paying for the transport service out of his own pocket.

Dr. BACH called for the Ministry to encourage the Bristol family folder scheme [*B.M.J.*, 1965, 1, 662] and asked what was the value of an intercom system.

Dr. KAY said that their intercom was at once a great help, particularly for doctors, midwives, and the mental welfare officer travelling in their cars, and a distraction—for example, when it disturbed a consultation. Dr. W. L. SELKIRK (Liverpool) had found it of great value, and they had agreed if a doctor did not answer the first signal that it would not be repeated for five minutes. Discussing the management of health centres, he suggested that the ideal person for this was a retired general practitioner. Every future health centre should consider appointing a manager.

Design and Function

Dr. BRIAN DIDSBURY (Ministry of Health) discussed the design and function of health centres. The present-day ones, in his view, were good examples of how they should not be built. Far too many of them had neglected the key role of the family doctor, not only in relation to traditional medical practice but also to the remainder of the community services. Thus some health centres were basically branch surgeries; others had separate wings for general practitioners and local authority services. He called for enlightened participation by general practitioners at the design stage of health centres. The advantage of the English system was the flexibility of design to meet local conditions of practice.

Practical difficulties were encountered in health centres serving over 25,000 patients; above this figure many facilities had to be duplicated—otherwise an institutional atmosphere was created.

Sir GEORGE GODBER asked what was the optimum size of a health centre. Dr. WIGRAM said that it was not the size that was of critical importance but the number of groups of doctors working within it. Dr. CARTER said that at Peterlee there were 18 doctors, eight partnerships, and four consulting-rooms—and the system worked well. Dr. SLEE thought that six doctors was the right size for a group. They had made it a rule for the doctor always to speak to a patient if he telephoned, and with this number of doctors the telephonist could always contact them. Dr. LEWIS said that at Harlow in Essex they had found that one large partnership served the needs of the new town best. This was a special sort of community, with unsettled, newly moved people who often liked to change their doctor until they found what they thought was the right one.

Speaking of interesting young doctors in general practice, Dr. VASEY said he had recently shown a group of students from Cardiff round their health centre. They had made two main comments. Firstly, they were quite taken aback that the general practitioner was expected to see a patient every five minutes. Secondly, they thought that general practitioners ought to have some institutional responsibility, whether a few general-practitioner beds or in a general-practitioner maternity unit.

Correspondence

Letters to the Editor should not exceed 500 words.

Requests for Abortion

SIR,—The anticipated increase in requests for termination of pregnancy would appear to have materialized. At my gynaecological outpatient clinic in the Hospital for Women, Birmingham, on 12 December there were seven such referrals from local doctors. The majority of these patients had been given urgent bookings at the clinic at the special request of their general practitioners. The time required for proper assessment of these patients interfered materially with the proper treatment of the remaining patients, and incidentally with the lunch-time arrangements of my staff and myself. One termination was advised, one patient was referred to the cardiologist for his opinion, and one was referred to the medical social worker for her assessment. In no case was referral to a psychiatrist deemed necessary.

These patients included one whose referring practitioner advised specifically against ter-

mination, and another girl, aged 20 and unmarried, who had previously had a pregnancy terminated last July and was now pregnant by another man. My mail the same morning had contained a letter from a nurse, who was also a doctor's daughter, requesting an appointment to discuss termination, but who could not get a referring letter because her practitioner was her father's partner. My antenatal clinic the following day included one more patient requesting termination against the advice of her practitioner.

If every unexpected conception is to be referred to a gynaecologist for comprehensive consideration of indications for termination, it is difficult to see how this can be contained within the present gynaecological structure of the National Health Service.—I am, etc.,

WILFRID MILLS.

Edgbaston,
Birmingham.

Clomiphene for Ovulation

SIR,—I apologize for this rather long and detailed reply to Dr. Arnold Kloppe's letter (16 December, p. 680), but as I disagree with practically everything he says and as our disagreement is one of fundamental principle rather than technical detail I must answer his points *seriatim* and rather fully.

He takes me to task for saying that steroid chemists should "get on with their research work" rather than waste their time doing innumerable oestrogen (and pregnanediol) assays to select suitable patients for clomiphene therapy and to monitor the day-to-day response to the treatment. As a do-it-yourself gynaecologist who is familiar with the laboratory as he is with the clinic and operating theatre, I would have thought he would have agreed that steroid chemists still have an enormous amount of research to do, especially in methodology, and that few laboratories were so equipped as to afford the time, the pairs of hands, and the money to do so much routine work as your leading article (25 November, p. 434) suggested was essential when there are other adequate methods of assessment and monitoring.

He contends that the selection of suitable women for treatment, the identification of amenorrhoeic subjects with sufficient residual ovarian activity to respond to the treatment, and the detection of women with regular but persistently anovular cycles require "accurate hormone assays." Hasn't he got the picture somewhat out of focus? Suppose one just gave a course of clomiphene to such an amenorrhoeic woman and saw whether it produced a period or not. This would demonstrate whether she had sufficient residual ovarian activity to respond to the treatment.

Suppose one supplemented this with daily basal temperature records. This, in my experience of careful charting of many thousands of records over at least 20 years, would tell you in at least 80% of the cases whether the response, if there was one, was ovulatory. Incidentally, I have found that it is very rare to have regular anovular cycles. Furthermore, suppose one had a vaginal cytology unit at one's disposal, which should be much more likely than a steroid chemistry unit capable of performing "accurate hormone assays," one could certainly answer these questions.

He says that "few would deny" that vaginal cytology is inadequate for "categorizing" the women subjected to treatment or determining the nature and timing of their response. How many gynaecologists in this country have sufficient experience of endocrine vaginal cytology and its capabilities? The answer is "few" and it is these few who would deny Dr. Kloppe's contentions. Most certainly serial vaginal smears can "categorize" and determine the nature and timing of the response.

He says that by means of hormone assays (and I suppose he means urinary oestrogen estimations) "most advanced laboratory services" can predict the day of ovulation. Dr. Sommerville's Endocrine Laboratory Unit at Chelsea can't and I should have been very surprised if it could. Just because the urinary oestrogen level is so many $\mu\text{g.}$ on day x of the cycle it certainly doesn't mean it will reach an ovulatory peak on day y . Nor is it our experience that the hormone assay pattern of one cycle is necessarily likely to repeat itself in subsequent cycles.

He implies that one can only determine that there is any ovarian response, that the oestrogen response is equal to or much above that of the normal cycle, whether ovulation occurred, or how adequate the luteal phase was by the urinary hormone assay. We contend at Chelsea that we can answer these questions equally well by means of serial vaginal cytology—and let him produce adequate vaginal cytological evidence to disprove our contention!

His belief is that the individual doctor should not be allowed to treat his patient with clomiphene unless the patient has been selected as suitable by, and unless the treatment is carried out under the supervision of, daily 24-hour urinary hormone assays. At least six years' intensive study both in the United States and in this country has been devoted to the clinical effects—and side-effects—of clomiphene. Both the Food and Drug Administration and the Dunlop Committee have agreed that it is sufficiently safe to be administered by gynaecologists and endocrinologists. No doubt it will be administered frequently to the wrong type of patient—it only induces ovulation and should therefore not logically be administered to a patient who is ovulating—but let us not have Dr. Kloppe and your leading article preventing us from using it unless our patients are prepared to become urinary prisoners of some rare laboratory.

This present correspondence applies in particular to clomiphene. It could equally apply in general to other drugs and other diagnostic investigations. I believe too much hospital time, too much public money, and too much interference with the routine of the patient's private life is being spent on many such investigations.—I am, etc.,

PETER BISHOP.

Chelsea Hospital for Women,
London S.W.3.

SIR,—The recent studies reported by Dr. D. Ferriman and others (25 November, p. 444) and Dr. E. Rabau and colleagues (p. 446) on the use of clomiphene therapy in the management of patients with infertility have stimulated me to present some preliminary results with low dosage oestrogen.

The patterns of follicle stimulating hormone and luteinizing hormone excretion in the normal menstrual cycle as reported by Stevens,^{1,2} in association with the usual oestrogen excretion pattern,³ together with the data observed following the use of oral contraceptives on gonadotrophin² and oestrogen/pregnanediol excretion,^{4,5} led to the theory that precise endogenous oestrogen production may be necessary to stimulate normal gonadotrophin secretion and the chain of events leading to ovulation.

After a discussion on the problems of infertility the hypothesis was further developed, and I suggested that such patients should be studied during oestrogen medication, the daily dose being determined by stepwise reduction every four weeks, the medication being prescribed daily for five to ten days. Each patient where possible was followed by

oestrogen and pregnanediol excretion. In some instances gonadotrophin excretion was determined. Very small doses of conjugated oestrogen (Premarin) gave encouraging results in a group of patients who had been followed most carefully. A number of these patients clearly ovulated, and in some instances pregnancy followed.⁶ Ethinyl oestradiol has also been used with some success in a dosage of 0.001 mg. That these small doses do stimulate F.S.H. secretion has recently been demonstrated by Stevens.⁷ At the recent World Congress of Obstetrics and Gynaecology, held in Sydney, McBride reported on the successful induction of ovulation in 12 of 18 women treated with 0.001 mg. of ethinyl oestradiol daily for 10 days. Although only four pregnancies were reported at the time the number has risen to eight.⁸

Clomiphene citrate is a non-steroidal com-

pound with both oestrogenic and antioestrogenic activity, but its precise mode of action in relation to ovulation stimulation is not clear. In view of the chemical similarity to chlorotrianisene (Tace) it is not unlikely that it may operate in a similar manner to very low dosages of Premarin or ethyl oestradiol.—I am, etc.,

Aylesbury, Bucks.

H. J. E. COX.

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Nursing Services in General Practice

SIR,—I read with great interest the article on the above subject by Dr. J. Weston Smith and Mrs. E. M. Mottram (16 December, p. 672), and I would like to compliment them on the initiative and enterprise shown in meeting present-day problems in general practice. In all branches of medicine we need to look again at the established traditional ways of providing a service, particularly in view of the shortage of doctors in all three branches of the National Health Service. I would like to make a plea that the work of a nurse in a practice be undertaken by a fully trained district nurse attached to the practice. In a practice such as Dr. Smith's, the work could be undertaken by two nurses, one S.R.N. and one S.E.N., and this would include the work outlined in the article and the home-nursing and any treatment in the surgery.

The merit of this recommendation is that there would be no need to introduce another worker into the practice, which inevitably causes certain difficulties. The advantage of the attached district nurse undertaking practice duties is that she has a knowledge of, and direct access to other local authority health and welfare services—mental welfare officer, child care officers, home helps, medical loans, etc. This is particularly true of the district nurse with district training; and any other training to meet the particular needs of a practice can usually be arranged by the local authority.

In this county we have several district nurses, S.R.N. and S.E.N., attached to practices, and the scope of their work outside traditional district nursing is a matter that is left to the individual practice. The fear of interference by the local authority is much more imaginary than real, as details of working arrangements are fully discussed and agreed before attachment takes place. Not all doctors want district nurses attached to their practice, and not all district nurses are suitable for this work, but a great deal more can be done by experiment and trial to provide the nursing cover best suited to present-day general practice. We have found that where attachment schemes have been agreed better understanding and closer working relations have been established between general practitioners and nurses. It is the policy of this authority to foster attachment of district nurses to general practitioners, and I would be very willing to discuss such schemes with

any general practitioner in the county who is interested.—I am, etc.,

County Health Offices,
Mold, Flintshire.

G. W. ROBERTS.

SIR,—It would be a pity to allow the highly significant article by Dr. J. Weston Smith and Mrs. E. M. Mottram (16 December, p. 672) to pass without comment.

The National Health Service set out to provide medical treatment free at the time. Patients were left with the responsibility of deciding when a doctor was needed. Now, 20 years later, we are told they are not prepared to accept this responsibility but require a new service to advise them whether they need a doctor, to treat illnesses not serious enough to require a doctor, and to secure the provision of free medicine for these minor ailments.

Thus, a nurse was able to deal with over a third of first visits (requested before 10.30 a.m.) in a two-man partnership, and in only 67 out of 537 first visits did she find it necessary to ask a doctor to call subsequently (Table I of the article). She might recommend the doctor to prescribe "a simple cough linctus or antacid." Not only did the patients accept the arrangement, they began to ask for the nurse directly, and the "threshold at which a visit is requested has become lower." Dr. Weston Smith has dramatically extended the scope of the National Health Service. Without breaking the regulations, without an Act of Parliament, perhaps without even a word with the Minister, he has introduced a new service which will no doubt uncover further hidden needs. Others are doing the same by introducing, for example, organ transplantation. They will be competing with Dr. Weston Smith for the available public funds. For, although this article confirms that doctors all over the country are performing the duties of a nurse or wise grandmother at a time of medical manpower shortage, it does not offer the nurse as a solution. On the contrary, the doctors had the impression that, "far from lessening the amount of work done by doctors the amount of consultative work has actually increased."

Here, then, is a vivid illustration of the insatiable demand for medical care and of public readiness to abdicate personal responsibility in health matters. We can choose whether to extend the scope of the National

Health Service in the direction of serious illness and introduce charges for minor illness or whether to extend it in all directions at even lower standards. We can even choose to support Dr. Weston Smith's new service and pay through taxation. But, at a time when child poverty needs relief and old-age pensions are inadequate to provide both food and fuel, there is something seriously wrong with a system which can nevertheless provide an ever-increasing army of expensive social workers, doctors, and nurses to visit, console, and treat the victims.—I am, etc.,

Holywell,
Flintshire.

DAVID L. WILLIAMS.

Early Work with Blood Transfusion

SIR,—Sir Geoffrey Keynes (18 November, p. 410) refers to the tercentenary of blood transfusion. The idea of transferring blood from a healthy person to a sick one had been mooted long before 1667, and apparently attempts had been made to carry out transfusions. In 1492 Pope Innocent VIII died after receiving blood from three youths,¹ all of whom also died, so that it would seem to be a fair presumption that this transfusion was a massive one, and even if by some near miracle all three of the donor bloods were compatible with that of His Holiness the circulation must have been grossly overloaded.

My primary concern in referring to the article mentioned is to draw attention to the fact that in Dublin in the early eighteenth century there was at least one man interested in the possibility of carrying out intrahuman transfusion. This was Richard Pockrich (1695–1759). His own description of the process is nowhere to be found, but a presumably full account appears as a footnote to "The Projector," a "Poem in an Epistle to Richard Pockrich, Esq.," by the satirist Brockhill Newburgh.² Though this was published in 1769 it had apparently been written in 1743. Newburgh was related to his subject on the latter's distaff side.

As the description appears in this work it reads "Take an Inflex Tube in the Nature of a Scyphon, fix it at the extreme Ends in the Veins of two different Persons to be open'd to receive them, the one youthful, adult, and sanguine, the other aged, decrepid, and wither'd. . . . The redundant fermenting Blood of the one, will immediately flow like Wine decanted into the empty shrivel'd Veins of the other. The Effects will be found no less uncommon than surprising. The wither'd Skin Braces, the Flesh plumps up and softens, the Eyes sparkle, the Visage blooms, and the Blood is invigorated with new Supplies of vital Warmth. When the Blood or Spirits begin to fail, or any Symptoms of Mortality do approach, the Experiment is only to be repeated, and so on, with equal success *ad infinitum*. 'Tis a common practice in Housewifery, to renew strong stale Beer for twenty, thirty, or any other Number of Years. Why may not the Fluids of the human Body be renew'd in like Manner? 'Tis certain the Experiment has been try'd on other Animals with Success and if such creatures have happen'd afterwards to die, it has been wholly owing to the Neglect of the propos'd Discipline."

Pockrich apparently realized either that there were major difficulties or possibly never made any effort to carry out practical experiments, but he was so convinced that his blood-transfusion scheme could be successful that he proposed that a Bill be introduced in Parliament which would provide that a person could be legally declared dead when

he reached 999 years, and that among others the local clergyman might claim the fees he would normally receive for the burial service. Pockrich was a most remarkable rather off-beat character who produced visionary schemes which caused him to be referred to at a recent meeting of the Section of History in the Royal Irish Academy of Medicine in Ireland as a poor man's Leonardo da Vinci.

—I am, etc.,

Blackrock,
Dublin.

JOHN FLEETWOOD.

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"Acrosclerosis"

SIR.—The recent article by Drs. A. W. Dellipiani and M. George (11 November, p. 334) on the syndrome of sclerodactyly, calcinosis, Raynaud's phenomenon, and telangiectasia, prompts us to report a further case.

A 75-year-old lady was admitted because of a hemiplegia due to cerebrovascular disease. She was noted to have tight shiny skin on some of her fingers, together with very rigid flexion deformities. Both thumbs showed dislocation of the distal interphalangeal joints. The tissues of the affected fingers were curiously hard and thickened. There were telangiectases on the lips,



FIG. 1.—Hand showing deformity and discharging area.



FIG. 2.—X-ray of hand.

face, and the palmar surface of the affected fingers.

Until the onset of the hemiplegia, which has been accompanied by severe dementia, she had been able to look after herself—including cooking, shopping, and doing housework—with some social support. History from friends and relatives gave no evidence of bleeding from the nose or gastrointestinal tract, nor was there any family history of bleeding. The patient had been troubled with Raynaud's phenomenon for as long as anyone could remember.

Later during her admission the skin of one of the affected fingers became inflamed and broke down, resulting in the discharge of a white pulsatious material, which on analysis proved to be composed of calcium and phosphate. The rest of the physical examination was not contributory.

Investigations revealed no definite evidence of involvement elsewhere, but the serum proteins were low at a total of 4.7 g./100 ml., with 3.4 g./100 ml. albumin, and 1.3 g./100 ml. globulin; electrophoresis showed a rather low γ and a high α_2 globulin. The white cell count persisted at a level of 20,000/cu. mm. and she has an iron deficiency anaemia with a haemoglobin of 7.6 g./100 ml. and a mean corpuscular haemoglobin concentration of 27%. However, these findings can be explained by the presence of a large bed-sore. X-ray of the hands showed extensive soft tissue calcification. There being no history or clinical evidence of dysphagia, a barium swallow did not seem justified in our patient. An electrocardiograph revealed nothing compatible with scleroderma.

This patient's history and progress support the contention that this syndrome has a benign course, but the deformities produced in our patient must have been at least to some degree incapacitating.

We are grateful to Dr. Harold Davis for his permission to publish details of this patient.

—We are, etc.,

STEPHANIE A. DAVIES.
FRED WOODROFFE.

Royal Free Hospital,
London W.C.1.

Disinfectants and Plastic Mop Heads

SIR.—Prompted by the letters of Dr. D. A. Leigh and Miss Christine Whittaker (12 August, p. 435) and Dr. L. Steingold, Mr. L. J. Dunn, and Mr. S. Henman (2 September, p. 620) we have investigated the effect of polyvinyl acetate, polyurethane, and cellulose sponges on the germicidal activity of various phenolic disinfectants:

One-inch (2.5-cm.) cubes of the plastics were immersed in 50 ml. of the disinfectant solution; allowed to soak for 24 hours; then the solution, with plastic still immersed, was inoculated with 0.5 ml. of a culture of *Pseudomonas aeruginosa*. Reinoculation was made each day over a seven-day period, and 7½, 15, and 30 minutes after each inoculation a 0.1-ml. sample of the disinfectant was withdrawn and examined for surviving bacteria. Not more than 10 survivors from the 0.1-ml. sample at 30 minutes was regarded as a satisfactory result. Controls of disinfectant without plastic were satisfactory over the whole seven-day period even at the seven-and-a-half-minute sample.

Polyvinyl acetate had the greatest effect. At the normal dilutions of use none of the disinfectants retained activity for more than the first inoculation. Polyurethane had only slightly less effect than polyvinyl acetate, none of the disinfectants at their normal dilution of use surviving more than one or two inoculations. Cellulose sponge, however,

did not affect germicidal activity to any great extent, the use-dilutions of all the disinfectants being satisfactory during the complete seven-day inoculation period.

When the disinfectants were tested at one and a half to three times their normal use-dilutions against polyvinyl acetate and polyurethane activity was retained for periods ranging from two to seven days. We found some evidence that the plastics and disinfectants behave in different ways—for example, disinfectant A was less affected by polyvinyl acetate than disinfectant B, while with polyurethane the reverse occurred. We repeated the investigation with polyvinyl acetate and polyurethane, pre-soaking the sponge for 24 hours in disinfectant before transferring it into a fresh solution at the same concentration for testing. While interference with the germicidal activity could still be found it was much less severe than in the earlier investigation, all the disinfectants retaining activity at one to two times their normal use-dilution over the seven-day period.

It would appear that cellulose sponge is the plastic of choice to avoid loss of phenolic germicide from solution. With other sponge materials the problem can be overcome by pre-soaking (preferably in overstrength) disinfectant and/or changing the solutions frequently as a matter of good housekeeping.

—We are, etc.,

Microbiology Laboratory,
Izal Limited,
Thorncliffe,
Sheffield.

J. W. GIBSON.
MAVIS LOXLEY.
JANET RIDGE.

Carcinogenicity of Tobacco and Tobacco Smoke

SIR.—Dr. M. Glass has asked two pertinent questions (5 August, p. 373), reiterated (9 December, p. 621), to which, he says, he has had no answer. I doubt if anyone can answer completely the vexed question of the pathogenesis of lung cancer in cigarette smokers, but the possibility that "some other essential factor, in addition to cigarette smoke," may be involved cannot be excluded. The important point is that in the absence of cigarette smoking, as opposed to smoke, to which non-smokers are often exposed, other possible factors that may be concerned in the evolution of cancer of the lung are less carcinogenic.

The absence of neoplastic reactions in the skin of the often heavily stained fingers of habitual chain-smokers may be related to the paucity, or absence, of pilosebaceous follicles in the lateral aspects of the fingers; assuming that the distillate from the tobacco contains fat-soluble potential carcinogens. There is experimental evidence from several independent sources which would support this explanation, which I reviewed in a different connexion.¹

The more difficult problem of the sequence of events in the pathogenesis of lung cancer in man, though unsolved, is not without clues. The demonstration² of basal cell hyperplasia and squamous metaplasia in the tracheobronchial tree in smokers, with or without lung cancer, as a more frequent finding than in non-smokers; and the observation³ that the increased incidence of primary lung cancer in smokers is practically limited to the epidermoid and undifferentiated

types suggests that these facts are causally related. Coughing, a regular accompaniment of smoking in many people, may be a contributory factor in the detachment of ciliated epithelium.

These may be some of the "other possible factors" postulated by Dr. Glass to which smokers are more liable than non-smokers.—I am, etc.,

Glasgow W.2.

P. R. PEACOCK.

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Antibiotic Combination in Staphylococcal Infections

SIR,—A recent *in vitro* study¹ has shown the advantages of kanamycin and cephalothin or kanamycin and methicillin in combination against methicillin-resistant strains of *Staphylococcus aureus*. It was suggested that combination therapy be initiated against all methicillin-resistant strains while awaiting the outcome of the appropriate *in vitro* tests. Others have recently extended this recommendation and have suggested combination therapy in all serious staphylococcal infections even before it is known whether or not the infecting strain is methicillin-resistant.^{2,3} Before accepting this latter recommendation, especially since infections with methicillin-resistant strains are uncommon, it is important to know whether antagonism occurs when the combination is used against methicillin-sensitive strains of *Staph. aureus*.

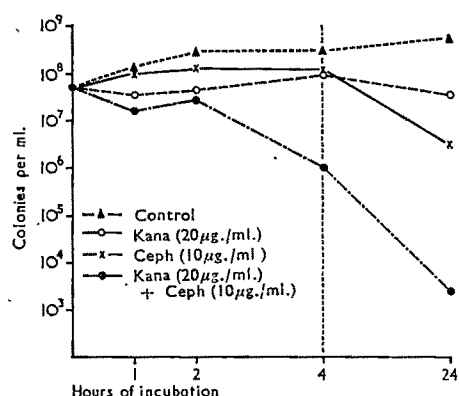
Ten strains of methicillin-sensitive coagulase-positive *Staph. aureus* isolated from clinical specimens were used to investigate this possibility. Pure cultures were obtained by transfer of single-colony isolates. Routine disc sensitivity tests were done on all strains according to the method of Bauer and Kirby.⁴

Routine tube dilution minimal inhibitory tests (M.I.C.) were performed simultaneously, comparing kanamycin, cephalothin, and kanamycin/cephalothin. All tests were made of an inoculum of 10^7 organisms per ml. using tryptose-phosphate broth; tubes were read for macroscopic turbidity after 18 hours of incubation. Subcultures of 0.01 ml. of all clear tubes were made on to agar plates; the concentration of antibiotic which yielded no growth was considered to be the minimal bactericidal concentration (M.B.C.), although this test guarantees only that there are less than 10^3 survivors/ml. With two strains, dynamics of growth were studied

in the presence of antibiotics singly and in combination, with counts of colony-forming units made at 0 time, 1, 2, 4, and 24 hours. The rate of killing over the first four hours is thought to be particularly important in evaluating antibiotic combinations.⁵

The patterns of antibiotic resistance and the M.I.C. and M.B.C. are shown for all 10 strains in the Table. On the basis of minimal bactericidal concentrations, the combination was of some advantage in five cases, but in the others was only as effective as cephalothin used alone. Nine of the 10 strains were killed in 0.5 µg./ml. of each of the agents in combination.

Growth curve characteristics of strain 2576 are shown in the Figure and illustrate some synergism. The second strain tested in this fashion showed no difference in the rate of killing between the combination and cephalothin or methicillin used alone.



Against a large inoculum of a methicillin-sensitive strain of *Staphylococcus aureus*, the kanamycin/cephalothin combination, in concentrations easily attainable in the blood stream, shows greater bactericidal activity than either agent used alone.

In these studies of 10 methicillin-sensitive strains of *Staph. aureus* there were no evidences of antagonism. Since cephalothin and kanamycin are bactericidal in different ways, it would be predicted that there would be no antagonism and that synergism might occur.⁶

On the basis of these tests, it seems reasonable to consider using the kanamycin/cephalothin or kanamycin/methicillin combinations when confronted with a life-threatening staphylococcal infection. If disc tests show sensitivity to methicillin, the kanamycin may be stopped, although some experts prefer the combination in endocarditis, regardless of sensitivity to methicillin. If

the infecting strain is methicillin-resistant, the combination could be used until appropriate *in vitro* tests confirm its efficacy.—I am, etc.,

ROGER J. BULGER.

University of Washington,
Seattle.

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Dysmenorrhoea

SIR,—Mr. A. Davis (11 November, p. 357) supports Muir's hypothesis that dysmenorrhoea results from myometrial ischaemia due to hypercontraction of the uterus, but this view is not supported by the studies of Wilson and Kurzrok.¹ Severe ischaemia of the uterus often occurs during the early hours of the puerperium and is not associated with pain.^{2,3} Pain indistinguishable from dysmenorrhoea can be provoked in all women by means of chemical, mechanical, and electrical stimulation of the cervix uteri. A simple and precise method for measuring the critical electrical stimulus which when applied to the cervix causes pain was described in your columns.⁴ If these results are confirmed a foundation for dysmenorrhoea will be established.

A lowered threshold to pain arising in the uterus does not mean, as Mr. Davis suggests, that "it's all up here." He is well aware that but a small proportion of signals arising in the periphery reaches consciousness, for there are many "censors" in the nerve pathways concerned. The operation of these censors can be affected either way by impulses both from the higher centres and from the periphery. Further, the actual cells in the apperception area can similarly be affected. There is no need to stress the point that it is the destination of the signals which determines their message. Experimental studies^{5,6} show that the effects caused by stimulating the hypogastric nerve vary with the hormonal state of the subject.

Such a concept would explain why the same individual can have both painful and painless periods, the degrees of intensity of the pain, why women complaining of severe dysmenorrhoea may have painless periods when admitted to hospital for investigation, as well as the undoubted benefit derived from the varied and multitudinous methods of treatment, ranging from exercise, hygiene, and spinal manipulation to presacral neurectomy. It would also explain why any and all of these treatments may prove unavailing.—I am, etc.,

G. W. THEOBALD.

University College Hospital,
London W.C.1.

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Minimal Inhibitory (M.I.C.) and Minimal Bactericidal Concentrations (M.B.C.) Obtained with Ten Methicillin-sensitive Strains of *Staphylococcus Aureus* against Kanamycin, Cephalothin, and the Kanamycin/Cephalothin Combination

Strain	Antibiogram*	Kanamycin		Cephalothin		Kana/Ceph	
		M.I.C. µg./ml.	M.B.C. µg./ml.	M.I.C. µg./ml.	M.B.C. µg./ml.	M.I.C. µg./ml.	M.B.C. µg./ml.
2994	P	32	32	<0.25	0.5	<0.25/0.25	0.5/0.5
3024B	Ch, T	64	128	<0.25	0.5	<0.25/0.25	0.5/0.5
3076	P, E, S, Ch, T	64	64	<0.25	4	<0.25/0.25	4/4
2572	P, Ch, T, K	>128	>128	<0.25	0.5	<0.25/0.25	0.5/0.5
1893	P	32	32	0.5	1.0	<0.25/0.25	0.5/0.5
2529B	P, S, T	16	16	<0.25	0.5	<0.25/0.25	<0.25/0.25
2024	P, T	128	128	<0.25	0.5	<0.25/0.25	0.5/0.5
2560	Sensitive to all	32	64	<0.25	0.5	<0.25/0.25	<0.25/0.25
2562	P	32	32	<0.25	1.0	<0.25/0.25	0.5/0.5
2576	P	16	64	<0.25	1.0	<0.25/0.25	0.5/0.5

* Refers to antibiotics to which the strain is resistant on testing with high concentration discs according to the method of Bauer *et al.*⁴. Antibiotics tested were: Penicillin G (P), Erythromycin (E), Streptomycin (S), Chloramphenicol (Ch), Tetracycline (T), Kanamycin (K), Cephalothin (C), and Methicillin (M).

Improving the Psychiatric Services

SIR,—Being very interested in and committed to the task of trying to plan and provide suitable hospital services for elderly people, I think that Dr. H. Jacobs's letter (16 December, p. 681) calls for some comment.

I refer to the very popular notion of "x weeks in and x weeks out geriatric service." Such service is not necessarily the sort of panacea that many people seek. It is very difficult indeed to keep to any such timetable. One knows that shutting the elderly from here to there will in itself very often affect them adversely and one had found that at the end of the allocated stay in hospital the patient is much worse than at the time of admission. Although one is keen to help the relatives and benefactors of frail elderly people by giving them respite, and is able to do this in selected cases, I have come after many years to believe that the primary task of the geriatrician is to treat vigorously whichever patients have tractable diseases, tempering such treatment with, one hopes, humanity and common sense.

As for day hospitals, I am completely sold on their virtues and efficacy. I am beginning to think that these, paralleled by local authority day centres, might very well reduce dramatically the expense of providing in future for the needs of the elderly.—I am, etc.,

St. Edmund's Hospital, J. H. RAPHAEL.
Northampton.

Tetanus Prophylaxis

SIR,—I was very interested to read your leading article on tetanus prophylaxis (16 December, p. 635). I was pleased to see that you made it very clear that prophylaxis in the non-immune wounded patient for practical purposes rests between antibiotics and antitetanus serum. Neither of these has been proved to be 100% effective, but nevertheless clearly must be largely effective, for, as you state, the number of tetanus cases in this country is quite small.

I do wish, however, that you had made it very clear that tetanus toxoid has no practical value in the immediate prophylaxis of tetanus. We see a number of patients in this hospital who have had their initial treatment of wounds at a neighbouring hospital where the staff seem to be convinced that either tetanus toxoid alone, or tetanus toxoid plus one injection of penicillin, is adequate prophylaxis. At the recent symposium on tetanus held in Leeds in April,¹ which is referred to in your leading article, both Mr. Sharrard and I emphasized that a course of antibiotics was necessary for adequate prophylaxis. This point you have brought out in your leading article. Recently, however, my colleague Dr. J. J. L. Ablett lectured on the treatment of tetanus to a society some 40 miles from here. As a matter of interest, at the end of the lecture he inquired from all those present what method of prophylaxis they themselves used in the patient at risk. The majority of those present stated that they gave tetanus toxoid and one injection of penicillin. I am sure that Mr. Sharrard will join with me in condemning this as inadequate and in stressing once more that tetanus toxoid is of no immediate prophylactic value.

All except one of our last 10 patients undergoing treatment in our tetanus unit had

been given this form of prophylaxis, emphasizing its inadequacy from a different point of view.—I am, etc.,

Tetanus Unit,
General Infirmary,
Leeds.

M. ELLIS.

REFERENCE

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Low Back Pain

SIR,—I was interested in Dr. W. I. D. Scott's comments on back troubles in industrial and general practice (9 December, p. 618). I would agree with him that strict bed rest in simple lumbago is impractical. Indeed, I would suggest that it may be harmful in some patients by providing yet another somatic outlet for their psychological stresses.

After all, the acute prolapsed disc is rarely seen in general practice, and most cases of lumbago-sciatica fall into the category of musculo-ligamentous strains.

These cases respond admirably, in my experience, to infiltration with local anaesthetic solutions, with or without hydrocortisone, together with manipulation and early mobilization.—I am, etc.,

Elgin,
Morayshire.

A. M. BLAIN.

Bromism

SIR,—We should like to point out once more the dangers of the long-term administration of carbromal, especially as the amount prescribed may go somewhat unnoticed when it is combined with a hypnotic such as pentobarbitone as in Carbrital (carbromal 250 mg., pentobarbitone 100 mg.). The danger lies in the fact that bromide (to which most of the carbromal is metabolized) is much more slowly excreted from the body than pentobarbitone and therefore has a cumulative effect. A recent case illustrates this.

A 75-year-old man who had been taking Carbrital as a hypnotic for many years, and who possibly took more than his usual dose of two capsules four days prior to admission, was admitted in a very confused state with nystagmus, marked ataxia, and generalized diminution of sensation. His serum bromide level at this time

was 60 mg./100 ml. Without treatment this had fallen to 40 mg./100 ml. in five days and the above symptoms and signs had disappeared.

In the past nine years he has had five admissions to mental hospitals with episodes of confusion, delusions, and hallucinations. On each occasion these settled down without any specific treatment, within a few days of admission. A number of psychiatric diagnoses were suggested, but none were consistent with the transient nature of the symptoms.

As the serum bromide was not recorded during these admissions we have no definite proof that they were due to bromism, but in view of his recent illness and the well-documented evidence of psychiatric symptoms in bromide intoxication^{1,2} we consider that these were manifestations of a toxic level of bromide.

We would like to thank Dr. J. E. G. Pearson for his permission to report on this case.

—We are, etc.,

A. F. BOYLES.
D. J. MARTIN.

Bristol Royal Hospital,
Bristol.

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² Wuth, O., *J. Amer. med. Ass.*, 1927, 88, 2013.

Cause of Death

SIR,—Why in the obituary notices of doctors published in the *British Medical Journal* is the cause of death never stated? In the *Journal of the American Medical Association* it invariably is.

The American practice is, I suggest, more seemly. After all, the *British Medical Journal* is written by doctors for doctors, and deals mainly with disease and death; and it would be easy to make provision for that very small minority of deaths in which a public statement of the cause might distress relatives. Certainly a changed practice in this respect would have the incidental advantage of reminding us in a most direct way that we too are mortal. And lastly, one task of medicine is to discover and to set forth the truth, and reticence of the kind in question would seem to be at variance with it.—I am, etc.,

Little Missenden,
Amersham, Bucks.

S. BRADSHAW.

Hospital Management

SIR,—In your leading article (28 October, p. 187) you draw attention to the report on *The Shape of Hospital Management in 1980* by the King Edward's Hospital Fund.¹ The report of the joint working party set up by the Joint Consultants Committee and the Ministry of Health on the "Organization of Medical Work in Hospital"² has also just been published (4 November, p. 252). These two documents form an interesting comparison and deserve careful study by members of the medical profession who work in hospitals.

Considerable attention has rightly been given to the question of remuneration and to hospital buildings, but the administration of hospitals has tended to be considered of less importance. This, I think, is a mistake. Given a reasonable standard of remuneration and freedom from financial worry most doctors can put up with considerable difficulties as

regards their buildings, provided that the administration of the hospital satisfies them. In my view one of the causes of frustration and the so-called "brain drain" is the administration of hospitals. Members of the medical staff have difficulty in getting their views made plain and in getting their needs carried out efficiently, quickly, and economically. Although the consultant medical staff are not trained administrators they do have to make many decisions quickly and under difficult circumstances. It therefore causes them irritation when they see what appears to be quite a minor decision being shelved or wrongly made. Committee structure and multiplicity is often wrongly blamed for this when the trouble is the shortage of trained administrators of adequate calibre. Decisions are put off and shelter taken behind committee procedure.³ I would like at this point

to specifically exclude the administration of my own hospital group, for which I have a high regard.

There are certain issues that need to be clarified in the Joint Working Party's Report. The first and most important is the method of appointing the chief of staff, and the second is what his exact responsibility and powers would be. It would seem that they are really intended to be advisory. However, I think in the view of many this would not be sufficient. An executive committee needs executive powers and is not purely advisory. Economy can best be achieved by delegating the responsibility for estimates and budgets to the department head concerned. The question of the divisions needed would be a problem. In the development of hospital services many of the new specialties have already developed departmental set-ups with secretarial services. The older service specialties such as x-ray and pathology also have these arrangements. Anyone who has worked in a specialty which has a department with secretarial services and methods of keeping their own statistics knows how valuable this is and would be very loath to lose them to a broader divisional network.

Clarification is also needed about where the manpower, the secretarial services, and the space for them are going to come from. Unless these were very quickly provided this suggested administrative network would be doomed from the start. Consultants have suffered from lack of secretarial help for too long. Only recently has it been recognized that they should have secretaries of personal secretary grade. This is one of the reasons why I think they have given up many of the old administrative functions that they used to carry out and why hospital statistics and hospital activity research are not often done.

Business analogies should not be pursued too far where hospitals are concerned. The fundamental purpose of a hospital is to care for and to treat sick people. The consultant staff have the ultimate responsibility for ordering the expenditure of the very considerable sums that are now necessary to treat patients. To my mind, therefore, it is essential that the consultants should be able to take part in the management of hospitals at the highest level. They need to be involved in more than an advisory capacity and be given both executive and financial responsibility. There are many difficulties to be ironed out, but, given the sympathy and support of the consultants and proper secretarial backing, I think the suggestions of the Joint Working Party would be a great start towards a more efficient and human administration of hospitals. It is to be hoped that the Joint Working Party will consider the total administration of hospitals in addition to the medical side, as it would seem to me, from the point of view of the medical staff, an alternative to the present situation, and the "Shape of Hospital Management in 1980" is badly needed.—I am, etc.,

Bury St. Edmunds,
Suffolk.

J. WEDGWOOD.

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- ¹ *The Shape of Hospital Management in 1980*, King Edward's Hospital Fund for London, 1967, London.
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- ³ Robinson, G. A., *Hospital Administration*, 2nd ed., 1966. London.

SIR,—It is sad to note in the letter written by Mr. J. Blundell and Dr. J. Lowry (9 December, p. 617), regarding the subject of managing the hospitals, that they confuse opinion with fact in dealing with the hoary old chestnut of the takeover of the running of the hospital by lay administrators.

As a member of the King's Fund and Institute of Hospital Administrators Working Party on *The Shape of Hospital Management in 1980* I bore certain responsibility for the issue of its report.¹ I have a copy before me as I write, and it is very clear that the general manager envisaged would, without question, be the best manager available, whether medical, lay, or nursing, or from other sources. The report made it quite clear that the manager could be a doctor, nurse, or lay administrator with the appropriate management attributes—these are the facts.

Taking this further the report itself stresses that all persons, medical, nursing, and administrative, who in future would hold managerial appointments in the hospitals should have received both training and experience in management and management needs to be able to measure performance. It also provides training posts for this to be achieved in each sphere of activity. Good management must be done and be seen to be done in the future so that we may run our hospitals more efficiently for the benefit of our patients as well as the satisfaction of the staff.—I am, etc.,

King's College Hospital Medical School,
London S.E.5. JOHN ANDERSON.

REFERENCE

- ¹ *The Shape of Hospital Management in 1980*, 1967. King Edward's Hospital Fund for London.

Approval of Emergency Treatment Service

SIR,—Dr. W. P. Fitt (9 December, p. 623) questions the need for the Emergency Treatment Service in a well-organized general-practitioner service. Since he suggests that a four- or five-partnership rota is desirable, why not also the next logical step of an efficiently organized larger rota, the Emergency Treatment Service, particularly as it has been proved successful in practice?

The other question, "Are doctors really happy about State-registered nurses answering the phone?" would be answered with an emphatic "yes" by those of us lucky enough to have had the chance to use such a service. It is certainly to be preferred to the previous alternatives, ranging from non-medical secretaries to au pair girls. But perhaps of greater importance than the satisfaction of the subscribing doctors to the Emergency Treatment Service is its acceptability and indeed popularity with the patients whom it serves.—I am, etc.,

St. George Health Centre,
Bristol 5.

A. DOWLING.

service "in keeping with the traditions of our profession."

Let us look at some facts. An analysis of my patient contacts in the past month has shown that less than 4% of my patients seen at home and 0.8% of total patient contacts were by an Emergency Treatment Service doctor. My off-duty, however, has been increased by 48 hours per week over what it was in our three-doctor practice prior to using the Emergency Treatment Service. It has been our experience that patients urgently requiring medical aid wish in the first place their own doctor, but if he is not available then they do not care particularly if it is one of a large group practice or another doctor provided he copes adequately with the situation, and provided he arrives promptly. Dr. Fitt talks about increasing efficiency. Is it more or less efficient to have nine doctors actually working with two-way radios in their cars so that always at least one is available for an urgent call, or to have 200 doctors tied to the phone or on call from the golf course? As for his point about nurses answering the phone, a ring round his colleagues will show that it is much more likely that the phone will be answered by the doctor's wife, an unqualified receptionist, or a Robophone than the doctor himself.

I am firmly in support of the value of a personal doctor, but his real value is in coping not with an acute appendix but with medical, emotional, and social problems of a more long-term nature. To cope adequately with these it is essential in the long term to have adequate time off call, and this can be done by allowing an efficiently run deputizing service like E.T.S. to cover urgent out-of-hours calls.—I am, etc.,

Bearsden,
Glasgow.

KENNETH HARDEN.

Points from Letters

Casualty Staffing

Mr. J. W. WILSON (Belfast City Hospital) writes: It appears from the report of the proceedings of the Central Committee for Hospital Medical Services (4 November, *Supplement*, p. 36), and the more recent letter of Mr. G. Rigby-Jones (11 November, p. 360), that the staffing of casualty departments is again the subject of interest, if not possibly of the anxiety that it merits. This problem is not one that can be dealt with in isolation; decisions taken here affect the whole hospital beneficially or adversely. The whole question of the department's responsibilities to the public, and equally to its nursing and medical staffs as regards teaching and career possibilities, must be fully appreciated before any acceptable decision on its staffing can be made. . . . It is to be hoped that when the Central Committee for Hospital Medical Services sets up its subcommittee to study this question it will seek the advice of, or, better, co-opt, consultants with wide experience in this very important hospital department.

Anaphylactic Reaction and Soap Enema

Dr. TORGILS AANELAND (Bærum, Norway) writes: In the very interesting article by Dr. Donald Smith (28 October, p. 215) there is no information about former contact between the patient and the "proprietary brand of soap-flakes," or a similar one. As long as this important information is lacking the soap allergy will continue to be a "foggy" problem in the future too.

SIR,—It is interesting to note that in the opinion of Dr. W. P. Fitt (9 December, p. 623) I, along with over half the general practitioners in Glasgow, belong to a service (the E.T.S.) of which there is need, and also by so belonging we are failing to provide a

Obituary Notices.

G. L. ROBERTS, M.B., CH.B., B.D.S., F.D.S. R.C.S., F.F.D. R.C.S.I.

Professor G. L. Roberts, for 32 years professor of dental surgery and director of dental studies at the University of Sheffield, died suddenly in his office at the Charles Clifford Dental Hospital on 14 December. He was 63.

George Laurence Roberts was born on 14 January 1904, and received his medical education at the University of Liverpool, where he had a distinguished career as both

a medical and dental student. He graduated M.B., Ch.B. with honours and a distinction in surgery in 1927. In 1928 he was successful in obtaining the degree of Bachelor of Dental Surgery with first-class honours. He held teaching posts in the universities of Liverpool, Leeds,



and Birmingham before being appointed to the chair of dental surgery in 1935.

Laurie Roberts started his work in Sheffield in a very tiny dental school which was housed mainly in a small part of the Sheffield Royal Hospital. He immediately persuaded the university and hospital authorities to build a new dental school. This was about to be done, when the second world war postponed the building indefinitely. Although deeply disappointed, Roberts, with a handful of loyal general practitioners and one full-time lecturer, developed the teaching to a standard which compared well with other schools in Great Britain. After the war he supervised the planning of the new school, and was responsible more than any single person for its coming into being. One of the proudest days of his life was in 1953, when the Charles Clifford Dental Hospital was opened by the Duchess of Gloucester. Although the new building appeared at first to be much too large for the requirements of a small dental school, Laurie Roberts had so built up its strength and students by 1964 that considerable additions, in the form of a new floor and extra laboratories and facilities for staff, were added. Again these improvements would not have been possible but for his skill in persuading others of the need and desirability of the extensions.

Professor Roberts was not only active in his own university, where his great experience enabled him to express views which were always listened to with respect, but was a great force in the wider world of dentistry. He was a leader in the Faculty of Dental Surgery of the Royal College of Surgeons of England, of which he was vice-dean in the session 1963-4, and member of the General Dental Council and the chairman of many important committees concerned with the affairs of the Council. He was consultant

adviser in dental surgery to the Ministry of Health, and adviser on dental health to the World Health Organization.

Laurie Roberts was always anxious to have what he used to refer to as a happy ship. He was, like all great captains, able to inspire his staff and to gain their respect by his obvious sense of "service." All who knew him were certain that all his actions and thoughts were concerned only with the advancement and improvement of his dental school and his profession. He gave all he had to his profession,

V. H. J. DAVIES, M.D., F.R.C.S.ED., D.OBST.R.C.O.G.

Mr. V. H. J. Davies, formerly senior consultant gynaecologist and obstetrician to the Swansea and Morriston Hospitals, died suddenly in his consulting-rooms on 15 December. He was 66.

Vyvyan Henry Jeremy Davies was born in Landore, Swansea, on 17 July 1901. He received his early education at the Swansea Grammar School, and from there pursued his medical studies at Charing Cross Hospital, London. He took the Conjoint diploma in 1924, and after holding posts as house-physician and resident obstetric officer at Charing Cross Hospital, he became resident medical officer at Queen Charlotte's Hospital. He settled in general practice in Swansea in 1927, and in the same year married Dr. Margaret Hughes Brown, who had been a contemporary of his at Charing Cross. He soon became established and built up a large practice. In 1932 he was appointed honorary anaesthetist at Swansea Hospital, and in 1935 police surgeon to the county borough. In 1934 he took the D.Obst.R.C.O.G. and in 1935 graduated M.B., B.S., proceeding to M.D. in 1937 with midwifery and gynaecology as his special subjects. In 1943 he became F.R.C.S.(Ed.), and thereafter his course was set. He left general practice and resigned from all his other appointments in 1946, when he became honorary consultant gynaecologist to Swansea and Gorseinon Hospitals. In 1948 he was appointed consultant gynaecologist to the Gwent Hospital Management Committee Group, a post he retained until his retirement in September 1966. He was consultant obstetrician to the county borough of Swansea, and in that capacity played a considerable part in the establishment of the "flying squad," and was also obstetric adviser to the local branch of the Family Planning Association.

He took an active interest in all local medical affairs, and was chairman of the Swansea Division of the British Medical Association from 1942 to 1945. Subsequently he was a member of the Gwent Hospital Management Committee for six years, chairman of the medical staffs committee, and also chairman of the Swansea and Morriston Hospitals standing medical committees. In 1967 he was made a Fellow of the British Medical Association, an honour of which he

to which he added dignity and integrity. He was fortunate in living at a time when great advances were taking place in dentistry. Few have done more to bring about these changes than he.

Whenever the story of G. L. Roberts's achievements is told the support and help given to him by his wife, Joyce, will never be forgotten. Without her patient help and support it would have been impossible for him to live the busy life his work demanded. To his wife and two sons, David and Alex, we extend our deepest sympathy. —E. L. H.

was very proud, and which was singularly well merited.

Vyvyan Davies was an eminent doctor and general practitioner, but undoubtedly he found his greatest fulfilment as a gynaecologist and obstetrician. Possessed of an able, keen, and analytical mind, he was an astute clinician and first-class diagnostician. As a surgeon he was careful, painstaking, dextrous, and very gentle. His years in general practice made him very approachable, and he was ever mindful of the difficulties of his general-practitioner colleagues, and always ready to be of service to them and their patients. He took a great interest in his junior hospital staff, and it is worthy of note that five of his former senior registrars now hold consultant posts. In committees he did not speak much, but when he did he was pertinent and to the point, and his opinion always carried great weight.

He had very little time to devote to hobbies. Always a great family man, he loved having his wife and children with him, and took great pride in his 10 grandchildren. Golf was his main recreation, and he had been a member of Pennard Golf Club for many years. In his day he was no mean performer and a doughty opponent. In May 1967 he had a major operation, and, although he was desperately ill for several days, he was most courageous and eventually made a good recovery. He died suddenly in his consulting-room while seeing one of his old patients, and it was a tragic coincidence that his death should have occurred on the same day that the old Swansea Hospital closed down—the place where he had done so much work during the past 40 years. Thus ended a life full of purpose, endeavour, and achievement, and his departure from the scene will leave a gap in the community of Swansea and its environs which will not easily be filled. He will be mourned and missed by many, particularly by those of us who had known him so well and worked with him over the years. It has been a great privilege to have enjoyed his friendship, his companionship, and his confidence.

He is survived by his wife, Dr. Margaret Davies, two sons, and one daughter, and to them we extend our deep sympathy. —C. H. D.

**C. R. WHITTAKER, F.R.C.S.ED.
F.R.S.ED.**

Dr. C. R. Whittaker, a former lecturer on anatomy at the School of Medicine of the Royal Colleges, Edinburgh, died on 4 December. He was 88.

Charles Richard Whittaker, a Lancashire man, took the triple qualification of the Royal Scottish Corporations in 1904, and was admitted a Fellow of the Royal College of Surgeons of Edinburgh in 1907. He devoted his life to teaching. In his early days this took the form of coaching, and his revision classes in anatomy and surgery for undergraduates and postgraduates working for their Fellowship were extremely popular, spiced as they were with witty and imaginative touches which served to fix the facts in the minds of his hearers. He busied himself also with writing, and was the author of *Surface Anatomy*, which went into three editions, *A Manual of Surgical Anatomy, Nerves of the Human Body*, and *An X-ray Atlas of Normal and Abnormal Structures of the Body*.

Extramural teaching in Edinburgh has now ceased, but it has a long and honourable history. This was especially true of anatomy. When Whittaker qualified the teaching of anatomy extra-academically was in the safe hands of a fellow Lancastrian and, curiously enough, a namesake, Joseph Ryland Whitaker, a notable teacher whose vacation courses drew large numbers from south of the border. Charles was Ryland's deputy, and the apprenticeship was a lengthy one, for it was not until 1931 that he succeeded as senior lecturer. He worthily maintained the tradition. A member of the British Medical Association, he was vice-president of the section of anatomy and anthropology at the Annual Meeting in 1939.

Among his outside interests painting was pre-eminent. It took him to several European countries, and resulted in the acquisition of a considerable art library. He found congenial company in the Scottish Arts Club, of which he later became president. He held office in the Scottish Society of Artists and the Scottish Artists' Benevolent Association. A number of his own works, in the abstract idiom, were hung in the annual exhibitions of the Royal Scottish Academy. In 1950 he was elected to honorary membership of the R.S.A. and appointed honorary professor of anatomy, an office which dates back to the days when that institution had its own life classes, and which had long been in abeyance. This appreciation by artistic circles in the capital gave him much pleasure and helped to fill a void in his life created by the death of his wife and only son.

Charles Whittaker did not wear his heart on his sleeve, but he was warm-hearted and generous and he was a good friend to generations of students, many from distant parts.—W. A. A.

**G. HAMILTON, M.A., M.B., B.CH.
B.A.O., D.A.**

Dr. G. Hamilton, formerly consulting anaesthetist to the Northern Ireland Hospital Authority, died on 7 December at the age of 80.

George Hamilton was born on 7 March 1887. He took up medicine after a business career and engaging in parish work. Having

graduated at Trinity College, Dublin, he entered the School of Divinity and served in the parish of Mohill, Co. Leitrim. He was there during the time of the "troubles" and had many harrowing experiences. Later he worked in the parishes of Dundonald and Killinchy. He then decided to embark on the study of medicine and he became a student at the Queen's University of Belfast, where he graduated M.B., B.Ch., B.A.O. in 1927. He set up in practice in Belfast, combining general practice with hospital work, and was for several years a clinical assistant in the ear, nose, and throat department of the Royal Belfast Hospital for Sick Children. He distinguished himself in the field of anaesthetics, and worked for many years in the Royal Belfast Hospital for Sick Children and the Royal Victoria Hospital. When the Health Service began he was appointed a consultant anaesthetist to the Hospitals Authority. He was honoured in 1947 by being elected to the Diploma of Anaesthetics of the Royal College of Surgeons in Ireland. His wide interest in medicine also embraced the field of occupational medicine, and he was for many years medical officer to Messrs. James Mackie & Sons Ltd., and to the Great Northern Railway. He was an active member and fellow of the Ulster Medical Society, and was at one time a member of its Council. He had also served on the executive committee of the Belfast Division of the British Medical Association. He continued his lifelong interest in church matters while practising as a doctor.

He is survived by his wife, Irene, and son, Trevor, who carries on the medical practice in Belfast.—G. T. C. H.

**H. C. JENNINGS, M.A., M.B., B.S.
D.P.H.**

Dr. H. C. Jennings, formerly county medical officer for Oxfordshire, died at his home in Eastbourne on 19 November. He was 74.

Henry Cecil Jennings was born on 6 January 1893, and received his medical education at Oxford University and St. Thomas's Hospital, where he qualified with the Conjoint diploma in 1915 and graduated M.B., B.S. two years later. During the first world war he served in the Royal Navy, and after demobilization decided to take up a career in public health work, taking the D.P.H. in 1920. After service with the Leeds City Council he became medical officer for the Holland Division of Lincolnshire, and then went on to take up his appointment as county medical officer for Oxfordshire, an appointment he held for 21 years. In 1935 he took the B.Sc. and B.A. with honours in natural science, and four years later proceeded M.A. He was an examiner in public health at Oxford University, and a Fellow of the Society of Medical Officers of Health. A member of the British Medical Association, he was chairman of the Holland Division in 1928-9. In the second world war he served as colonel in the Home Guard. After his retirement in 1953 he accepted the appointment of chairman of the Banbury Hospital Management Committee. In this capacity he undertook his responsibilities with great thoroughness, making himself familiar with every aspect of hospital administration and never hesitating to say what he thought at committee meetings. In 1964

he moved to Eastbourne, where his former colleagues were always very pleased to see him and to renew their happy associations with a man who was always friendly and a very good companion.

While he was at Oxford Henry Cecil Jennings took a great interest in the university and maintained an active membership of the Union. He was the first chairman of the Oxford Medical Officers of Health Liaison Committee, and it is to his credit that such a happy relationship has always existed between the public health and hospital board staff in the Oxford region. In addition to his academic pursuits he was very interested in all forms of sport. He himself was a good golfer and a keen follower of university cricket and rugby. Not infrequently he was to be seen in the Parks or at Ilfley Road, following the game with a sure eye for its finer points. He was an excellent raconteur with a good sense of humour, and was never at a loss to illustrate a point with a story or incident. All who knew him will enjoy warm memories of his companionship, and will wish to extend their very sincere sympathy to his wife and two daughters who survive him.—M. J. P.

N. J. E. writes: Dr. Jennings will be remembered for his championship of the use of general practitioners in the public health service. He made full use of their services in preference to appointing whole-time staff. The strain of the war years was to justify his good judgement in that an adequate public health service was well maintained. His insistence that the general practitioner must be a key figure in the public health service led to a much wider use, in the post-war years, of the health visitors by the general practitioners. This in its turn led to the establishment of a health-visitor school in Oxfordshire. He was a keen member of the County Medical Officers of Health Society and a past chairman.

**W. R. SADLER, L.R.C.P.ED., L.R.C.S.ED.
L.R.F.P.S.GLASG.**

Dr. W. R. Sadler, a general practitioner in the east end of Glasgow, died at his home on 5 December. He was 62.

William Ross Sadler was born on 20 April 1905, and spent a number of years in the family business in Glasgow before deciding, in his middle thirties, to embark on a medical career. He took the Scottish triple qualification in 1945 at the age of 40. After spending a year as an assistant at Thornliebank, he went to a country practice at Barnhill in Ayrshire for two years; then he moved to a practice in the Shettleston district of Glasgow, where he served his patients faithfully for 19 years until his death. He was a member of the Glasgow Local Medical Committee for 15 years until failing health necessitated his resignation. Before entering medicine he was interested in the Masonic movement, in which he held high office. For almost all of his professional life in Glasgow he was an elder in Shettleston Old Parish Church. He was a very able physician with an alert mind and sound judgement, and a man of personal integrity beyond question.

To his wife, his two sons, and two daughters we extend our deepest sympathy.—J. G. W. C.

News and Notes

EPIDEMIOLOGY

Hospital Inpatients

The publication by the Ministry of Health and the General Register Office of the Commentary completes the report on the hospital inpatient inquiry in England and Wales for the two years 1960 and 1961. The data were based on a 10% sample of inpatients in all N.H.S. hospitals. Mental hospitals and mental deficiency hospitals were excluded; they have been reported on separately. Patients in psychiatric departments of general hospitals and private patients were also excluded.

The report is divided into six main sections: (1) geographical variations, (2) administrative and general aspects, (3) diseases by system, (4) maternity patients, (5) surgical operations and investigations, and (6) occupation.

Variations between regions were considerable. The rate of admission was highest in the Liverpool region in 1961, with 93 per 1,000 population, and lowest in East Anglia in 1960, with 64 per 1,000 population. High 1961 rates were recorded in the N.W. and N.E. Metropolitan regions, 92 and 90, respectively. Low 1961-2 rates were

recorded in Sheffield, 68 and 67. Average duration of stay in hospital ranged from 22 days in the Liverpool region during 1960 to 16 days in the Newcastle region in 1961. For the whole country the admission rate for non-maternity beds was 39 per 1,000 population and for maternity beds 3.8. The hospitals in rural areas had a smaller admission rate than in urban areas, but there is no consistent trend between towns of varying size.

Females had a greater rate of bed occupancy than males even after excluding maternity cases. Average duration of stay was lower for females from ages 15 to 64 but higher after age 65, rising to about 50% above the male rate at ages 85 and over.

The largest number of admissions for children up to age 14 were for tonsils and adenoids, 17,359; appendicitis, 3,627; head injuries, 2,549; other fractures, dislocations, injuries, and reactions to treatment, 3,789; other infectious and parasitic diseases 2,170; pneumonia, 2,083; strabismus, 2,028. Malignant neoplasms caused an admission rate of 44.0 per 1,000 in 1961. The sites with large rates were: digestive system, 8.0; lung, 7.5; and breast, 5.6. The admission rate for cancer of the lung in London was

10.9, compared with the national average of 6.7.

The average number of available maternity beds rose from 19,410 in 1959 to 20,004 in 1961. During this period the percentage of hospital deliveries steadily increased, 60.4 in 1959, 61.2 in 1960, and 62.7 in 1961. The average duration of postnatal stay fell continuously from 10.0 days in 1957 to 8.4 days in 1961. For the same period the percentage discharged on or before the seventh day rose from 12.5 to 27.9.

The number of operations performed in hospitals in this inquiry during 1961, apart from those performed in maternity units, was almost 1½ million. Gastrointestinal and abdominal surgery accounted for one-quarter of all operations. For males aged 16 years and over the data have been tabulated by occupation and shown by age, duration of stay, and deaths in hospital. The rates of admission to hospital vary with occupation, and the composition of the occupational group varies with age. For these reasons the rates have been standardized. Miners and quarrymen had the largest admission rates in each age group up to age 55.—*Report on Hospital In-patient Inquiry for the Two*

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 9 December (No. 9) and corresponding week 1966.

Figures of cases are for the countries shown and for Greater London. Figures of deaths and births are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	0	0	
Dysentery ..	523	49	118	4	1	563	78	153	13	9
Encephalitis, acute ..	0	0		0		2	1		0	
Enteric fever: Typhoid ..	1	0	0	0		1	1	0	0	
Paratyphoid ..	2	0	0	0		0	0	0	0	
Food-poisoning	105	31	8	1		118	54	5	2	
Infective enteritis or diarrhoea under 2 years				28	38				31	41
Measles* ..	1,385	51	81	25	119	13,864	2498	442	106	110
Meningococcal infection ..	5	0	3	2		3	0	0	0	1
Ophthalmia neonatorum	11	2	0	0		20	0	2	0	
Pneumonia† ..	153	25	135	6	3	178	26	119	20	2
Poliomyelitis, acute: Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic ..	0	0	0	0		0	0	0	0	
Puerperal fever§	72	24	1	0		78	25	1	0	
Scarlet fever ..	386	67	17	19	8	501	74	45	17	11
Tuberculosis: Respiratory ..	225	41	35	7		227	52	32	7	
Non-respiratory ..	34	7	8	2		48	9	1	2	
Whooping-cough	914	106	33	16	33	671	115	64	10	15

DEATHS	1967					1966				
	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Gr. Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		1	1		0	
Encephalitis, acute ..				0						0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	9	1	4	2	3	9	0	0	0	2
Influenza ..	36	4	0	0	0	17	6	2	0	1
Measles ..	0		0	0		0		1	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	959	109	19	26	13	873	140	23	24	15
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0		0		0	0	0
Tuberculosis: Respiratory ..	48	12	2	0	1	47	12	1	1	1
Non-respiratory ..				0	0				0	0
Whooping-cough	0	0	0	0	0	1	0	0	0	0
Deaths 0-1 year	329	64	28	7	9	365	57	18	9	10
Deaths (excluding stillbirths)	11,742	1771	550	109	221	11,505	1855	576	144	196
LIVE BIRTHS	14,171	2362	789	216	407	15,123	2505	813	243	430
STILLBIRTHS	206	39	8			250	37	14		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.

Years 1960 and 1961, Part III, Commentary, 1967, H.M.S.O. (38s. net).

Tees-side Gastroenteritis

Gastroenteritis in recent weeks among babies under 1 year had caused 37 cases on Tees-side by 22 December, when we went to press. Eight babies have died, but the infection was not the direct cause of death in four of them. Eight babies are still dangerously ill. The infecting organisms were *Escherichia coli* 0128 (the more dangerous) and *E. coli* 0119.

The infection began some weeks ago with a case at West Lane (Infectious Diseases) Hospital, Middlesbrough. The infection spread from there when babies were transferred to the Stockton Children's Hospital and the Middlesbrough General Hospital.

Eire in Third Quarter

The birth rate in Eire during the third quarter of 1967 was 21.2 per 1,000 of the population, and was 0.9 below the rate for the third quarter of 1966. The infant mortality rate was 23 and the neonatal mortality was 15 per 1,000 registered births; these were the same and one less, respectively, than the rates for the corresponding quarter of 1966.

Deaths from the principal infectious diseases included 35 from gastroenteritis under 2 years, eight from influenza, three from whooping-cough, two from acute infectious encephalitis, one from diphtheria, and one from measles. Deaths from tuberculosis

were 35 from the respiratory form and 13 from other forms, and these were 21 fewer and four more, respectively, than the preceding third quarter. Of the 1,279 deaths assigned to malignant neoplasms 588 were due to those of the digestive system and 219 to those of the respiratory system. The general death rate was 9.9 per 1,000 population, being the same as the rate for the September quarter of 1966.

Infectious Diseases

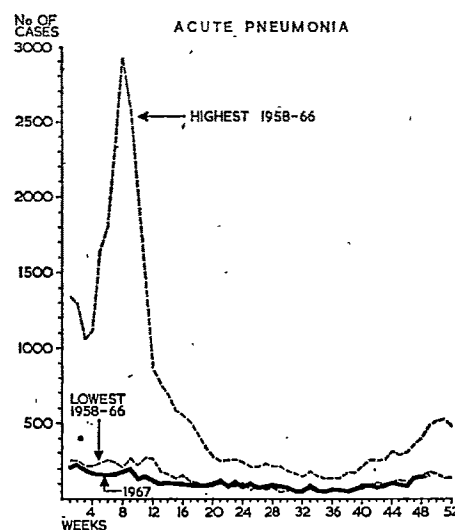
Areas where numbers of notifications were high in the latest two weeks for which figures are available.

Dysentery	Week Ending 1 Dec.	8 Dec.
Berkshire ...	15	18
Devonshire ...	10	16
Exeter C.B. ...	5	15
Durham ...	53	58
Blaydon U.D. ...	29	27
Stanley U.D. ...	7	13
Greater London ...	58	49
Camden ...	4	12
Kent ...	5	28
Lancashire ...	103	115
Barrow-in-Furness C.B.	1	10
Ashton-under-Lyne M.D.	26	38
Suffolk ...	0	13
Deben R.D. ...	0	13
Warwickshire ...	111	43
Coventry C.B. ...	99	31
Yorkshire West Riding ...	38	66
Barnsley C.B. ...	1	11
Leeds C.B. ...	11	20
Saddleworth U.D. ...	6	10

Dysentery (contd.)	Week Ending 1 Dec.	8 Dec.
Edinburgh ...	17	43
Glasgow ...	59	36
Influenza Deaths		
England and Wales ...	27	36
Lancashire ...	11	18

Graphs of Infectious Diseases

The graph below shows the uncorrected number of cases of acute pneumonia in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



MEDICAL NEWS

Universities Collaborate in Medical Education

The universities at St. Andrews and Manchester have agreed to co-operate in medical education. A joint liaison committee will operate the scheme, which it is hoped will include interchange of staff.

From 1973 onwards the enlarged clinical school in Manchester University will draw its students from the preclinical schools in both Manchester and St. Andrews. Students at St. Andrews will study for three years in the faculty of science on an extended pre-clinical course and will take a B.Sc. ordinary degree, or an honours B.Sc. with an extra year of study. Those wishing to qualify in medicine will be able to go to Manchester for three more years' work leading to the M.B., Ch.B. degrees. The partnership will make it possible to provide for a wider range of applicants drawn from both England and Scotland. For many it will also be an advantage to spend part of their time in a relatively small and closely knit community and the rest in a large civic university.

Manchester will continue to expand its pre-clinical as well as its clinical capacity in accordance with Government policy. An enlarged clinical school is now being developed. The university will retain its close association with the United Manchester Hospitals and form a new association with the

regional hospital board, notably at Withington Hospital, which will become a full teaching hospital.

The scheme, it is claimed, represents a considerable contribution to the national need to increase the supply of doctors and does so cheaply by making full use of resources and skills already in existence.

New Health Centres at Oxford

Opening two health centres in Oxford on 14 December, the Minister of Health, Mr. KENNETH ROBINSON, predicted that more than 100 health centres were likely to be in use in England and Wales within the next three years. "And four or five times that number within 10 years," he added. Oxford, he said, was the first county borough in England to have three operational health centres. In achieving as well 100% attachment of its nursing staff it had set an example to the rest of the country.

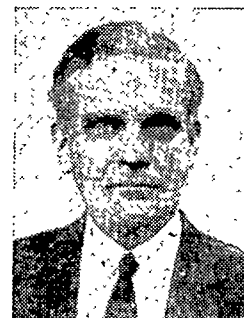
Population Census in 1971

The MINISTER OF HEALTH stated in a written reply on 18 December that the Government had decided to seek the authority of Parliament to take the next census in April 1971. It will mean "a full enumeration of the whole population." Preliminary tests on a voluntary basis will be carried out to ensure the efficiency of the operation. These will include a test census next April in 10 selected areas in England and Wales and 10 in Scotland.

Appointments to Professorships

The title of professor of neurosurgery has been conferred on Mr. VALENTINE LOGUE in respect of his post at the Institute of Neurology. Mr. Valentine Logue was educated

at Bishop's Stortford College and King's College, London, and graduated from St. George's Hospital in 1936. After four years in general surgery, during which time he was elected to the temporary wartime consultant staff of St. George's, he



transferred to neurosurgery in 1942, subsequently serving in the R.A.M.C. as neurosurgical specialist. In 1948 he was appointed neurological surgeon to the Maida Vale Hospital for Nervous Diseases and St. George's Hospital, and in 1957 he left to join the staff of the Middlesex Hospital. In 1965 he took the post of director of the newly established department of neurosurgical studies at the Maida Vale and National Hospitals for Nervous Diseases. Mr. Logue's interests are centred particularly around spontaneous intracranial haemorrhage and also the surgery of the spine and spinal cord. His published work includes articles

on the treatment of ruptured posterior fossa aneurysms and intermittent claudication of the cauda equina.

Dr. L. B. STRANG has had the title of professor of paediatrics conferred on him in respect of his post at University College Hospital Medical School. Dr. Strang, who is 42, was educated at the Royal Grammar School, Newcastle upon Tyne, and University of Durham, graduating M.B., B.S. in 1949. After holding junior house appointments at

the Royal Victoria Infirmary he became first assistant in the Department of Child Health in the University of Durham in 1956. In 1959 he obtained an M.R.C. research fellowship, and spent two years at Hammersmith Hospital in the department of medicine. From 1961 to 1962 he



Julia Bennett Studios

was research fellow at Harvard Medical School, and he then returned to Hammersmith as senior lecturer and consultant in the department of child health. He took up his appointment at U.C.H. in 1963. Dr. Strang obtained his M.D. with distinction in 1961 and he was elected F.R.C.P. this year. His publications in the clinical field include the original descriptions of the Harlequin syndrome, the secretion of catecholamines by neuroblastomas, and the existence of right to left shunts in infants with respiratory distress. In the past five years his main research work has used the foetal lamb preparation to study the adaptive change which takes place in the foetal lungs at birth. It has dealt with the control of pulmonary blood flow, the surface properties of the developing lung, and lymph flow from the lungs.

The title of professor of forensic medicine has been conferred on Dr. DONALD TEARE in respect of his post at St. George's Hospital Medical School. Dr. Donald Teare was educated at King William's College, Isle of Man, and Caius College, Cambridge. He qualified M.R.C.S., L.R.C.P. in 1936.



In 1937 he obtained the M.B., Ch.B. and the M.R.C.P. From 1938 to 1946 he was assistant curator of the museum at St. George's, his appointment being interrupted for a year when he was pathologist in the Emergency Medical

Service. In 1946 he was appointed pathologist to the hospital and lecturer in forensic medicine at the medical school and at St. Bartholomew's Hospital Medical College. He was elected a Fellow of the Royal

College of Physicians in 1962. The same year he was awarded the diploma in medical jurisprudence by the Society of Apothecaries of London. In 1963 he became a Founder Fellow of the College of Pathologists and reader in forensic medicine at St. George's. He was elected president of the Medical Defence Union in 1964.

People in the News

► Mr. KENNETH WYBAR has been appointed as Civilian Consultant in Ophthalmology to the Royal Navy.

News in Brief

From 1 January births in Wales and Monmouthshire may be registered in Welsh as well as in English.

Grants and Awards

A £12,000 research grant has been awarded to the Institute of Directors' Medical Centre by the British Heart Foundation. It will be used partly to finance a project to investigate the life expectancy of businessmen.

Coming Events

Medicine Today (B.B.C. T.V. programmes).—"Foetal Growth" (Dr. F. BRIMBLECOMBE and Mr. H. GORDON), 2 January, 1.15 p.m., transmitted on B.B.C. 2. Repeated on B.B.C. 1, 10 January, approximately 11 p.m.

Lister Centenary.—The exhibition at the symposium on "Operating-rooms a Century after Lister," arranged by the B.M.A. to commemorate the Lister centenary, will be on view in the Great Hall at B.M.A. House until 5 January (open 9 a.m. to 6 p.m.).

Hospital Physicists' Association and Urological Section of the Royal Society of Medicine.—Conference, "The Use of Electrical Stimulation in Urinary Retention and Incontinence," 12 January, 10.30 a.m., Royal Society of Medicine. Details from General Secretary, Hospital Physicists' Association, Tavistock House North, Tavistock Square, London W.C.1.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 1 January

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, Chelmsford and Essex Hospital, 5.30 p.m., clinical meeting.

INSTITUTE OF LARYNGOLOGY AND OTOLGY.—5.30 p.m., Professor I. Friedmann, Dr. D. A. Osborn, Dr. M. I. Wright: clinicopathological conference.

SOCIETY FOR MEDICAL AND DENTAL HYPNOSIS.—At Royal Society of Medicine, 8 p.m.; dental meeting.

Tuesday, 2 January

B.B.C. 2 TELEVISION.—1.15 p.m., *Medicine Today: Foetal Growth*. (Sponsored by A.S.M.E.)

BOLTON AND DISTRICT MEDICAL SOCIETY.—At Gymnasium, Bolton Royal Infirmary, 8.15 p.m., Dr. G. M. Berlyne: Haemodialysis.

ST. CHARLES'S HOSPITAL MEDICAL CENTRE.—8.45 p.m., Dr. A. I. Suchett-Kaye: Some Topics of Interest in Geriatrics.

Wednesday, 3 January

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, Chelmsford and Essex Hospital, 12 noon, surgical meeting.

STOKE MANDEVILLE HOSPITAL.—12.15 p.m., Dr. Lorna Davies: clinical cases.

Thursday, 4 January

EMERGENCY MEDICAL AID COMMITTEE FOR ISRAEL in conjunction with the BRITISH FELLOWSHIP OF THE

ISRAEL MEDICAL ASSOCIATION.—At the Medical Society of London, 11 Chandos Street, London W.1, 8.15 p.m., Professor Harold Ellis: Post-graduate Medical Education in Israel.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian lecture by Professor J. P. Reidy: The Nasal Septum.

Friday, 5 January

BIOCHEMICAL SOCIETY.—At Department of Biochemistry and Chemistry, St. Bartholomew's Hospital Medical College, 9.30 a.m., colloquium on Properties of Enzymes Attached to Solid Matrices, followed in afternoon by ordinary meeting.

Saturday, 6 January

ROYAL POSTGRADUATE MEDICAL SCHOOL.—9.30 a.m., anaesthetic teaching meeting: Overdose with Therapeutic Agents.

Sunday, 7 January

EDGWARE POSTGRADUATE MEDICAL SOCIETY.—At Edgware General Hospital, 10.30 a.m., Dr. J. Mowbray: Management of Chronic Renal Failure.

Universities and Colleges

ABERDEEN

M.D.—P. N. Bennett, A. S. Henderson, J. Reid.

M.B., Ch.B.—D. N. Anumudu, Jill D. Gurney, P. J. Hellstrom, D. P. J. McCarthy, O. Olatunji, With honours. In absentia.

DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

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British Medical Journal · Supplement

LONDON SATURDAY 7 OCTOBER 1967

CONTENTS

Committee on Medical Science, Education, and Research -	1	Private Practice Committee -	9
B.M.A. Emergency Treatment Service -	3	Discount Service -	10
Medical Staffing in the National Health Service in England and Wales -	3	H.M. Forces -	10
Medical Staffing in the National Health Service in Scotland	7	Diary of Central Meetings -	10
		Branch and Division Meetings -	10

Committee on Medical Science, Education, and Research

Owing to a suggestion by the Film Committee that its title and functions should be broadened to encompass the new department of audio-visual communication, the Committee on Medical Science, Education, and Research briefly discussed the future organization of the B.M.A.'s scientific activities. The question of how the Association could best help postgraduate centres was referred for investigation to a special committee, which would also consider the future of B.M.A. lectures. Professor O. L. Wade and Dr. W. W. Fulton were appointed to convene a working party to examine the usefulness of amphetamine preparations. Draft regulations for a B.M.A. research fellowship of £1,500 a year were approved. The Council is to be asked to press for adequate rehabilitation and long-term treatment facilities for drug addicts who have completed their initial treatment.

The Committee on Medical Science, Education, and Research held its first meeting of the session at B.M.A. House on 19 September. Mr. A. LAWRENCE ABEL was re-elected Chairman and Sir RONALD TUNBRIDGE was re-elected Deputy Chairman.

Size of Committee

The Committee considered a request from the Council that central committees should reduce their size to the minimum compatible with the work of the committee, and also reduce the number of subcommittees where possible.

It was agreed that a Chairman's subcommittee should be formed to consider urgent matters and matters which it was unnecessary for the full Committee to discuss. Mr. R. V. Cooke (President), the Chairman, the Deputy Chairman of the Committee, and Dr. R. Cove-Smith were appointed as the Chairman's Subcommittee.

Recruitment of Members

It was reported that the Organization Committee, in a recent report to the Council, had expressed a hope that each of the major medico-political committees of the Association would consider how best to recruit members.

Dr. W. W. FULTON said that in recruiting meetings held in various medical school areas much emphasis had been laid on the B.M.A.'s scientific work. He thought that sometimes the trade union aspects of the Association tended to get more prominence, and he suggested that every five years or so a brochure might be published describing its scientific activities. It should mention the awards for research available to members. Dr. D. P. STEVENSON, Secretary, supported Dr. Fulton's suggestion.

Film Committee

It was reported that, now the department of audio-visual communications had been established, the Film Committee thought that its title and terms of reference were inappropriate. Neither of them were broad enough to cover all aspects of the audio-visual field. It was considering, therefore, recommending to Council that the Committee should be renamed the "Audio-visual Communications (Film) Committee," and that its terms of reference should be, say, "to be responsible for the Association's activities in the sphere

of audio and visual communications." It was also proposed to strengthen the Committee by inviting members with experience of the subject to serve on it.

Dr. T. QUILLIAM, Chairman of the Film Committee, said that a director of the department of audio-visual communications had been appointed (*B.M.J.*, 13 May, p. 453), and the Film Committee had arranged for a meeting on the technological aspects of medical education and had planned a series of activities.

The CHAIRMAN said that this matter was still in the melting-pot, and he thought it was several months too soon to consider it.

Professor D. E. C. MEKIE said that the Film Committee should not take medical education under its wing. Dr. QUILLIAM replied that it was a matter of technology. The Film Committee's function was to improve the way in which teaching material was conveyed to the students. Dr. FULTON suggested that the title should be reviewed from year to year.

Dr. ARNOLD BROWN thought it would be wise to postpone a decision. The methods of audio-visual communication could change, and might be quite different in two years' time. Mr. R. MYLES GIBSON supported him.

Dr. STEVENSON pointed out that the department of audio-visual communications had to be responsible to somebody. It could not be responsible to the Film Committee, because its commitments covered a wider field, nor to the Committee on Medical Science, Education, and Research, since that Committee was not constituted to supervise the audio-visual field. He suggested that the Committee should agree to "a modest change" in the title of the Film Committee without prejudice to further discussions on the subject.

The Committee accepted this suggestion.

Biological Council

A suggestion was considered that the Association should apply for affiliation to the Biological Council, which was formed in 1945, to enable representatives of societies and associations in the biological sciences to meet periodically to discuss common problems and to draw on each other's experience. It was largely on the initiative of the Biological Council that the Institute of Biology was founded in 1950, and it was represented on committees dealing with scientific documentation and with biological education and the training of technicians, and it also maintained an interest in schemes designed to provide accommodation for scientific societies.

The Committee agreed to recommend to the Council that the Association should apply for affiliation to the Biological Council.

Amphetamine Preparations

The Committee received a report that the Council, on receiving the Committee's recommendations that the possibility of prohibiting the manufacture of amphetamine preparations except in liquid form should be explored, had amended the recommendation to read, "that the position be explored of the usefulness or otherwise of amphetamine preparations." Consideration had been given to the establishment of a working group to carry out this recommendation, and it was noted that the Home Office had asked to receive a copy of the group's report when available.

Dr. FULTON said that the recommendation of the Joint Formulary Committee, on which he served, had been that amphetamine preparations should be withdrawn from the *British National Formulary*. There was some objection to complete withdrawal of the drug, but its use as a stimulant or anti-depressant was condemned. He thought the aim should be to discontinue combinations of amphetamines with other preparations such as sedatives. The Joint Formulary Committee had considered that amphetamine had a use, but only a limited one.

It was agreed to appoint Dr. Fulton and Professor O. L. Wade to set up a working party on which the Psychological Medicine Group Committee and the General Medical Services Committee, among others, would be represented.

Lectures

The Committee agreed that the Sir Charles Hastings Lecture should be further suspended during 1967-8. A report was received that during the 1966-7 session 144 B.M.A. lectures had been arranged for Branches, Divisions, and medical students' societies in the United Kingdom.

The Committee considered a suggestion from the honorary secretary of the North Wales Branch that B.M.A. lectures should be abandoned. His view was that postgraduate centres would rob the B.M.A. of any reason for having scientific lectures, and he thought the B.M.A. lectures should become an integral part of a week-end course at a postgraduate centre.

Dr. STEVENSON said this was an important point. The Association was now offering all its facilities to the postgraduate centres, of which there were some 200. He thought the future of medicine lay in postgraduate centres, and the B.M.A., which had much to offer these centres, must adapt itself accordingly.

Mr. MYLES GIBSON pointed out the contributions that the department of audio-visual communications could make in this field. Dr. STEVENSON thought that the money now spent on B.M.A. lectures could be used to better advantage providing facilities in postgraduate centres. He suggested that the day of the formal lecture was past.

Professor J. H. MIDDLEMISS thought that the B.M.A. should approach postgraduate deans. Professor MEKIE did not think the usefulness of the B.M.A. lectures had passed. More important, however, was the question of the continuing influence of the Association in postgraduate centres. Dr. J. WEDGWOOD said that clinical teachers would welcome help from the B.M.A.

Dr. FULTON said there should be a continuous programme arranged and syllabuses should be approved in advance so that the lectures qualified for postgraduate grants, which would be a great incentive. Social activity was important. The B.M.A. could not compete with the big symposia arranged by drug houses, which were very costly. There was a place for non-scientific B.M.A. lectures, and one held in Glasgow in 1966 on sculpture had been the most successful one in Glasgow for 22 years.

Dr. I. FIELD, Assistant Secretary, said the Committee could, if it wished, make representations to the Council to amend the present constitution of the B.M.A. lectures.

It was agreed to establish a committee to investigate the position and to prepare a report for the next meeting on how the B.M.A. could best help postgraduate centres. The President, Dr. Wedgwood, Professor Mekie, and Dr. Fulton were appointed as the Committee, together with a nominee of the Film Committee.

Computer Courses

It was reported that, after two successful computer courses in London in May and June, arrangements were in hand for a course on computers in medicine in Manchester on 12 October and one in Edinburgh on 26 October. Arrangements were being made to hold a similar course at Rhyl in January 1968.

Dr. FIELD reported that the joint symposium on the application of mathematical and computer methods to problems in medicine was arranged for 6 December, and would be an all-day meeting. This would be a combined effort of the B.M.A. and the Institute of Mathematics. It would be designed for those who already had an interest in this field.

The Committee agreed to ask the Finance Committee for a contribution of up to £100 towards the cost of the symposium.

Budget

The Committee considered the following statement on its estimated expenditure for 1967 and its expected expenditure for 1968:

	1967 £	1968 £
Research scholarships and grants	2,400	2,400
Prize expenses, awards, etc.	550	550
B.M.A. lectures	3,750	3,750
First-aid conference	250	—
B.M.A. Nuffield Library expenses	7,200	8,350

There was criticism of the increase in the library expenditure, though its importance was recognized. Dr. FIELD said most of the increased expenditure would be owing to rises in the cost of periodicals. It was agreed to ask the Library Committee to re-examine expenditure as the year progressed.

Research Fellowship

The Committee considered draft regulations for a B.M.A. Research Fellowship for whole-time research in any subject related to the causation, prevention, or treatment of disease. The Fellowship would be awarded only to

members of the Association. It would be an annual one and to the value of £1,500. It would be renewable for a second and final year if required, subject to a satisfactory progress report. The Association would also be prepared to consider a grant, not exceeding £300 a year, to cover approved expenses of the candidate. It was assumed that the head of the department in which the research fellow worked would be his supervisor.

Lister Centenary

The Committee considered a preliminary report of its steering committee set up to make recommendations on suitable ways for the Association to celebrate in 1967 the Lister Centenary. The report dismissed the idea of a single lecture in favour of a symposium designed to launch an exhibition in B.M.A. House, which would emphasize the links between Lister and the B.M.A. The steering committee recommended a half-day symposium, under the chairmanship of the President of the B.M.A., on the structural design of operating-theatres in relation to the control of infection.

Mr. G. E. MOLONEY, a member of the steering committee, who attended by invitation for this item, said the basic idea was to get together all those interested in operating-theatres to produce something creative as a commemoration. As many workers in related fields as possible should be invited to take part.

Mr. MYLES GIBSON, also a member of the steering committee, said it was understood that the Army would help with a demonstration of mobile theatre units. It would be possible to organize the event in early December.

The Committee decided to recommend to the Council that a symposium on the lines suggested should be held in December, and to ask the steering committee to make the detailed arrangements.

Drug Addiction

The Committee considered a resolution of the Annual Representative Meeting 1967 recommending that there should be adequate provision for rehabilitation and long-term follow-up for patients who have completed treatment for drug addiction. The Government, the resolution stated, should be urged to implement all the other recommendations of the Brain Committee.

The CHAIRMAN said that treatment was almost useless without rehabilitation. Dr. FULTON said everything existed on paper but not in fact, and the Committee must stress that facilities should be provided as soon as possible.

The Committee agreed to recommend to the Council that action should be taken and also that the matter should be taken up at the Parliamentary and Scientific Committee.

Conference on Medical Education

The Committee considered a letter from the Secretary-General of the World Medical Association concerning the organization of

the fourth World Conference on Medical Education (*B.M.J.*, 23 September, pp. 749 and 795). It asked the B.M.A., among other associations, to establish a group of medical education experts to provide the W.M.A. council with guidance, continuing suggestions, and constructive criticism on the programme for the conference.

Dr. STEVENSON said that the conference would be held in Europe probably in 1972. Dr. FULTON said it would be a pity if the British medical scene was totally neglected. Dr. STEVENSON thought it would be possible for the Association to pay the fares of a substantial number of speakers if the conference was held in Europe.

Legislation on Drugs and Medicines

The Committee considered the Government's White Paper on Forthcoming Legislation on the Safety, Quality, and Description of Drugs and Medicines (*B.M.J.*, 16 September, pp. 689 and 734).

Several speakers much regretted the proposed legislation and said they would prefer the existing system to continue. The CHAIRMAN said that the new system would need an army of civil servants to administer it.

Dr. FULTON criticized Clause 15 as too vague, and said the Committee should express its reservation at this stage. He went on to attack Clause 48, which would permit

in certain circumstances sales over the counter and the manufacture of herbal remedies not containing drugs. He said that some herbal remedies could be quite potent. Dr. M. WEATHERALL said that Clause 48 seemed much too loose as it stood. It was perfectly possible to make lethal mixtures. He was also surprised at the retention of the Poisons Boards. He said there should be only one body.

Dr. FULTON said that there was no doubt that the whole set-up of the marketing of drugs needed codification and the White Paper was a commendable attempt.

It was agreed to submit a report to the Council on the White Paper.

B.M.A. Emergency Treatment Service

The Chairman of the Inner London Executive Council of the National Health Service, Mr. G. F. Rowe, denied last week that the council was to blame for the temporary abandonment of the British Medical Association Emergency Treatment Service, which was to have been operated in London by Telephone Answering Services Ltd.

Doctors in the London area were informed by the Emergency Treatment Service (a deputizing service) at the beginning of September that the response from doctors was too small to justify operating the scheme. The Chairman of the Central Advisory Committee of the B.T.S., Dr. I. M. Jones, and the managing director of Telephone Answering Services Ltd., Mr. J. W. Tayler, stated in a letter that there had been "considerable delay" in obtaining official approval for the service, and they considered

that the slow response from the doctors might "in some measure" have arisen from the delay. They said that the deputizing service would begin when enough doctors had enrolled.

Mr. Rowe's statement last week said that the B.M.A. first informed the Inner London Executive Council in December 1966 of the intention to start the deputizing service. A meeting between the organizers and sponsors and the Deputizing Arrangements Committee of the executive council could not be arranged until 19 May. Though the executive council was satisfied that the service sponsored by the B.M.A. would be of a high quality, the council had, in the interests of the doctors who would use the service, to require it first to sort out its own company structure, which was then being changed. The executive council had been "very concerned at the booklet which had been issued

by the British Medical Association to London doctors." This had not given information on, among other important matters, the name of the company with whom the doctors would be contracting, and the contract form was "quite unacceptable." The booklet had since been withdrawn.

Any delay from that stage was due, Mr. Rowe points out, to the need for action by the organizers to meet the executive council's objections. The alteration of the company structure of Telephone Answering Services Ltd. was completed in August, and the appropriate committee of the executive council approved the deputizing service on 22 August. "The scheme," Mr. Rowe's statement concluded, "had legal implications for subscribers which the council had to deal with, and in no circumstances can the blame for any delay be laid at the door of the executive council."

Medical Staffing in the National Health Service in England and Wales

The introductory text printed below and the Table reproduced overleaf have been provided by the Ministry of Health. Similar information relating to Scotland, provided by the Scottish Home and Health Department, is printed at p. 7.

The accompanying Table shows the number of doctors in posts above house-officer grade in National Health Service hospitals and in general practice. Doctors employed by local health authorities and doctors who do not have contracts with hospital authorities or executive councils are not included.

The Table attempts to indicate for each specialty the relation between numbers undertaking specialty training and the number of permanent posts expected to become vacant in the specialty. In tabulating this information it has been necessary to oversimplify the true position and to make some assumptions which may be queried.

Column I gives annual output of the senior registrar grade on a three-year basis, though it is recognized that four years of training at the senior registrar level is often required

unless sufficient experience has been gained at registrar level.

Column J gives estimated figures for annual deaths and retirements of consultants and S.H.M.O.s with allowance from all causes. These figures are estimated actuarially from a knowledge of the age structure of these grades in 1966 and from past experience of actual deaths and retirements in the specialty concerned.

Column K gives the average annual expansion of the consultant grade in the specialty over the past three years. Column L gives the sum of columns J and K. Column M represents an attempt to show in which specialties there seem to be too few or too many doctors undertaking specialty training at senior registrar level in relation to likely consultant vacancies. In most specialties

expansion of the consultant grade over the last year has led to improved prospects for senior registrars in training. This improvement is reflected in an increasing number of asterisks in column M. Growth of the consultant grade has continued through 1967, and it is expected that the 1967 Table, to be prepared as early as possible in 1968, will show further improvement in prospects for senior registrars. The Table is similar to that for 1965 (*Supplement*, 24 December 1966, p. 240). It relates to the position at 30 September 1966. It is constructed from returns provided by hospital boards and executive councils. Collection and checking of these returns takes some time, but the Table this year has been produced three months earlier than last year, and every effort will be made to provide the information earlier in future years.

Medical Staffing and Prospects in the N.H.S., England and Wales, at 30 September 1966

A Specialty	B Consultants	C S.H.M.O.s with Allowance	D S.H.M.O.s without Allowance	E Medical Assistants	F Senior Registrars	G Registrars	H S.H.O.s	I Annual Output from Senior Registrar Grade (3-year Basis: U.K. and Republic of Ireland Born)	J Consultant and S.H.M.O. with Allowance Posts Falling Annually	K Average Annual Expansion in Consultant Posts 1965-6	L Expected Annual Consultant Vacancies	M Pros- pects
Anaesthetics	Under 35 35-39 40-49 50-59 60-64 65 and over Total	40 181 412 326 104 14 1,077	21	39	24	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	42	34	33	67	****
Cardiology	Under 35 35-39 40-49 50-59 60-64 65 and over Total	— 4 30 10 1 45	—	—	2	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	4	1	2	3	
Dermatology	Under 35 35-39 40-49 50-59 60-64 65 and over Total	5 12 58 61 14 154	2	2	1	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	7	5	3	8	**
Diseases of the chest	Under 35 35-39 40-49 50-59 60-64 65 and over Total	— 3 113 117 59 356	58	104	28	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	2	17		Uncertain	Uncertain
General medicine ¹	Under 35 35-39 40-49 50-59 60-64 65 and over Total	8 83 279 373 109 870	7	24	17	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	45	34	15	49	**
General practice	Principals Under 35 35-39 40-49 50-59 60-64 65 and over Total	19,790 2,754 2,956 6,326 4,738 1,628 37,482		Assistants 740	Trainee Assistants 121				Principal posts falling vacant annually 800	Minimum increase in number of principal posts needed to prevent growth of list sizes annually	Annual rate of principal appointments required	***
General surgery	Under 35 35-39 40-49 50-59 60-64 65 and over Total	2 63 286 359 144 811	14	18	30	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	45	40	5	45	*
Geriatrics	Under 35 35-39 40-49 50-59 60-64 65 and over Total	5 23 73 30 15 156	7	18	20	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	3	5	11	16	***
Infectious diseases	Under 35 35-39 40-49 50-59 60-64 65 and over Total	— 2 8 14 9 37	4	20	4	U.K. and Republic of Ireland born Total	U.K. and Republic of Ireland born Total	1	3	-1	Up to 2	Uncertain

¹ Includes clinical physiology and social medicine.

Medical Staffing and Prospects in the N.H.S., England and Wales, at 30 September 1966—contd.

A	B	C	D	E	F	G	H	I	J	K	L	M
Specialty	Consultants	S.H.M.O.s with Allowance	S.H.M.O.s without Allowance	Medical Assistants	Senior Registrars	Registrars	S.H.O.s	Annual Output from Senior Registrar Grade (3-year Basis: U.K. and Republic of Ireland Born)	Consultant S.H.M.O. with Allowance and Post Rating Vacant Annually	Average Annual Expansion in Consultant Posts 1963-6	Expected Annual Consultant Vacancies	Prospects
Neurology ^a	Under 35 3 35-39 17 40-49 48 50-59 37 60-64 10 65 and over 115 Total	—	—	3	Under 35 7 35-39 9 40 and over 2 U.K. and Republic of Ireland born 16 Total 28	U.K. and Republic of Ireland born 46 Total 57	U.K. and Republic of Ireland born 17 Total 28	5	3	4	7	**
Neurosurgery	Under 35 10 35-39 27 40-49 25 50-59 6 60-64 1 65 and over 69 Total	—	—	—	Under 35 7 35-39 11 40 and over 2 U.K. and Republic of Ireland born 14 Total 20	U.K. and Republic of Ireland born 17 Total 48	U.K. and Republic of Ireland born 11 Total 33	5	2	1	3	.
Obstetrics and gynaecology	Under 35 47 35-39 190 40-49 215 50-59 58 60-64 11 65 and over 521 Total	5	14	9	Under 35 21 35-39 50 40 and over 6 U.K. and Republic of Ireland born 74 Total 77	U.K. and Republic of Ireland born 153 Total 369	U.K. and Republic of Ireland born 177 Total 449	25	19	9	28	**
Ophthalmology	Under 35 9 35-39 41 40-49 97 50-59 123 60-64 54 65 and over 10 Total 334	7	110	9	Under 35 42 35-39 20 40 and over 11 U.K. and Republic of Ireland born 55 Total 73	U.K. and Republic of Ireland born 62 Total 126	U.K. and Republic of Ireland born 22 Total 92	18	15	4	19	.
Otolaryngology	Under 35 8 35-39 24 40-49 117 50-59 108 60-64 43 65 and over 14 Total 314	—	3	5	Under 35 26 35-39 13 40 and over 6 U.K. and Republic of Ireland born 29 Total 45	U.K. and Republic of Ireland born 44 Total 131	U.K. and Republic of Ireland born 19 Total 101	10	14	1	15	***
Pædiatrics	Under 35 5 35-39 18 40-49 115 50-59 88 60-64 21 65 and over 251 Total	—	1	4	Under 35 14 35-39 18 40 and over 2 U.K. and Republic of Ireland born 28 Total 34	U.K. and Republic of Ireland born 74 Total 158	U.K. and Republic of Ireland born 92 Total 205	9	8	8	16	***
Pædiatric surgery	Under 35 3 35-39 8 40-49 3 50-59 3 60-64 1 65 and over 15 Total	—	—	—	Under 35 2 35-39 2 40 and over 4 U.K. and Republic of Ireland born 4 Total 4	U.K. and Republic of Ireland born 4 Total 18	U.K. and Republic of Ireland born 9 Total 22	1	—	1	1	.
Pathology ^a	Under 35 9 35-39 112 40-49 457 50-59 322 60-64 64 65 and over 978 Total	7	17	29	Under 35 78 35-39 30 40 and over 24 U.K. and Republic of Ireland born 121 Total 132	U.K. and Republic of Ireland born 145 Total 231	U.K. and Republic of Ireland born 80 Total 143	40	26	30	56	***
Physical medicine and rheumatology	Under 35 2 35-39 22 40-49 50 50-59 37 60-64 15 65 and over 127 Total	1	6	3	Under 35 8 35-39 5 40 and over 1 U.K. and Republic of Ireland born 12 Total 14	U.K. and Republic of Ireland born 24 Total 40	U.K. and Republic of Ireland born 8 Total 17	4	4	6	10	***

^a Includes clinical neurological physiology. ^b Includes blood transfusion.

Medical Staffing and Prospects in the N.H.S., England and Wales, at 30 September 1966—contd.

A	B	C	D	E	F	G	H	I	J	K	L	M
Specialty	Consultants	S.H.M.O.s with Allowance	S.H.M.O.s without Allowance	Medical Assistants	Senior Registrars	Registrars	S.H.O.s*	Annual Output from Senior Registrar Grade (3-year Basis: U.K. and Republic of Ireland Born)	Consultant S.H.M.O. with Allowance and Posts Filling Vacant Annually	Average Annual Expansion in Consultant Posts 1963-6	Expected Annual Consultant Vacancies	Prospects
Psychiatry	Under 35 24 35-39 141 40-49 382 50-59 319 60-64 93 65 and over 10 Total 969 of whom 734 mental illness 92 mental subnormality 143 child psychiatry	25 of whom 19 mental illness 5 mental subnormality 1 child psychiatry	141 of whom 113 mental illness 23 mental subnormality 5 child psychiatry	157 of whom 130 mental illness 27 mental subnormality — child psychiatry	Under 35 97 35-39 80 40 and over 38 U.K. and Republic of Ireland 182 Total 215 of whom 185 mental illness 4 mental subnormality 26 child psychiatry	U.K. and Republic of Ireland 255 Total 433	U.K. and Republic of Ireland 72 Total 153	61	30	23	63	M.L. M.S. G.P.
Plastic surgery	Under 35 — 35-39 3 40-49 21 50-59 30 60-64 5 65 and over 2 Total 61	—	—	2	Under 35 3 35-39 10 40 and over 4 U.K. and Republic of Ireland 12 Total 17	U.K. and Republic of Ireland 10 Total 31	U.K. and Republic of Ireland 26 Total 26	4	2	2	4	•
Radiology	Under 35 12 35-39 77 40-49 226 50-59 189 60-64 11 65 and over 11 Total 559	1	2	1	Under 35 41 35-39 25 40 and over 7 U.K. and Republic of Ireland 56 Total 73	U.K. and Republic of Ireland 86 Total 119	U.K. and Republic of Ireland 14 Total 17	19	16	13	29	••••
Radiotherapy	Under 35 2 35-39 20 40-49 73 50-59 53 60-64 12 65 and over 1 Total 161	—	9	2	Under 35 14 35-39 12 40 and over 5 U.K. and Republic of Ireland 24 Total 31	U.K. and Republic of Ireland 31 Total 58	U.K. and Republic of Ireland 9 Total 24	8	4	3	7	
Thoracic surgery ⁴	Under 35 — 35-39 2 40-49 44 50-59 39 60-64 11 65 and over 96 Total 192	—	—	3	Under 35 9 35-39 10 40 and over 3 U.K. and Republic of Ireland 14 Total 22	U.K. and Republic of Ireland 25 Total 67	U.K. and Republic of Ireland 7 Total 42	5	3	2	5	•
Traumatic and orthopaedic surgery	Under 35 1 35-39 40 40-49 164 50-59 202 60-64 39 65 and over 5 Total 451	7	18	49	Under 35 23 35-39 39 40 and over 4 U.K. and Republic of Ireland 58 Total 66	U.K. and Republic of Ireland 109 Total 314	U.K. and Republic of Ireland 71 Total 377	19	15	13	28	•••
Urology	Under 35 — 35-39 7 40-49 14 50-59 19 60-64 7 65 and over 1 Total 48	—	—	—	Under 35 6 35-39 5 40 and over 2 U.K. and Republic of Ireland 11 Total 13	U.K. and Republic of Ireland 7 Total 15	U.K. and Republic of Ireland 9 Total 21	4	2	3	5	••
Venerology	Under 35 — 35-39 2 40-49 20 50-59 46 60-64 13 65 and over 3 Total 84	3	13	5	Under 35 2 35-39 4 40 and over 4 U.K. and Republic of Ireland 7 Total 9	U.K. and Republic of Ireland 10 Total 14	U.K. and Republic of Ireland 6 Total 14	2	4	—	4	•••

⁴Includes cardiac surgery.

Medical Staffing in the National Health Service in Scotland

The accompanying Tables show the number of doctors in posts above house-officer grade in National Health Service hospitals and in general practice in Scotland. Doctors employed by local health authorities and doctors who do not have contracts with executive councils are not included.

The Scottish figures are not shown in exactly the same form as are the figures for England and Wales. This mainly arises because of differences in the forward estimating of development of the consultant establishment. There are also some minor deviations in the specialty headings owing to the small numbers involved.

In column H the estimated annual number of consultant posts to be filled in Scotland takes into account losses due to retirement and illness and expansion to the numbers recommended in the Report on Medical Staffing Structure in Scottish Hospitals (Wright Report). It also allows for a small

element of expansion beyond this number to allow for developments in teaching, research, and new advances in medicine which involved no service commitment at the time the Wright Committee was deliberating.

At present the senior registrar establishment in Scotland is estimated broadly on a four-year training basis, but this is only an average figure, and the actual number of years spent in training varies considerably between specialties. The 1967 establishment for senior registrars is 312, while the number in post at 30 September 1966 (column E) was 263. The Tables are based on staff in post on 30 September, and this is a common time for changeover in posts. There is therefore a relatively large number of transitional vacancies.

Adjustments have been made in the establishment to allow for likely developments in certain specialties. Because of these variations and adjustments, column I is not simply column E divided by four but is rather an

estimate of the output which it is hoped to attain within the next few years. The senior registrar establishment is adjusted each year to take account of movement out of and into Scotland and of incidental losses. The excess of column I over column H is accounted for by the present net average movement out of Scotland of 10 senior registrars per year. The aim is to produce a situation in which every senior registrar with the requisite qualifications and experience can expect to obtain a consultant post and at the same time ensure that there is a reasonable number of candidates available for each post. This may not always be possible, since some specialties are less attractive than others and experience difficulty in obtaining suitable candidates. The ratio of the number of registrars born in the U.K. and Republic of Ireland to the number of senior registrars in each specialty will express to some extent the prospects in that specialty.

TABLE I.—Hospital Medical Staffing (Including Honoraries) in Scotland at 30 September 1966

A Specialty	B Consultants	C D Medical Assistants and S.H.M.O.s without Allowance		E Senior Registrars	F Registrars	G S.H.O.s	H Average Annual Number of Consultant Posts to be Filled	I Planned Average Annual Output of Senior Registrars
		S.H.M.O.s without Allowance	Medical Assistants					
All specialties	Total 1,338 Under 35 46 35-39 181 40-49 526 50-59 468 60-64 96 65 and over 21	121	121	Total 263 Under 35 135 35-39 98 40 and over 30 (Born in U.K. or in Republic of Ireland, 246)	703 (Born in U.K. or in Republic of Ireland, 488)	437 (Born in U.K. or in Republic of Ireland, 262)	60-63	72-74
General, medicine, ¹ infectious diseases, chest medicine, neurology	Total 280 Under 35 2 35-39 25 40-49 111 50-59 113 60-64 25 65 and over 4	39	34	Total 54 Under 35 25 35-39 21 40 and over 8 (Born in U.K. or in Republic of Ireland, 50)	170 (Born in U.K. or in Republic of Ireland, 107)	86 (Born in U.K. or in Republic of Ireland, 52)	10	12
Dermatology	Total 25 Under 35 2 35-39 1 40-49 8 50-59 10 60-64 3 65 and over 1	—	1	Total 3 Under 35 1 35-39 2 40 and over — (Born in U.K. or in Republic of Ireland, 3)	16 (Born in U.K. or in Republic of Ireland, 12)	8 (Born in U.K. or in Republic of Ireland, 4)	1-2	1-2
Venereal diseases	Total 7 Under 35 — 35-39 — 40-49 3 50-59 2 60-64 2 65 and over —	3	4	Total — Under 35 — 35-39 — 40 and over — (Born in U.K. or in Republic of Ireland, —)	1 (Born in U.K. or in Republic of Ireland, 1)	1 (Born in U.K. or in Republic of Ireland, 1)	Less than 1	Less than 1
Medical paediatrics	Total 36 Under 35 3 35-39 5 40-49 15 50-59 13 60-64 — 65 and over —	3	1	Total 8 Under 35 6 35-39 2 40 and over — (Born in U.K. or in Republic of Ireland, 7)	30 (Born in U.K. or in Republic of Ireland, 21)	11 (Born in U.K. or in Republic of Ireland, 5)	1-2	2
General surgery ²	Total 151 Under 35 4 35-39 16 40-49 51 50-59 62 60-64 16 65 and over 2	5	4	Total 36 Under 35 20 35-39 15 40 and over 1 (Born in U.K. or in Republic of Ireland, 33)	103 (Born in U.K. or in Republic of Ireland, 70)	67 (Born in U.K. or in Republic of Ireland, 45)	9	10
Surgical paediatrics	Total 11 Under 35 — 35-39 1 40-49 3 50-59 6 60-64 1 65 and over —	—	—	Total — Under 35 — 35-39 — 40 and over — (Born in U.K. or in Republic of Ireland, —)	3 (Born in U.K. or in Republic of Ireland, —)	6 (Born in U.K. or in Republic of Ireland, 3)	1	1
Urology	Total 11 Under 35 — 35-39 2 40-49 4 50-59 3 60-64 1 65 and over 1	—	—	Total 3 Under 35 1 35-39 1 40 and over 1 (Born in U.K. or in Republic of Ireland, 3)	1 (Born in U.K. or in Republic of Ireland, 1)	4 (Born in U.K. or in Republic of Ireland, 2)	1	1
Neurosurgery	Total 12 Under 35 1 35-39 2 40-49 6 50-59 3 60-64 — 65 and over —	1	—	Total 3 Under 35 2 35-39 1 40 and over — (Born in U.K. or in Republic of Ireland, 3)	6 (Born in U.K. or in Republic of Ireland, 3)	9 (Born in U.K. or in Republic of Ireland, 2)	1	1

(Continued overleaf)

TABLE I.—Hospital Medical Staffing (Including Honoraries) in Scotland at 30 September 1966—*contd.*

A Specialty	B Consultants	C D Medical Assistants and S.H.M.O.s without Allowance		E Senior Registrars	F Registrars	G S.H.O.s	H Average Annual Number of Consultant Posts to be Filled	I Planned Average Annual Output of Senior Registrars
		S.H.M.O.s without Allowance	Medical Assistants					
Plastic surgery	Total 9 Under 35 — 35-39 1 40-49 3 50-59 4 60-64 1 65 and over —	—	—	Total 1 Under 35 — 35-39 — 40 and over 1 (Born in U.K. or in Republic of Ireland, 1)	6 (Born in U.K. or in Republic of Ireland, 2)	5 (Born in U.K. or in Republic of Ireland, 1)	Less than 1	Less than 1
Thoracic surgery	Total 11 Under 35 — 35-39 — 40-49 6 50-59 4 60-64 1 65 and over —	—	—	Total — Under 35 — 35-39 — 40 and over — (Born in U.K. or in Republic of Ireland, —)	4 (Born in U.K. or in Republic of Ireland, 3)	5 (Born in U.K. or in Republic of Ireland, 3)	Nil	Nil
Orthopaedic surgery	Total 72 Under 35 2 35-39 8 40-49 32 50-59 28 60-64 1 65 and over 1	3	2	Total 12 Under 35 8 35-39 3 40 and over 1 (Born in U.K. or in Republic of Ireland, 12)	41 (Born in U.K. or in Republic of Ireland, 22)	21 (Born in U.K. or in Republic of Ireland, 10)	2	4
E.N.T. surgery	Total 48 Under 35 2 35-39 5 40-49 19 50-59 13 60-64 9 65 and over —	1	2	Total 7 Under 35 2 35-39 3 40 and over 2 (Born in U.K. or in Republic of Ireland, 5)	22 (Born in U.K. or in Republic of Ireland, 15)	7 (Born in U.K. or in Republic of Ireland, 2)	2-3	2-3
Anaesthetics	Total 138 Under 35 9 35-39 29 40-49 54 50-59 39 60-64 5 65 and over 2	17	9	Total 21 Under 35 13 35-39 7 40 and over 1 (Born in U.K. or in Republic of Ireland, 20)	66 (Born in U.K. or in Republic of Ireland, 59)	42 (Born in U.K. or in Republic of Ireland, 32)	5	6
Ophthalmology	Total 47 Under 35 4 35-39 6 40-49 21 50-59 14 60-64 1 65 and over 1	14	10	Total 8 Under 35 6 35-39 2 40 and over — (Born in U.K. or in Republic of Ireland, 6)	17 (Born in U.K. or in Republic of Ireland, 11)	20 (Born in U.K. or in Republic of Ireland, 3)	1	2
Obstetrics and gynaecology	Total 99 Under 35 — 35-39 13 40-49 33 50-59 44 60-64 6 65 and over 3	2	6	Total 16 Under 35 7 35-39 7 40 and over 2 (Born in U.K. or in Republic of Ireland, 16)	53 (Born in U.K. or in Republic of Ireland, 41)	71 (Born in U.K. or in Republic of Ireland, 42)	5	5
Radiodiagnosis	Total 80 Under 35 1 35-39 12 40-49 37 50-59 23 60-64 6 65 and over 1	1	1	Total 12 Under 35 4 35-39 5 40 and over 3 (Born in U.K. or in Republic of Ireland, 12)	13 (Born in U.K. or in Republic of Ireland, 10)	10 (Born in U.K. or in Republic of Ireland, 6)	4	4
Radiotherapy	Total 22 Under 35 — 35-39 2 40-49 12 50-59 6 60-64 2 65 and over —	—	4	Total 6 Under 35 2 35-39 4 40 and over — (Born in U.K. or in Republic of Ireland, 6)	3 (Born in U.K. or in Republic of Ireland, 1)	6 (Born in U.K. or in Republic of Ireland, 2)	Less than 1	1-2
Mental illness, mental defi- ciency, child psychiatry	Total 129 Under 35 8 35-39 25 40-49 52 50-59 35 60-64 8 65 and over 1	20	36	Total 34 Under 35 18 35-39 10 40 and over 6 (Born in U.K. or in Republic of Ireland, 32)	94 (Born in U.K. or in Republic of Ireland, 59)	37 (Born in U.K. or in Republic of Ireland, 30)	8	9
Laboratory medicine (3)	Total 150 Under 35 8 35-39 28 40-49 56 50-59 46 60-64 8 65 and over 4	12	7	Total 39 Under 35 20 35-39 15 40 and over 4 (Born in U.K. or in Republic of Ireland, 37)	54 (Born in U.K. or in Republic of Ireland, 50)	21 (Born in U.K. or in Republic of Ireland, 17)	8	10

¹ General medicine includes cardiology, physical medicine, geriatrics, social medicine, homeopathy, rheumatic diseases, clinical physiology, electrotherapy, and tropical diseases. ² General surgery includes surgical science and casualty. ³ Laboratory medicine includes pathology, biochemistry, bacteriology, blood transfusion, haematology, morbid anatomy, and neuro-pathology.

TABLE II.—General Practitioners in Scotland at 1 October 1966

Principal:	Assistants	Trainee Assistants	Principal Posts Falling Vacant Annually	Minimum Increase in Number of Principals Needed to Prevent Growth of List Sizes Annually	Annual Rate of Principal Appointments Required
Total 2,595 Under 35 336 35-39 402 40-49 938 50-59 599 60-64 145 65 and over 175	80	33	80	10	90

Private Practice Committee

The Committee deplored the lack of active support given by the Association to its official policy to promote private practice. It also decided to request the Council to implement its undertaking to "do all in its power" to support Independent Medical Services Limited.

The Private Practice Committee held its first meeting of the session on 27 September. Dr. I. M. JONES was unanimously re-elected chairman, and Dr. J. E. MILLER re-elected vice-chairman.

The CHAIRMAN welcomed Dr. J. P. Grier and Dr. P. G. Jones as new members of the Committee, and he paid tribute to the retiring members, Drs. R. Green, R. D. Summers, R. Hale-White, and W. B. Adam.

Charges for Services

The Committee considered the following resolution of Council at the request of the Organization Committee: "That all Association committees be invited to consider the question of charges for services, if any, in their respective fields and to make recommendations."

Dr. J. E. MILLER thought the resolution must mean that if any project initiated by the Private Practice Committee attracted the interest of non-members of the Association consideration should be given to charging those of them who availed themselves of any benefits resulting from the project. Dr. Miller said he felt strongly about non-members benefiting from the services of the Association for which members paid handsomely. He pointed out that non-members had benefited without charge from the B.M.A.'s work in assisting doctors with car parking, particularly in the London area. The idea of making a charge might be extended in that connexion, said Dr. Miller.

Dr. G. R. SMITH suggested that the legal position should be investigated, and the Committee agreed to seek guidance on the matter from the Association's solicitor.

Road Traffic Subcommittee

In presenting the report of the Committee's Road Traffic Subcommittee (formerly the Car Parking Subcommittee), Dr. W. A. H. STEVENSON said that he would welcome closer liaison between the Inner London Local Medical Committee and the Subcommittee on the matter of car parking.

He reported that arrangements had been made for the supply of 2,000 self-adhesive signs bearing the words in fluorescent red: "Doctor—Emergency Duty. Issued by the British Medical Association." It was recommended that the signs should be sold to members of the Association at 2s. each and to non-members at 10s. each, including postage.

The recommendation was adopted.

Referring to the supply of 2,000 self-adhesive plastic car badges with white insert cards, the CHAIRMAN asked the Committee to consider a suggestion by Dr. A. N. Mathias that from the earliest possible date the fee for the provision of the special parking badge for non-members should be at least two guineas. The original recommendation of the Private Practice Committee had been that the badges should be sold to members of the Association for 7s. 6d. each, including postage, and at 10s. each to non-members.

The Council had adopted the recommendation, with the substitution of £1 for 10s.

On the motion of Dr. G. R. SMITH, duly seconded, the Committee agreed to recommend to the Council that the charge for the badge to non-members should be £2, including postage.

Fees

The Committee considered a proposal from the North of England Branch Council that the scale of recommended fees for certificates and reports provided outside the Health Service should be printed on a card which doctors could keep readily available.

The CHAIRMAN reminded the Committee that when it considered the matter in January it had decided to take no action. It had always been the policy of the Association, he said, that a fee charged for any service to a patient was a matter for arrangement between the patient and the doctor.

Dr. MILLER pointed out that the fees concerned were recommended for the guidance of doctors and were not statutorily laid down. Some local medical committees had actually printed a small card setting out recommended fees.

The Committee rejected the Branch Council's proposal.

Notification by Police

The Committee agreed that a letter should be sent to all chief constables requesting that when the police were called after the discovery of a dead person they should notify the person's doctor as soon as practicable.

Alternative Medical Services

The CHAIRMAN drew attention to the following resolution of the A.R.M., 1967: "That this Meeting requests Council to introduce an item-of-service insurance scheme for private practice. Such a scheme of insurance for private practice must include medical care within hospitals and nursing homes and should not be restricted to specialists."

The Chairman, speaking also as Chairman of the Committee of Management of Independent Medical Services Ltd., said that I.M.S. had decided some time ago that at the earliest date it would try to evolve a partial reimbursement scheme. The scheme was now almost complete, and full details would be available for the Committee at its next meeting.

Dr. P. G. JONES said that in his view the Association had failed lamentably in its support of Independent Medical Services. The schemes produced by I.M.S. were practical and workmanlike, but he had yet to see it fully advertised, for instance, in the *British Medical Journal*.

Dr. S. F. LOGAN DAHNE agreed. There had been powerful opposition to I.M.S. and not enough active support, he said.

Dr. M. LANDAU said there had been publicity for I.M.S. The Chairman had addressed B.M.A. Branch and Division meetings up and down the country, but if doctors

did not turn up in any numbers to those meetings what could be done?

The CHAIRMAN said that he had attended many meetings, and, though I.M.S. was officially supported by the Association, it had been rare for another member of the Council to be present. "I am told that many members of Council do not support it," he continued, "but when it was put to the vote in Council only two members voted against it."

Dr. LANDAU suggested that I.M.S. might have come into being at an unfortunate moment for it, in that doctors were now doing better out of the N.H.S. than they had been a few years ago.

Dr. H. FIDLER said that it was up to the Council of the Association to support the I.M.S. scheme.

Sponsored by B.M.A.

Dr. MILLER said that Independent Medical Services had been sponsored by the Association, and on repeated occasions the Council and those in positions of responsibility had paid lip service to their support of it. It had, however, been nothing more than lip service. "The least we are entitled to expect is that the force and the power of the B.M.A. will be behind the operation of I.M.S." Dr. Miller said that he thought this was the opportunity for the Committee—which, by definition, encouraged private practice—to go on record as saying that it was dissatisfied, disappointed, and resentful of the negative attitude of those in a position to assist and encourage I.M.S. If as a result of that negative attitude I.M.S. failed, he said, then the blame could be laid fairly and squarely on those who were responsible for frustrating its efforts at the very beginning.

Dr. P. G. JONES suggested that a letter should be sent to every member of the Association setting out the policy of the Association towards Independent Medical Services. Dr. G. R. SMITH said that the Association was not critical enough of the National Health Service. There was a feeling in the periphery that the B.M.A. had one foot over the Ministry fence. The General Practitioners Association and the Medical Practitioners Union had gained prominence because they had voiced strong criticism. Dr. Smith suggested that I.M.S. ought to look into the N.H.S. doctors' contract, to point out where it was at fault, and to indicate its deficiencies. The profession must feel that I.M.S. could offer members something.

Dr. MILLER, in reply to Dr. Smith, pointed out that the General Medical Services Committee was extremely critical of Ministry policy. On occasions a stronger line might have been taken, he said, but it should not be thought that the G.M.S. Committee was bending over backwards to fall into line with Ministry policy.

Dr. LOGAN DAHNE proposed that the Committee should deplore the lack of active support given to the policy of the Association for the promotion of private practice, and that it should request the Council to implement its past undertaking to do all in its

power to carry out Association policy in support of Independent Medical Services.

The Committee supported this proposal.

Road Accidents

The Committee agreed that renewed representations should be made to the Ministry of Transport for payment of an adequate fee for emergency treatment under the Road Traffic Act, and that steps should be taken to ensure that the fee was paid to the doctor first attending the patient whether it was at the scene of the accident or at the hospital.

Discount Service

As foreshadowed in the Supplementary Annual Report of the Council (*Supplement*,

1 July, p. 13), discount trading facilities are to be provided for doctors by Independent Medical Services Ltd. The Annual Representative Meeting, 1967, gave its approval to this proposal when it accepted the report of the Private Practice Committee (*Supplement*, 22 July, p. 94).

The service will operate as the Facilities Division of Independent Medical Services Ltd., and it will arrange the supply at a discount of a wide range of goods, professional equipment, car purchase, car hire, purchase, and credit facilities. It is stated that further facilities will be added later. The service will be available exclusively to members of the B.M.A., to doctors who have subscribed to the funds of I.M.S., and to medical students belonging to the B.M.S.A. There is no entrance or membership fee.

Information may be obtained from the Manager, Facilities Division, Independent Medical Services Ltd., Tavistock House South, Tavistock Square, London W.C.1.

H.M. Forces

ROYAL NAVY

ROYAL NAVAL RESERVE

Surgeon Lieutenant-Commander C. Fleming has re-entered into the Active List of the permanent R.N.R.

Surgeon Lieutenant M. W. G. Wren to be Surgeon Lieutenant-Commander.

ARMY

Major-General M. H. P. Sayers, O.B.E., Q.H.P., late R.A.M.C., has retired on retired pay.

Brigadier R. A. Smart, C.B.E., late R.A.M.C., to be Major-General.

Colonel H. C. Jeffrey, late R.A.M.C., to be Brigadier.

HOUSEHOLD CAVALRY, ROYAL HORSE GUARDS

Surgeon Captain J. P. A. Page to be Surgeon Major.

ROYAL ARMY MEDICAL CORPS

Majors J. McEwan and T. D. Jones to be Lieutenant-Colonels.

Association Notices

Diary of Central Meetings

OCTOBER

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| 9 Mon. | Armed Forces Committee, 2 p.m. |
| 10 Tues. | G.M.S. Advisory Committee on Vocational Training and Continuing Education, 2 p.m. |
| 11 Wed. | Public Health Committee, 10 a.m. |
| 11 Wed. | Journal Committee, 10.30 a.m. |
| 11 Wed. | Road Traffic Act Subcommittee (Private Practice Committee), 10.30 a.m. |
| 11 Wed. | Film Committee, 2 p.m. |
| 12 Thurs. | G.M.S. Committee (at B.M.A. Scottish House, 7 Drumsheugh Gardens, Edinburgh), 10.30 a.m. |
| 13 Fri. | Public Health Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m. |
| 17 Tues. | Tuberculosis and Diseases of the Chest Group Committee, 2 p.m. |
| 19 Thurs. | Finance Committee, 2 p.m. |
| 19 Thurs. | Joint Consultants Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 10.15 a.m., followed by meeting with Scottish Home and Health Department at St. Andrew's House, 2.30 p.m. |
| 20 Fri. | Central Committee for Hospital Medical Services, 10.30 a.m. |
| 21 Sat. | Central Committee for Hospital Medical Services, 10 a.m. |
| 24 Tues. | Joint Consultants Committee (at Royal College of Physicians and Surgeons of Glasgow, 242 St. Vincent Street, Glasgow), 10 a.m. |
| 25 Wed. | Council, 10 a.m. |
| 26 Thurs. | S.H.M.O. Group Council, 2 p.m. |

NOVEMBER

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| 1 Wed. | Annual Meetings Committee, 12 noon. |
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DECEMBER

- | | |
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| 13 Wed. | Journal Committee, 2 p.m. |
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Branch and Division Meetings to be Held

Honorary Secretaries of Branches and Divisions are asked to send notices of meetings to the Editor at least 14 days before they are to be held.

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

BIRKENHEAD AND WIRRAL DIVISION.—At Larch House, Clatterbridge Hospital, Tuesday, 10 October, 8 for 8.30 p.m., Dr. R. Winston Evans: "Recent Advances in Cancer Research."

BRADFORD DIVISION.—At Bradford Royal Infirmary, Wednesday, 11 October, 8.15 p.m., Dr. J. Henry: "The Swan Song of an A.F.D."

BRIGHTON AND MID-SUSSEX DIVISION.—At Sussex Postgraduate Medical Centre, Brighton General Hospital, Tuesday, 10 October, 8.30 p.m., annual general meeting.

BROMLEY DIVISION.—At Elmswood Recreation Hall, Farnborough Hospital, Wednesday, 11 October, 8.15 for 8.30 p.m., Dr. G. F. Vaughan: "Child Psychiatry." Dr. C. H. C. Upjohn will open the discussion.

BUCKINGHAMSHIRE DIVISION.—At Archway Unit, Stoke Mandeville Hospital, Friday, 13 October, 8.15 p.m., annual cheese and wine party. Ladies are invited.●

CAMDEN DIVISION.—At B.M.A. House (Room "D"), London W.C., Tuesday, 10 October, 8 p.m., jointly with City and St. Marylebone Divisions, symposium on "Drug Addiction." Speakers, Dr. A. J. Hawes, Dr. W. Lindsey Neustatter, Dr. D. Stafford-Clark, Mr. H. B. Spears (Home Office). Guests are invited.

CITY OF EDINBURGH DIVISION.—At 7 Drumsheugh Gardens, Wednesday, 11 October, 8.15 p.m., "Young Doctors' Night." Guests are invited.

COVENTRY DIVISION.—(1) At Warwick Road Congregational Church, Sunday, 15 October, 6.30 p.m., annual church service. (2) At Hotel Leofric, Thursday, 12 October annual dinner. Guest of honour, Reverend Lawrence Jackson.

DONCASTER DIVISION.—At Rogerthorpe Manor Country Club, Friday, 13 October, 8 for 8.30 p.m., ladies' night dinner and dance.●

DORSET DIVISION.—At Ballroom, Harrison Hospital, Dorchester, Friday, 13 October, 8 for 8.30 p.m., annual dinner. Guest of honour, Dr. J. Revans.●

EAST YORKSHIRE BRANCH.—At Hull School of Nursing, Hull Royal Infirmary, Anlaby Road, Wednesday, 11 October, 8.30 p.m., Mr. W. W. Slack: "Surgery of Non-neoplastic Conditions of the Colon."

FINCHLEY DIVISION.—At Board Room, Finchley Memorial Hospital, Tuesday, 10 October, 8.30 p.m., Dr. A. M. Ramsay: "The Expanding Field of Infectious Diseases."

GLASGOW DIVISION.—At Livingstone Tower, Strathclyde University, Tuesday, 10 October, 8 for 8.30 p.m., joint meeting with Glasgow and West of Scotland Branch of Pharmaceutical Society of Great Britain, Mr. C. G. Jeffery (Home Office): "The Drugs Problem."

GLOUCESTERSHIRE BRANCH.—At Carlton Hotel, Cheltenham, Thursday, 12 October, 6.30 p.m., presidential address by Dr. K. M. Tomlinson: "A Country Tomb." Followed by dinner.

GREENWICH AND DEPTFORD DIVISION.—At 25 Manor Way, Blackheath, Wednesday, 11 October, 8.30 p.m., wine and cheese party for members and wives.●

HUNTINGDON AND PETERBOROUGH DIVISION.—At Nurses' Home, Peterborough Memorial Hospital, Wednesday, 11 October, 8.30 p.m., B.M.A. lecture by Dr. J. A. Clarke: "Drug Addiction."

KINGSTON-UPON-THAMES DIVISION.—At Outpatients Department, Kingston Hospital, Tuesday, 10 October, 7.30 p.m., clinical meeting.

LEEDS DIVISION.—At Parkway Hotel, Thursday, 12 October, 7.45 for 8.15 p.m., annual dinner and dance.

MEDWAY AND GRAVESEND DIVISION.—At Boardroom, St. Bartholomew's Hospital, Rochester, Sunday, 8 October, 10.30 a.m., annual general meeting.

MERSEYSIDE BRANCH.—Wednesday, 11 October, annual general meeting.

NUNEATON DIVISION.—At Chase Hotel, Tuesday, 10 October, 8 for 8.30 p.m., annual valedictory dinner and ladies' night, Professor A. P. Griffiths: "The Incipient Drug Problem."●

PLYMOUTH DIVISION.—Wednesday, 11 October, 6 p.m., visit to new District General Hospital Site at Derriford.●

RENFREWSHIRE DIVISION.—At Kilmacolm Hydro Hotel, Friday, 13 October, 7.15 for 8.15 p.m., annual dinner and dance.●

SOUTH-EAST ESSEX DIVISION.—Tuesday, 10 October, visit to cosmetics factory of Messrs. Yardley. Meet at main gates, 2.10 p.m. Ladies are invited.●

SOUTH SHIELDS DIVISION.—At Nurses Lecture Unit, Ingham Infirmary, South Shields, Wednesday, 11 October, 8.30 p.m., B.M.A. lecture by Dr. J. Fry: "Medical Care Behind the Iron and Golden Curtains."

SUTTON DIVISION.—At Worcester Hotel, Worcester Park, Wednesday, 11 October, 7.30 for 8 p.m., annual dinner and dance.●

WORCESTER AND BROMSGROVE DIVISION.—At Mitre Oak Hotel, Crossway Green, near Hartlebury, Thursday, 12 October, 8.30 p.m., wine tasting and buffet supper.●

British Medical Journal Supplement

LONDON SATURDAY 14 OCTOBER 1967

CONTENTS

Scottish Committee for Hospital Medical Services	11	Full-time Medical Teachers and Research Workers	15
Type D General Practice Allowances	12	Hospitality	15
Hospital Junior Staffs Group Council (Scotland)	13	"Mediflash"	15
Occupational Health Committee	13	Central Ethical Committee	15
Planning Unit's Progress	14	Association Notices	16

Scottish Committee for Hospital Medical Services

The Scottish Committee for Hospital Medical Services (formerly the Central Consultants and Specialists Committee (Scotland)) held its first meeting on 25 September at B.M.A. House in Edinburgh. Mr. N. G. C. HENDRY and Dr. A. ALLISON were appointed Chairman and Deputy Chairman respectively.

Dr. J. G. M. HAMILTON was reappointed Treasurer of the Central Consultants and Specialists Committee (Scotland) Fund, and it was agreed that consideration should be given to renaming this fund so that it would correspond with the new name of the Committee.

Outpatient Prescriptions

Further consideration was given to the question of prescribing for hospital outpatients, and to the use for this purpose of a form (Form R.B.P.) intended for prescribing drugs unobtainable in the hospital pharmacy for outpatients not being referred to their general practitioners. Two regions thought that an attempt was being made to reduce the use of this form, and the Committee had regarded this as a possible interference with a doctor's clinical freedom.

The Committee agreed to make the following three comments on the matter through the Joint Consultants Committee (Scotland) to the Scottish Home and Health Department: (1) that this valuable facility should not be withdrawn; (2) that the profession could accept only with reservations the fact that the charge for the drugs so prescribed had to go on the hospital budget; and (3) that if there appeared to be any interference with the freedom of hospital doctors to prescribe the matter would be brought up with the Department again.

Dr. A. J. SANGSTER said he believed that the cost of prescriptions on Form R.B.P. was being charged to boards of management, and as a result they had not enough money to purchase essential equipment.

It was agreed to ask secretaries of regional committees for hospital medical services to seek definite information on this point.

The Committee received a report that a Scottish hospital memorandum was being prepared on the recognition of overseas and of general-practitioner service in placing newly appointed hospital doctors on an appropriate salary scale. It was also reported that there was no further information about proleptic appointments.

Negotiating Machinery

The Committee considered a paper from the chairman's subcommittee on the new negotiating machinery for hospital doctors in the United Kingdom. The subcommittee suggested that, with the agreement of the Scottish Home and Health Department and of the Joint Consultants Committee (Scotland), matters which in England and Wales came within the remit of the negotiating subcommittee of the Central Committee for Hospital Medical Services should be referred directly to the Department by the Scottish Committee for Hospital Medical Services. The matter could be reconsidered at the end of a year, when it would be possible to assess the working of the negotiating subcommittee in London.

The CHAIRMAN questioned whether it was possible at present to identify enough items relating particularly to Scotland and requiring special reference to Scotland for discussion and decision which at the same time were matters other than those which were the concern of the Royal Colleges. He understood that the Scottish Home and Health Department would meet whatever arrangements the profession chose to make.

Dr. HAMILTON, Chairman of the Joint Consultants Committee (Scotland), pointed out that other constituent members of his Committee would have to be consulted before any changes were made. He suggested that it would be wise to wait to see how matters progressed in England under the Joint Consultants Committee (U.K.) with its new terms of reference, and with the negotiating subcommittee of the Central Committee for Hospital Medical Services.

The Committee agreed with Dr. Hamilton, and decided to reconsider the matter again in a year's time.

The Committee was informed that the Scottish Panel of the "Group of Nine" (the committee appointed in December 1966 by the Joint Consultants Committee (U.K.) to conduct negotiations with the Ministry of Health on the memorandum "Current Problems of Hospital Medical Staff" (*Supplement*, 13 May, p. 93)) had agreed on the principle of an "acting-up" allowance in circumstances such as those which had occurred in Aberdeen, where senior registrars were seconded from Aberdeen to undertake consultant work in Orkney and Shetland in the absence of consultants. The amount of money to be paid in such cases would be a matter for decision by the Review Body.

It was also reported that, after discussions with the Home and Health Department, the Joint Consultants Committee (Scotland) now hoped that arrangements could be made for a special responsibility payment to be paid to general practitioners who undertook unsupervised specialist work in remote hospitals. The General Medical Services Committee (Scotland) proposed to put its views on this matter to the Department in support of the action already taken by the Joint Consultants Committee (Scotland).

Staffing of Departments

Dr. A. ALLISON reported that a meeting had taken place in Glasgow with the Western Regional Hospital Board to discuss the problems that were being encountered in the establishment of and making appointments to the chest service in the region.

The regional board had not disclosed its plans for manning the chest service, but it was already advertising posts for physicians with an interest in chest diseases. Some senior S.H.M.O.s who had been engaged in the work for years thought that the practice of advertising the posts seriously interfered with their chances of being appointed. The Western Regional Committee for Hospital Medical Services had asked the Board that the S.H.M.O.s with special experience should have that experience taken into account in making the appointments.

Dr. W. F. TYRRELL expressed the concern of S.H.M.O.s in this matter. The Committee agreed, however, to wait to see how the appointments that were now being advertised were filled.

The Committee was informed that a paper emphasizing the deficiencies in the staffing of radiological departments in district hospitals had been presented to the Home and Health Department,

which had referred it to the Advisory Committee on Consultant Establishments, and had also agreed to discuss it with senior administrative medical officers. Dr. P. AITKEN welcomed this information and hoped that the question of staffing in diagnostic radiology would continue to be kept under review.

Anaesthetic Services

The CHAIRMAN congratulated Professor A. C. Forrester, Chairman of the Anaesthetic Services Subcommittee, on his appointment to the Chair in Anaesthetics at Glasgow University.

Professor FORRESTER said that his subcommittee had decided that it would be necessary to reconsider its memorandum on senior registrars in anaesthesia in Scotland in view of the recent changes in the consultant establishment in the specialty. In the past year 22 new anaesthetic consultant posts had been filled; 12 of them had been recommended in the Wright Report and 10 more posts had been added.

The subcommittee had welcomed the Report on Dental Anaesthesia by the joint subcommittee of the Standing Medical and Dental Advisory Committee of the Central Health Services Council. Anaesthetists looked forward to the time when dental anaesthetics would be given by specialist anaesthetists, said Professor Forrester. He agreed that the training of doctors in dental anaesthesia could be improved. A start had been made in Glasgow, where registrars now worked in dental departments, and it was hoped that this instruction would be extended to other doctors, in due course.

A further point made by Professor Forrester was that there had been no reference to training and education in anaesthetics in the report of the Working Party on Postgraduate Medical Education. He said that anaesthetics was now one of the largest specialties, and this lack of reference to training in anaesthetics had been a bad omission in an otherwise valuable document.

Medical Assistant Posts

The Committee thought that from reports from regions it appeared that the system of consultation with the profession before the institution of medical assistant posts was reasonably satisfactory.

In answer to a question, Dr. ALLISON said that in the Western Region local views were obtained when the regional committee for hospital medical services received a request for an opinion from the regional hospital board. Dr. SANGSTER asked whether local opinion about the proposed new posts had been conveyed to the advisory committee on consultant establishments. The CHAIRMAN said he thought this always happened, and that further steps were being taken to ensure that the advisory committee had the fullest information. Replying to Dr. G. C. TIMBURY, the CHAIRMAN said that information was being collected by the advisory committee about the filling of medical assistant posts throughout Scotland.

Terms of Service

The Committee next discussed medical examinations of prospective hospital staff, which were usually carried out by hospital

junior doctors. It was queried whether this work was included in the doctors' contract, and what was the precise interpretation of the terms of service in the contract.

Dr. S. J. HADFIELD, Scottish Secretary, informed the Committee that the imposition of this extra work was causing growing concern among hospital junior staff. It had been reported to the Hospital Junior Staffs Group Council (Scotland) recently that the work seemed to be continually increasing. It had also been said that the results of the examinations were not always taken into account by those who engaged the staff.

Professor E. M. MCGIRR referred to the possible introduction in the near future of a hospital occupational health service, and he thought this might help to solve the problem. Dr. HAMILTON agreed that this work represented a continual and unreasonable load over and above the ordinary clinical work of the junior staff.

The Committee agreed to seek evidence from the hospital junior staff regional groups on this matter.

It was reported to the Committee that the Scottish hospital memoranda on study leave, sick leave allowances, removal expenses, and minimum time off duty for junior and intermediate grades of staff had been issued by the Home and Health Department after consultation with the Joint Consultants Committee (Scotland).

Referring to the circular relating to minimum time off duty, Dr. SANGSTER pointed out that even if there were more housemen available there was no extra money for them, nor was there any extra money for the additional accommodation which would be required to house them.

The CHAIRMAN said that in existing circumstances it seemed there was no question of employing extra staff. It was more likely that the services to the public would have to be curtailed if it was not possible to reorganize them within the present budget and with the present staff.

Research and Intelligence Unit

Dr. M. A. HEASMAN, of the research and intelligence unit of the Scottish Home and Health Department, attended the Committee by invitation and spoke on the unit's work. It was set up two years ago with four main functions: (1) to collect information on the working of the Scottish health services; (2) to circulate this information; (3) to engage in research into the working of the health services; and (4) to stimulate others to undertake research. Since that time a fifth function had been added in that the unit had become responsible for the development of computer policy.

Dr. Heasman said that the main points on which data were obtained were on inpatient and outpatient statistics, matters relating to hospital waiting-lists, and information on the discharge of patients from hospital. He said that the material available was not used outside the Health Department as much as it should be. Most of it could be obtained by clinicians for the asking. In difficult cases a clinician could visit the unit and extract the information he wanted.

Dr. Heasman mentioned the Scottish Health Service statistics which were published annually. He said that his unit proposed in future to send to hospitals a summary of

the data on their work. Such data tended to be an indigestible mass, but it was hoped that the data for 1967 would be produced in a more usable form, and would give individual consultants some information on their work and the work of their specialty. The sort of information that would be available would be the age distribution of patients, the length of stay in hospital, and when admitted and when discharged. National averages would also be provided.

Another activity of the unit was the financing of research. Dr. Heasman regretted that so far there had been few applications for financial help from non-university clinicians.

In reply to a question by Dr. P. AITKEN about the statistics on services such as radiology, Dr. HEASMAN said the unit's work did not include this yet, because it was dealing only with clinical data. Dr. A. A. BROWN asked for more information about the distribution of statistical reports on the work of consultants, and Dr. HEASMAN said that in addition to the copy sent to the consultant a confidential copy would be sent to the senior administrative medical officer. What the unit was providing was patient-care evaluation for discussion within the profession.

The CHAIRMAN thanked Dr. Heasman for attending the meeting, and for his helpful exposition of the work of his department.

Increased Junior Representation

Representatives to other committees and the members of subcommittees were appointed, and a recommendation of the chairman's subcommittee that the representation of hospital junior staff on the Scottish Committee for Hospital Medical Services should be increased from two to three was adopted.

Type D General Practice Allowances

The Ministry of Health has introduced a new scheme of special allowances known as "Type D" initial practice allowances (*Supplement*, 23 September, p. 136). The details are set out in a circular (H.C.N. 631) to general practitioners. Special rates of initial practice allowance will be offered to doctors with the necessary qualities and experience who are willing to enter practice in new towns and redevelopment areas concurrently with the arrival of the new residents. The allowance will ensure that the doctors' earnings will remain at the same level as in their previous post, subject to a net maximum of £4,000 a year.

The Type D allowance will continue for a maximum of three years or until the doctor takes a partner, whichever is the sooner. If a partner is appointed a "Type C" initial practice allowance (designed for doctors who join in a partnership) will ordinarily be available, provided the area is a designated one. Doctors appointed to practices which qualify for the Type D allowance will normally be expected to have had about ten years' experience, including two years in hospital appointments, five years in a busy general practice, and experience in obstetrics.

Hospital Junior Staffs Group Council (Scotland)

The first meeting of the session of the Hospital Junior Staffs Group Council (Scotland) was held in Edinburgh on 19 September. Dr. W. P. U. KENNEDY was appointed Chairman, and Dr. G. M. McANDREW Deputy Chairman.

The CHAIRMAN began by making a special appeal for unity among hospital junior staff, and he asked members of the Group Council to encourage their colleagues to support the leadership of the Hospital Junior Staffs Group in London.

Senior Registrars

The Group Council was informed that, with the agreement of the Joint Consultants Committee (Scotland), the question of an "acting-up" allowance for senior registrars required to undertake consultant duties in Orkney and Shetland had been discussed with the Home and Health Department and referred to the Scottish Panel of the "Group of Nine." The Scottish Panel had agreed on the principle of additional payments for these duties, but it was reported that the amount of the payment was a matter for decision by the Review Body.

Dr. R. N. M. MACSWEEN asked that the existing arrangements for the appointment of honorary senior registrars should be changed. Dr. B. GRODEN said that registrars in the National Health Service thought that lecturers who were made honorary senior registrars blocked the establishments, and that there should be more control over the number of these appointments.

The Group Council agreed that it would like to see the document on senior registrar and consultant establishments, which was being prepared by the Subcommittee on Senior Registrars and Consultant Establishments, before it was presented to the Scottish Committee for Hospital Medical Services.

Disciplinary Procedures

The Group Council received a report that no further progress had been made on the question of disciplinary procedures which were under revision in the General Whitley

Council. The matter was held up until a report was available from the Ministry of Labour's Advisory Committee on Disciplinary Procedures and Appeals. Members of the Group Council thought that it was not enough that doctors should be included in any general machinery which was decided upon. Hospital doctors had to adhere to an ethical code and were subject to special discipline, and it was essential, especially since it was thought that distinctions were difficult to make between personal misconduct and professional misconduct, that there should be one disciplinary procedure for doctors to deal with all cases of misconduct.

Dining Accommodation

The Group Council then discussed the question of dining accommodation. Members stated that there was no consultation with hospital junior staff when changes were to be made in the arrangements for residents, and it was believed that often there was no consultation with the senior staff either.

The Group Council thought that regional group committees should agitate for consultation in this matter, and it was resolved to request the Scottish Committee for Hospital Medical Services to ask the Joint Consultants Committee (Scotland) to express the dissatisfaction of hospital junior doctors in this matter to the Scottish Home and Health Department, and to stress the need for consultation with the junior staff when any changes were made in existing hospitals and when any plans were being formulated for new hospitals.

Scottish Hospital Memoranda

A report was received of the progress achieved by the Group of Nine and by the Scottish Panel in the negotiations between the Health Departments and N.H.S. hospital doctors and dentists, as set out in the first and second joint reports on the negotiations (*Supplement*, 27 May, p. 135, and 19 August, p. 119).

Reference was made to the Scottish hospital memoranda which had been issued on sick-

leave allowances, professional and study leave, off-duty time, removal expenses, and the provision of telephones for hospital medical staff.

Some speakers said they realized that there would be difficulties in many places in fulfilling the requirements of the circular dealing with minimum time off duty. Dr. MACSWEEN said that implementation of the circular on study leave was bound to be held up by lack of funds, because no extra money was being provided to pay extra staff, even if they existed.

It was agreed to ask the Scottish Home and Health Department what money was available for implementing the proposals in the hospital memorandum on minimum off-duty time.

It was reported that a hospital memorandum was being prepared on the question of taking into account overseas service by a candidate for a hospital post.

Several members of the Group Council expressed concern about the burden placed on hospital junior staff when they had to examine hospital employees and prospective employees for fitness for duty. The considerable turnover of hospital staff meant increasing work for hospital junior doctors, particularly registrars, who found it difficult to carry out this commitment in addition to their clinical work.

Committee Representation

The Chairman and the Deputy Chairman were appointed to represent the Group Council on the Scottish Committee for Hospital Medical Services, and Dr. Groden was nominated as the third representative, if, as was expected, the Scottish Committee for Hospital Medical Services decided that in future the hospital junior staff representation on that committee should number three representatives.

Dr. McAndrew and Dr. Groden were appointed to the Executive Committee of the Hospital Junior Staffs Group Council (U.K.), and Dr. Kennedy and Dr. A. Auld were appointed to serve on the Scottish Council of the Association.

Occupational Health Committee

The Occupational Health Committee held its first meeting of the session on 4 October. Dr. R. E. W. FISHER was re-elected to the chair.

The Committee considered the position of its Remuneration Subcommittee and of its Negotiating Panel.

The CHAIRMAN pointed out that in the past the subcommittee had advised the Committee on levels of remuneration in general, while the panel had acted as a body from which negotiators could be drawn.

It was proposed that there should be only one subcommittee, which would combine the functions of the remuneration subcommittee and the negotiating panel.

Dr. R. L. LUFFINGHAM said that the functions of the subcommittee and of the panel had been different. The subcommittee had been concerned with setting standards of remuneration, whereas the panel had had to negotiate on a more practical level.

The Committee agreed to the proposal that there should be one subcommittee combining the functions of the Remuneration Subcommittee and the Negotiating Panel.

Charges for Services

Dr. I. T. FIELD, Assistant Secretary, said that all committees had been requested by

the Organization Committee to consider making a charge for services given to non-members.

Mr. J. C. McMASTER thought that advice given to non-members in response to their requests should be charged for.

The CHAIRMAN said that in giving advice about, say, remuneration the B.M.A. was not only providing a service for the doctor or the employer but also a service for the profession, because it was in the interests of the profession that a doctor working in industry should be properly paid, and that the service should be properly run. The Chairman thought it would be difficult to separate the two functions, because one of the B.M.A.'s

responsibilities was to ensure that the health services were properly administered. He deprecated the idea of the Secretariat acting as a consultant body that charged fees.

Mr. McMASTER said that there was a strong feeling within the B.M.A. that services to non-members should be reduced. The Association needed to increase its membership, but if doctors could get its services free, they would not easily be persuaded to become members. The B.M.A. was financed from members' subscriptions. He agreed that the Secretariat should not refuse to give advice, but if this was required by non-members then they should be prepared to pay a small fee towards the cost.

Dr. FIELD said that it might be possible to charge non-members for copies of the booklet *The Doctor in Industry*, which contained the B.M.A.'s recommendations on the terms and conditions of service of industrial medical officers. But the booklet had always been sent to employers-free of charge, on the ground that the Association was providing a service to the whole of industrial medicine. Dr. Field thought that it would be difficult for the B.M.A. to start charging employers for providing them with information on its recommendations on different matters.

Dr. F. H. TYRER said that when a lay body or lay person sought advice no fee should be charged, but doctors who were non-members of the Association should be charged.

The matter was referred to the Committee's Planning Subcommittee for consideration.

Conference of Advisory Councils

The Committee received a report that the conference of Advisory Councils on Occupational Health in 1968 would be on 6 March. The chairman of the conference would be Mr. W. T. Parsons, of Brighton, and the subject for discussion would be "The Scope

and Functions of an Occupational Health Service."

Dr. J. A. SMILEY wondered if these conferences served any real purpose. Dr. TYRER thought they did. But it was unfortunate, he said, that there were still only a handful of advisory councils in the country. He would like to see three times as many. He agreed that the time might come when the question would have to be asked whether the value of the conference was worth what it cost the Association to hold it.

Dr. FIELD said the real question was whether the advisory councils were of any use. He believed that the conference was the one thing which made the councils feel it was worth while continuing. Without this many would fold up.

Dr. A. REEVES said that in the West Riding of Yorkshire the conference was an important matter. If expense was the difficulty he believed that advisory councils would be prepared to share the cost rather than lose the annual conference.

The Committee agreed to discuss the matter again at its next meeting.

Vibration Syndrome

The CHAIRMAN presented the report of a subcommittee which had been considering the vibration syndrome. He said that there was now probably good reason for the vibration syndrome to be proscribed under the National Insurance (Industrial Injuries) Act of 1965.

The subcommittee recommended that the Ministry of Social Security should be informed of this opinion and that a short memorandum supporting this view should be submitted at the same time to the Ministry. The memorandum should include the following points:

(1) There was increasing evidence that the use of vibrating tools was likely to produce minor but uncomfortable disability due to

Raynaud's phenomenon and, less commonly, to affections of the bones, joints, muscles, and nerves of the hand, arm, and shoulder.

(2) The commonness of the condition had not been appreciated because many who suffered from it were able to continue working and accepted the discomfort as an inevitable concomitant of their work.

(3) Not enough was known about the incidence of the condition nor of its varying degrees of severity. It was understood that a research project had started, and it was to be hoped that the research would provide definitive answers to these questions.

(4) The existence of the condition was now so well attested and its specificity to a particular cause was so clear that there seemed to be little purpose in further delaying proscription.

Dr. TYRER asked whether there were clear diagnostic criteria, and the CHAIRMAN replied that, in the view of the experts who had been consulted, there were.

Dr. SMILEY said that two other committees had examined the vibration syndrome, and had decided there was no accepted specificity to a particular cause. Raynaud's phenomenon occurred quite frequently without any contact with vibrating tools.

Dr. TYRER said that to get a disease proscribed it was not essential that a specific cause for it should have to be proved. If persons suffering from this syndrome were granted benefits under the Industrial Injuries Act it would not cost much, because the numbers were so few.

The Subcommittee's report was approved, and it was decided to recommend to the Council that it should write on the lines of the report to the Industrial Injuries Advisory Council.

It was agreed to nominate a deputation to attend the Industrial Injuries Advisory Council to discuss the matter, should that body wish it.

Planning Unit's Progress

The Association's Planning Unit (*Supplement*, 2 September, p. 126), under its director, Professor Henry Miller, continues its work of defining, investigating, and reporting upon specific problems in the National Health Service through a number of working parties of experts.

Mr. Duncan Guthrie, Director of the National Fund for Research into Crippling Diseases, is chairman of the working party on mechanical aids for the disabled. Its remit covers an assessment of the nature and value of available appliances, mechanical aids, and architectural adaptations and their cost; an examination of arrangements whereby these can be provided from public funds; and a review of existing research facilities and proposals for their further development. The medical members of the working party are Dr. J. Agate, Mr. George Bonney, Dr. D. A. Brewerton, Mr. J. Chalmers, Dr. F. Cooksey, Dr. P. J. R. Nichols, Dr. J. J. Walsh, Wing Commander C. B. Wynn Parry, and Dr. G. Yates, together with Mr. A. K. Godden, Department of Engineering Science, University of Oxford, and Mr. A. Kennaway, consulting engineer, London. Dr. Catherine

Dennis is the Ministry of Health's observer.

Under the chairmanship of Dr. E. J. Moran Campbell, of the Royal Postgraduate Medical School, a working party has been established on intensive care units. One group of the working party is investigating and collecting information, and another group will make a critical review of the information. Members of the investigating group are: Drs. E. J. M. Campbell, D. Benazon, E. Sherwood Jones, G. T. Spencer, G. Ford (Ministry of Health), and Miss C. Willman, sister of an intensive-care ward. The membership of the review group is Mr. A. G. Cox, Dr. D. N. S. Kerr, Professor L. P. Le Quesne, Mr. Walpole S. Lewin, and Dr. B. L. Pentecost.

Primary Care

It is probable that a working party will be set up shortly to study the provision of primary medical care. A study group is advising the unit on the best method of investigating the future of primary medical care. Its membership includes Drs. D. Irvine,

G. Curtis Jenkins, R. Logan, G. Marsh, and I. R. McWhinney. The chairman is Mrs. Margot Jefferys, Director of the Social Research Unit, Bedford College, University of London.

The unit has sought advice from the Medical Research Council's computer centre on the possibility of initiating an investigation into computer science in relation to medicine. It will be decided shortly how the unit can best contribute in this field.

Each B.M.A. Branch and Division has been invited to nominate a "forward-looking young doctor" to act as an "unofficial liaison officer" with the Planning Unit. So far over 50 liaison officers have been nominated.

The members of the main Planning Unit are Professor Henry Miller (Director), Newcastle; Dr. John Bennett, Liverpool; Dr. Charles Fletcher, London; Dr. W. G. Harding, London; Miss Josephine Barnes, London; Mrs. Mary Adams (representing lay consumers); Dr. Donald Irvine, Ashington and Northumberland; Mr. Walpole S. Lewin, Cambridge; and Professor O. McGregor, Department of Social Studies, London University.

Full-time Medical Teachers and Research Workers

At its first meeting of the session the Full-time Medical Teachers and Research Workers Committee re-elected Dr. K. S. ZINNEMANN as its chairman and Dr. M. M. BULL as deputy chairman.

The CHAIRMAN welcomed Dr. E. C. Fox (Birmingham), Mr. H. Gordon (London), Dr. J. H. Walker (Newcastle), and Dr. R. S. Kirk (Manchester), deputizing for Dr. H. Fox, as new members of the Committee, and Dr. G. M. Williamson (Pfizer Ltd.), who was co-opted to represent research workers outside the Medical Research Council.

Representative Committees

Reporting on a meeting of the Central Committee for Hospital Medical Services, Professor IAN RANNIE referred to the constitution of the Joint Consultants Committee. In September of last year the Central Consultants and Specialists Committee, as it was then called, had decided to assume the function of negotiating with the Minister on remuneration. The Joint Consultants Committee agreed to reconstitute itself and that negotiations on pay should be left to the C.C. and S. Committee. The C.C. and S. Committee then changed its name to that of Central Committee for Hospital Medical Services so that it could be seen to be representative of all hospital medical staff.

The composition of the Joint Consultants Committee had remained very much the same, but its function now was to deal with matters other than those of terms and conditions of service.

The College of Pathologists and the Royal Medico-Psychological Association had asked to be included in the new Joint Consultants Committee, but the Joint Committee had not yet agreed, nor had it agreed to a suggestion that the Full-time Medical Teachers and Research Workers Committee should be represented on it.

Another point of interest to the Committee was that the ballot on distinction awards had not yet been completed. It had been extended in time so that clinical university teachers with honorary consultant posts could take part in it.

Remuneration of Clinical Teachers

The CHAIRMAN reported that the Government had paid the increase in remuneration due to clinical teachers as from 1 October 1966 in one lump sum on 1 July 1967 instead of phasing the payment as the Government had intended.

The Chairman said that much help in this matter had been received from the Chairman of Council, who had attended every meeting at the Ministry.

The Chairman drew attention to a resolution of the A.R.M. 1967 requesting the Council to continue to press for the inclusion of medical teachers in the remit of the Kindersley Review Body. He said that the Minister of State for Education and Science in August last year had stated that he was thinking of

making the salaries of university teachers (including medical teachers) a standing reference to the Prices and Incomes Board, and he urged those concerned to give him their consent before Christmas last year. Dr. Zinnemann reported that the B.M.A.'s views had been given to the Minister before Christmas, but nothing had happened as yet. He believed that a reference to the Prices and Incomes Board was imminent.

Appointments for Dental Surgeons

The CHAIRMAN said that in July the Chief Dental Officer, Ministry of Health, had issued to the dental schools a paper headed "Appointments in the Hospital Service for Dental Surgeons." At the back of the paper was a diagram which equated senior lecturers and readers in the universities with senior registrars in the hospital service. That had caused the Committee much concern, and it had been pointed out to the Chief Dental Officer that senior lecturers and readers were equivalent to consultants in the hospital service, and that the B.M.A. took strong exception to the diagram.

Professor RANNIE proposed, and the Committee agreed, that the Council should be asked to press for the withdrawal of the diagram.

Grants to Students

Commenting on a report of a working party on grants and welfare presented to the annual general meeting of the British Medical Students Association 1967, Sir RONALD TUNBRIDGE said that students who had no private means and no parents should have enough to live on.

It cost a student who was modest in his demands £600 a year to maintain himself in London. That should be the basic grant. Adjustments might have to be made in cases where students were required to take up residence in hospital for a time and still retain their lodgings. If clinical students were considered as postgraduate students, as many of them in fact were, it would be a great help.

The Committee expressed general agreement with the comments made by Sir Ronald Tunbridge.

Hospitality

A German doctor's daughter living in Munich would like to stay with a British medical family for six weeks from 1 March to 15 April 1968. In exchange the family would be pleased to receive a British girl of similar age for six weeks in June or July.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

"Mediflash"

From 16 October Mediflash, a portable, flashing green light which can be fixed to the roofs of doctors' cars when travelling to emergencies, will be available to doctors through the British Medical Association (*Supplement*, 8 July, p. 23).

The light can be obtained only by doctors who sign an agreement with the B.M.A. to abide by the following conditions:

- (1) The light remains the property of the Association, and it must be returned to the Association if for any reason the member ceases to be engaged in active practice.
- (2) The light is to be used by registered medical practitioners only while travelling to medical emergencies.
- (3) The use of the light confers no special privileges, and the law, including general traffic regulations and speed limits, must be complied with.
- (4) The light must not be sold or transferred to any other person.
- (5) The Association must be informed immediately if the light is lost or stolen.
- (6) The Association may demand the return of the light if the Association is satisfied it has been improperly used.

No Special Privileges

In a letter to honorary secretaries of B.M.A. Branches and Divisions the Secretary of the Association states that it is essential that doctors should abide rigidly by the conditions, and that the "success of the project depends very much on the co-operation of the profession." Honorary secretaries have been asked to seek the co-operation of the police locally in introducing the lamp. In a letter to chief constables the Secretary emphasizes that the lamp is intended as an identification symbol for a doctor who is seeking the co-operation of the police and other road users to enable him to get through congested traffic as quickly as possible. The B.M.A. understood that it would not confer any special privileges in relation to general traffic regulations and speed limits.

The light will cost £6 6s. for members of the B.M.A. and £7 10s. for non-members.

Central Ethical Committee

At its first meeting of the session on 5 October the Central Ethical Committee appointed Dr. WALTER WOOLLEY to be its chairman. Dr. S. Noy Scott did not seek re-election.

Dr. Noy Scott had been chairman of the Central Ethical Committee since 1957, when he succeeded Dr. Robert Forbes, and before that he had been its deputy chairman since 1952. Tribute was paid by the Committee to his services, and Dr. WOOLLEY welcomed the fact that Dr. Noy Scott would continue to be a member of the Committee.

Dr. Woolley has been a member of the Central Ethical Committee for 18 years, and has been its deputy chairman since 1962.

Association Notices

Diary of Central Meetings

OCTOBER

- 17 Tues. Tuberculosis and Diseases of the Chest Group Committee, 2 p.m.
19 Thurs. Joint Consultants Committee (Scotland) (at 7 Drum-
heugh Gardens, Edinburgh), 10.15 a.m., followed by
meeting with Scottish Home and Health Department at
St. Andrew's House, 2.30 p.m.
19 Thurs. Finance Committee, 2 p.m.
20 Fri. Central Committee for Hospital Medical Services, 10.30
a.m.
21 Sat. Central Committee for Hospital Medical Services, 10 a.m.
24 Tues. Joint Consultants Committee (at Royal College of Physi-
cians and Surgeons of Glasgow, 242 St. Vincent Street,
Glasgow), 10 a.m.
25 Wed. Council, 10 a.m.
26 Thurs. G.M.S. Committee, 10.30 a.m.
26 Thurs. S.H.M.O. Group Council, 2 p.m.

NOVEMBER

- 1 Wed. Annual Meetings Committee, 12 noon.
1 Wed. Liaison Committee with the Royal College of General
Practitioners (at Royal College of General Practitioners,
14 Princes Gate, London S.W.7), 4.30 p.m.
2 Thurs. G.M.S. Planning Working Group on Medical Care in
Rural Areas, 2 p.m.
3 Fri. Ophthalmic Qualifications Committee, 1 p.m.
3 Fri. Common Market Committee, 2 p.m.
3 Fri. Ophthalmic Group Committee, 2 p.m.
15 Wed. Rural Practices Subcommittee (G.M.S. Committee),
2 p.m.
15 Wed. Alcohol and Road Accidents Committee, 2 p.m.
23 Thurs. Compensation and Superannuation Committee, 2 p.m.
23 Thurs. Dermatologists Group Committee, 2.30 p.m.

DECEMBER

- 13 Wed. Journal Committee, 2 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked * are asked to notify in advance the honorary secretary concerned.

ALDERSHOT AND FARNHAM DIVISION.—At Physiotherapy Department, Farnham Hospital, Wednesday, 18 October, 8.15 p.m., clinical evening.
BARNESLEY DIVISION.—At Queen's Hotel, Monday, 16 October, 9.15 p.m., annual general meeting.

BRISTOL DIVISION.—At Large Lecture Theatre, Medical School, Wednesday, 18 October, 8.30 p.m., annual general meeting.

DUDLEY DIVISION.—At Wordsley Hospital, Tuesday, 17 October, 7 for 7.15 p.m., Professor R. Milnes Walker: "Some Aspects of Cancer."

DUNBARTONSHIRE DIVISION.—At Queen's Hotel, Helensburgh, Friday, 20 October, annual dinner and dance.

ENFIELD AND POTTERS BAR DIVISION.—At Chase Farm Hospital Academic Centre, Friday, 20 October, 8.30 p.m., Dr. E. W. Emery: "Carcinoma of the Breast—a survey of 20 years' treatment at University College Hospital."

FERMANAGH DIVISION.—At Manor House Hotel, Killadeas, Enniskillen, Tuesday, 17 October, 8.30 p.m., Representative's report, film strip, and supper.*

GLASGOW DIVISION.—Tuesday, 17 October, visit to Ravenscraig Steel Works, Motherwell. Transport will leave Glasgow Regional Office at 5.30 p.m.*

GRIMSBY DIVISION.—At Humber Royal Hotel, Thursday, 19 October, 7.30 for 8 p.m., annual dinner. Guests are invited.*

HARROGATE DIVISION.—At Cairn Hotel, Tuesday, 17 October, 8.30 p.m., general meeting to discuss Presidency for 1970-1.

MID-GLAMORGAN DIVISION.—(1) At Redcroft, 30 Dinas Baglan Road, Port Talbot, Friday, 20 October, 8 p.m., wine and cheese party in aid of R.M.B.F.* (2) At Margam Abbey, Sunday, 22 October, 3 p.m., St. Luke's Day service.

MIDLAND BRANCH.—At Lecture Theatre, General Hospital, Birmingham, Thursday, 19 October, 8 for 8.15 p.m., clinicopathological section meeting, Dr. B. L. Pentecost, Dr. N. M. C. Mayne: "Coronary Care Units in Treatment of Myocardial Infarction."

MONMOUTHSHIRE DIVISION.—At Belle Vue Hotel, Newport, Thursday, 19 October, 7.30 for 8 p.m., dinner and symposium meeting: "Peripheral Arteriovascular Disease."*

NORTH MIDDLESEX DIVISION.—At Committee Room, North Middlesex Hospital, Tuesday, 17 October, 8.30 p.m., film: "Confidence by Choice" (contraceptive methods). Mr. A. Davis will open the discussion. Followed by buffet supper.*

NORTH OF ENGLAND BRANCH.—(1) At Royal Victoria Infirmary, Newcastle upon Tyne, Thursday, 19 October, 7 for 7.30 p.m., symposium by Dr. I. Kolvin, Mr. L. A. Gane, Mr. J. Gittins: "The Delinquent Child." (2) At Five Bridges Hotel, Gateshead, Saturday, 21 October, 7.15 p.m., annual meeting; 7.30 p.m., reception and dinner.

NORTH STAFFS DIVISION.—At Medical Institute, Hartshill, Wednesday, 18 October, 8.15 p.m., Mr. S. Bender: "Sex Hormone Therapy in General Practice."

OLDHAM DIVISION.—At Union Club, Oldham, Monday, 16 October, 9 p.m., B.M.A. lecture by Professor C. J. Polson: "External Signs of Injury."

PORTSMOUTH DIVISION.—(1) At the Cathedral, High Street, Sunday, 15 October, 11 a.m., St. Luke's service. (2) At Medical Centre, St. Mary's Hospital, Thursday, 19 October, 8.30 p.m., Dr. J. D. Pollitt: "Depression." (Preceded by supper, 7.45 p.m.)*

REDBRIDGE AND STRATFORD DIVISION.—At East Ham Memorial Hospital, 21-22 October, week-end general postgraduate course for general practitioners. Applications should be made to Dr. J. B. Enticknap at the hospital.

RICHMOND DIVISION.—At Watney's Brewery, Friday, 20 October, 8.15 p.m., meeting on "Road Traffic Act Provisions and Blood Alcohol Levels in Drivers." Speaker, Dr. B. M. Wright.

SHROPSHIRE AND MID-WALES BRANCH.—At Shrewsbury Medical Institute, Wednesday, 18 October, 8.30 p.m., annual general meeting.

SOUTH LANCASHIRE AND EAST CHESHIRE BRANCH.—At St. Ann's Church, St. Ann's Square, Manchester, Sunday, 22 October, 6.30 p.m., annual St. Luke's Day service.

STOCKPORT DIVISION.—At new Postgraduate Medical Centre, Stepping Hill Hospital, Sunday, 22 October, 10.30 a.m., clinical meeting.

SWANSEA DIVISION.—At St. Barnabas Church, Sunday, 22 October, 11 a.m., St. Luke's Day service.

TOWER HAMLETS DIVISION.—At St. Andrew's Hospital, Friday, 20 October, 3 p.m., Dr. A. T. Brain: "Some Geriatric Topics."

TROWBRIDGE DIVISION.—At Lansdowne Grove Hotel, Bath, Saturday, 21 October, 8.30 p.m., dinner dance.*

WALSALL DIVISION.—At Three Crowns Inn, Tuesday, 17 October, 8.15 p.m., Professor J. M. Bishop: "Pulmonary Heart Disease."*

WEST BROMWICH AND SMETHWICK DIVISION.—At West Bromwich and District General Hospital Thursday, 19 October, 8.15 p.m., symposium on "Hypertension" and discussion.

WEST SUSSEX DIVISION.—At Burlington Hotel, Worthing, Wednesday, 18 October, 7 for 7.30 p.m., dinner meeting, Mr. N. C. Tanner: "Modern Trends in Gastric Surgery."*

WIGTOWNSHIRE DIVISION.—At King's Arms Hotel, Glenluce, Friday, 20 October, 7.30 p.m., Professor J. W. Dundee: "The Influence of Various Medicaments on the Course of Anaesthesia and the Relief of Pain."

Branch and Division Officers Elected

ABERYSTWYTH DIVISION.—Chairman, Dr. W. H. Beasley. Vice-chairman, Dr. A. Davies. Honorary Secretary and Treasurer, Dr. J. B. Lloyd. Assistant Honorary Secretary, Dr. J. Griffiths.

CITY OF DUNDEE DIVISION.—Chairman, Dr. J. M. Langlands. Vice-chairman and Chairman-elect, Dr. D. M. Green. Honorary Treasurer, Dr. J. Scott Innes. Honorary Secretary, Dr. W. T. M. Yeaman.

FURNESS DIVISION.—Chairman, Dr. J. E. Horrocks. Chairman-elect, Dr. T. S. Moore. Vice-chairman, Dr. J. M. Stuart. Honorary Secretary, Dr. P. Gardner. Honorary Treasurer, Dr. A. MacLeod.

HEXHAM DIVISION.—Chairman, Dr. L. R. Routledge. Vice-chairman, Dr. W. Gibson. Honorary Secretary and Treasurer, Dr. M. McKendrick.

HUDDERSFIELD DIVISION.—Chairman, Dr. W. Brown. Chairman-elect, Dr. A. L. G. Smith. Vice-chairman, Dr. H. W. Davis. Honorary Secretary, Dr. A. M. Barlow. Assistant Honorary Secretary, Dr. W. Brown. Honorary Treasurer, Dr. J. F. Tomlinson.

KENYA MEDICAL ASSOCIATION.—President, Dr. J. S. Nesbitt. Vice-presidents, Dr. I. J. Khosla, Dr. M. Y. D. Kodwawala. President-elect, Dr. I. J. Khosla. Honorary Secretary, Mr. Andrew Hicks. Assistant Honorary Secretary, Dr. P. R. Mehta. Honorary Treasurer, Dr. L. L. Ghelani. Assistant Honorary Treasurer, Dr. B. P. Patel.

LEICESTERSHIRE AND RUTLAND BRANCH.—President, Dr. E. T. James. President-elect, Dr. Dudley Gotla. Vice-president, Dr. E. W. Goodwin. Honorary Secretary and Treasurer, Dr. L. Mitchell.

NORTH-EAST SUFFOLK DIVISION.—Chairman, Dr. G. Clayton. Honorary Secretary and Treasurer, Dr. W. J. Wren.

ROCHDALE DIVISION.—Chairman, Dr. R. Mallinson. Vice-chairman, Dr. W. T. Gordon. Honorary Secretary and Treasurer, Dr. A. H. Michael-Phillips.

SUNDERLAND DIVISION.—Chairman, Dr. B. Gordon. Chairman-elect and Vice-chairman, Dr. P. Inman. Honorary Secretary, Dr. C. Nelson. Honorary Treasurer, Dr. B. Tindle.

SWINDON DIVISION.—Chairman, Dr. J. A. M. Ager. Vice-chairman, Dr. D. F. Alexander. Honorary Secretary and Treasurer, Dr. F. J. Lowe. Assistant Honorary Secretary, Dr. H. Barnard.

WEST LOTHIAN DIVISION.—Chairman, Dr. G. M. Dewar. Vice-chairman, Dr. A. F. Lang. Honorary Secretary and Treasurer, Dr. M. Gardiner. Assistant Honorary Secretary, Dr. J. Callander.

WEST NORFOLK DIVISION.—Chairman, Dr. R. S. McKelvey. Chairman-elect and Vice-chairman, Dr. Humphrey Booth. Honorary Secretary, Dr. J. H. Ballantyne. Honorary Treasurer, Dr. R. V. Smith.

YORK DIVISION.—Chairman, Dr. A. I. MacLeod. Chairman-elect and Vice-chairman, Mr. C. Smith. Honorary Secretary and Treasurer, Dr. M. A. Wilson.

British Medical Journal. Supplement

LONDON SATURDAY 21 OCTOBER 1967

CONTENTS

Scottish Council - - - - -	17	Proceedings of Council - - - - -	23
Edinburgh Conference on Better Medical Care - - - - -	18	Inner London Executive Council - - - - -	23
Committee on Overseas Affairs - - - - -	20	Journal Committee Chairman - - - - -	23
Fees for Colliery Emergencies - - - - -	21	Armed Forces Committee - - - - -	24
Opinions on Distinction Awards - - - - -	22	Association Notices - - - - -	24

Scottish Council

By a large majority the Scottish Council approved the principle that charges might be made to non-members for certain services rendered them by the B.M.A. The Scottish Council was told that not enough money was provided for the ambulance service in Scotland.

At a meeting of the Scottish Council in Edinburgh on 3 October Dr. JOHN RIDDELL was re-elected chairman and Dr. MARY ESSLEMONT was re-elected deputy chairman.

The Chairman welcomed 14 new members. He pointed out that, while the Scottish General Medical Services, Public Health, and Hospital Medical Services Committees dealt with their special problems, the Scottish Council had an important part to play in getting agreement among all sections of the profession and in trying to reach conclusions acceptable to all parties.

It was reported that Dr. D. M. Baxendine had agreed to represent the Scottish Council on the Committee on Welfare of the Disabled of the Scottish Council of Social Service.

Car Parking

Copies were received of letters from the Scottish Development Department on the subject of parking concessions for doctors. They were to associations of local authorities and the Scottish Association of Executive Councils asking for their views on the Secretary of State's suggestion that doctors should be given recognition in parking schemes and that "Doctor" markings on the roadway near doctors' consulting-rooms should be authorized. The scheme suggested for road markings was broadly similar to the one which operated in the Westminster area in London.

Dr. W. W. FULTON said that representatives of the Scottish Development Department had said originally that the Secretary of State might well be more ready to give concessions, since he was also responsible for the National Health Service in Scotland. There was, however, no direct record that the question of road markings would be raised with chief constables. One of the letters stated that traffic wardens had the same powers of discretion as police constables, but Dr. Fulton questioned whether that was true in parking-meter zones. It must be quite clear where the powers of discretion began and ended. He said that the principle of one marking per consulting-room or surgery was no longer appropriate as the numbers in group practices increased. He thought it should rest with the B.M.A. and not the local authority to decide whether a roadway marking was justifiable.

Organizational Matters

A request was considered from the Organization Committee that the size of committees and the appointment of subcommittees should be reviewed. The Scottish Council found that "it could offer no recommendation to the Council" on this matter, since the Scottish committees were as small as was compatible with adequate representation and the smaller committees involved little expenditure.

Consideration was then given to the question of whether non-members should be charged for services provided by the Association.

Dr. J. E. MILLER said that he thought it probable that much time was given by B.M.A. staff to non-members. He thought there was a need for a membership card which would have to be produced or its number quoted whenever a service was requested. Other organizations adopted that method successfully. Dr. C. C. LUTON supported Dr. Miller, and said it was an important recruitment issue.

Dr. C. J. SWANSON disagreed with Dr. Miller and pointed out that the B.M.A. was there to promote the medical and allied sciences and interests of the profession. That non-members should take advantage of the B.M.A.'s services was between them and their consciences. It was all very well to have differential charges for material things such as car badges, but the high traditions of the Association should not be interfered with.

Dr. E. R. C. WALKER supported Dr. Swanson, and said that in his experience the use of the Association's Scottish Office by non-members was relatively slight. To be exclusive, he said, was a mistake.

Dr. MILLER said he accepted that much of the Association's work benefited everybody. When he was honorary secretary of the Glasgow Division non-members had said to him, "What can the B.M.A. do for me that it does not do for me as a non-member?" Those doctors, said Dr. Miller, had not got the conscience to which Dr. Swanson had referred "and therefore you cannot appeal to it." Schemes which had been mooted by the B.M.A. over the years and which should have been carried out had had to be abandoned for lack of money. "For donkey's years we have tried to encourage membership by working for non-members. The time has come to insist on membership," concluded Dr. Miller.

Dr. JOAN K. SUTHERLAND asked what services would be the subject of a charge, but the meeting decided against discussing the detail and to vote on the principle only.

It was moved by Dr. FULTON, with the agreement of Dr. MILLER, "That the Scottish Council approves the principle that charges may be made to non-members for certain services rendered to them by the Association where there is no charge for members."

The motion was carried by a large majority.

Road Safety Act

Reports were received of meetings held with the Scottish Home and Health Department and with the Crown Office to discuss the appointment of police surgeons and the arrangements and fees for taking blood specimens under the Road Safety Act, which was to come into force on 9 October.

Dr. SWANSON protested at the lack of public guidance given to doctors on what would be required of them. Doctors, he said, were in the dark on the matter. Dr. WALKER suggested that it might be necessary to set up a special committee to deal with problems associated with work for the police. Dr. G. H. HUGHES thought that such a matter should be dealt with on a U.K. basis—what was necessary was good liaison with London.

It was agreed that the Chairman and Scottish Secretary should look into the question of the appointment of a committee.

Ambulance Service

A request from the St. Andrew's Scottish Ambulance Service that the B.M.A. Scottish Office should arrange the appointment of two general practitioners to each of the six regional ambulance committees was agreed to.

Dr. FULTON, the general-practitioner representative on the central ambulance committee, suggested that when the ambulance service for a particular local medical committee area was under discussion the secretary of that local medical committee should be invited to the meeting. He said that unless the general-practitioner representation on these committees was increased all areas ought to have reasonably easy access to their appointed representatives. In the Western Region the area was very wide.

Dr. J. F. CAMERON said that in his area (Banff, Moray, and Nairn) a rotation of representation was arranged in appointing members to various committees, so that all local medical committees were represented in turn.

Dr. W. A. ROSS pointed out that local, and often very acceptable, ambulance arrangements were being replaced by central depots, and it was important that rural interests should be recognized by the appointment of a rural practitioner as one of the two general practitioners on each regional ambulance committee.

The Scottish Council supported that suggestion and also Dr. H. B. MURK's suggestion that deputies should be allowed when members could not attend meetings.

Dr. FULTON informed the meeting that not enough money was being provided for the ambulance service. That it was an expanding service was not recognized by merely increasing the financial allocation by 3½% each year.

The profession was constantly encouraging improvements in the hospital service (day hospitals, geriatric assessment units, etc.) and these placed increasing demands on the ambulance services. Those trying to run the ambulance service were suffering from a dearth of replacement vehicles. If the replacements were not ordered or were not forthcoming the money allocated could not be used, and any unused money each year went back to the Treasury.

Birsay Report

A report of comments by the Public Health Committee (Scotland) on the Birsay Report on General Medical Services in the Highlands and Islands was received.

Dr. CAMERON took exception to a recommendation by the Public Health Committee that relatives should not be employed as home helps. He said that in under-populated areas relatives were often the only people available. If they could not act as home helps there would be no home helps.

Dr. SWANSON agreed and said his subcommittee (the Highlands and Islands Practitioners Subcommittee) supported the Birsay Committee's recommendation that gave a blessing to relatives acting as home helps. Dr. Swanson informed the Scottish Council that a report by his subcommittee on the Birsay Report was to be presented to the G.M.S. Committee (Scotland) shortly. It was also stated that the Scottish Committee for Hospital Medical Services was awaiting a report on the subject from the Northern Regional Committee for Hospital Medical Services.

It was remitted to the Chairman to collect all the comments on the Birsay Report and to collate them in one document.

Committee Reports

Dr. SWANSON, in the absence of the Chairman of the G.M.S. Committee (Scotland), gave an account of its recent work.

The Secretary of State, he said, had been asked to allocate more money for health centres. Dr. Swanson also referred to a study of general practitioners working in hospitals, particularly those undertaking specialist duties unsupervised, and an unsuccessful attempt to get the lending power of the General Practice Finance Corporation extended to include equipment.

Reports were also received on the work of the Public Health Committee (Scotland) and of the Scottish Committee for Hospital Medical Services (*Supplement*, 14 October, p. 11). Under any other business, a suggestion by Dr. LUTTON that an annual one-page report on the work of the Scottish Council should be distributed was referred to the Chairman's Committee for consideration.

Dr. JOAN SUTHERLAND and others expressed dismay at the closing down of the Medical Practices Advisory Bureau in Edinburgh and its transfer to Glasgow. She was disappointed that there had not been full prior consultation with Scotland, and she was doubtful whether the move would effect economies.

Dr. SWANSON, speaking as one who practised neither in Edinburgh nor in Glasgow, said he saw a distinct advantage in having all the information concentrated in one bureau to which applications could be made.

Edinburgh Conference on Better Medical Care

"Better Medical Care—Which Road?" was the theme of a conference on 7 October arranged by the Edinburgh and South-east Scotland Branch of the B.M.A. and held in Edinburgh University. The conference was conceived along similar lines to a conference on "The Future of British Medicine" held in Newcastle upon Tyne in March (*B.M.J.*, 18 March, p. 693).

Present Position

Mr. GEORGE R. HODNETT, chairman of the Board of Governors, Royal Victoria Infirmary, Newcastle upon Tyne, opened the morning session of the conference, which was on the advantages and disadvantages of the present position. He said that the original requirements of the National Health Service had been underestimated. It had been thought that the health services could and should be paid for out of taxation, and the idea of private contribution had been swept aside. "Charity" and "means test" had become dirty words in the 1930s. However, when what had now developed was looked at not only had it not fulfilled expectations but the whole medical problem had become more difficult because of the progress of medical science, particularly on the hospital side.

At the moment there seemed to be no solution. Day-to-day directives received in hospitals gave the impression that all was going to happen, whereas the facts pointed to the probability that it would not happen. The Government in power could not move too far ahead of public opinion, particularly in respect of a problem which was either wholly or partly insoluble, unless that movement was going to justify itself in time for a general election.

Mr. Hodnett believed that the medical profession, which enjoyed and deserved the high regard of the community, should take a lead in forming public opinion. He asked the profession to consider whether below the Ministry there should be a medical board—a health board—which would be responsible for the recruitment, training, and employment of medical personnel and for the operation of the Health Service. It might possibly be under a Ministry which combined the social services, and which would have a pensions board, a health board, and an education board.

Mr. Hodnett believed that any Government should accept financial aid from any reasonable source. Old prejudices should be set aside and every means explored and pursued to raise funds from the public to supplement health programmes. He did not know how young qualified people who wanted

to go abroad could be prevented from doing so. He suggested for consideration, however, that young people in training might be under contract for a period of years, allowing within that period a secondment for overseas service and training. That would be followed by a return to Britain for a further period of service.

Administrative Musical Chairs

Dr. G. S. RIDDELL, medical officer of health for Fife, said the most significant factor to affect the National Health Service since its inception had been the seventh report of the Review Body and the Family Doctors' Charter. At the same time there had emerged a new interest in health centres. From these two factors organizational changes at local level which were possible within the existing administrative framework were starting to flow.

Radical changes in local administration at this stage might prove disadvantageous. The local authority services escaped some of the worst effects of central financial control and preserved some scope for independence, experiment, and diversity. Those were important and must not be lightly cast away for the sake of administrative expediency. The heart of the matter was not the administra-

tive structure but finance. Unless first an alternative, more flexible system of finance was evolved area health boards held no genuine promise of an improved Service and would merely involve playing administrative musical chairs.

Medical Aid System

Dr. C. C. LUTTON, general practitioner, Musselburgh, said that doctors were uneasy because the present medical system did not allow the high standard which should be possible. Unless there were changes in organization, finance, and use of the N.H.S. the standard would even deteriorate. The medical "industry" was inefficient and needed business analysis, so that the major effort could be properly organized and channelled to where it was most needed.

If patients wanted a better service then the world price for medical care must be paid, said Dr. Lutton. The time had come to examine the method of payment, because welfare regardless of need would eventually bankrupt any system. Most would agree that a free basic service was desirable, but on to this could be put various additional services to be paid for in proportion to use and income. Payments for prescriptions, consultations, appliances, and hospital board and lodging could be considered. Britain had a legal-aid system, so why not a medical-aid system, but on the basis of a health tax rather than a means-test system?

Dr. Lutton thought that the pattern of fewer general practitioners working in larger units would continue. Newly qualified doctors were reluctant to enter ill-equipped and under-capitalized practices. Meantime the promise by the Minister of Health of hundreds of health centres, for which money was not yet available, had effectively slowed down the improvements that many general practitioners were themselves undertaking. Failure to improve medical services further was likely to lead to a limited return to "insurance fund" private practice by those doctors who wished it and those patients prepared to pay.

Hospitals

Dr. J. G. M. HAMILTON, consultant physician, Edinburgh Royal Infirmary, said that twentieth-century medicine was rushing along so fast and expensively that it was difficult to conceive of enough money being made available for hospital services.

He criticized the closure of cottage hospitals—"those invaluable assets." Far from being abandoned, he thought that new ones should be created in towns and cities as well as in the country districts. There was no inherent professional reason why a general practitioner should not look after his own patient in his own hospital when that was practicable.

Dr. Hamilton said that the initial administrative and staffing problems which existed in the hospital service before 1948 were still there. They had been aggravated by the growing sense of frustration and unfulfilled dreams. They had not been overcome despite the flag-waving, fine words, and grand promises upon which the Service had been largely fed for nearly 20 years.

Dr. W. P. U. KENNEDY, hospital registrar, Edinburgh, argued that there was too "pussey-

footed" an attitude to specialization. Cardiac departments, for instance, were still expected to take their quota of admissions along with the other medical wards. How could they possibly fulfil both functions? Such departments should be accorded full specialty status.

He proposed a concept of a central specialist hospital providing for advanced diagnostic studies, research, and complex therapeutic facilities. Together with the undergraduate and postgraduate medical schools for the region it could comprise a medical complex that could be the spiritual centre of the region. Its limbs would be the district general hospitals, providing a comprehensive hospital service for their own area. All hospitals would take part in teaching students and training their own medical staff. In every hospital much greater importance would be attached to the intensive-care area and to mobile teams equipped to deal with acute emergencies.

The Future

The opening speaker at the afternoon session, on the subject "The Future Organization of Medical Care," was Mr. ESMOND WRIGHT, M.P. for the Pollok Division of Glasgow, formerly professor of modern history at Glasgow University, and a member of the Committee on General Medical Services in the Highlands and Islands—the "Birsay Committee" (*Supplement*, 8 July, p. 23).

Mr. Wright submitted a 10-point programme for the medical profession. There must, he said, be more cottage hospitals and more hospices, especially in the Highlands and Islands of Scotland. The nurse-patient ratio in geriatric units must be "urgently improved." Also needed was an inspectorate of all geriatric units. There was also need to pay more attention to the crippling diseases rather than the killer diseases.

People were, in Mr. Wright's view, prepared to pay for medical services. That being so, there should be alongside and supplementary to the National Health Service a provision that allowed people to pay extra. Health insurance premiums should be tax deductible. He saw no reason why health insurance should not be regarded as important as life insurance.

In a "Common Market" world Mr. Wright thought the medical profession should be far more international in its recruitment than it had been. It was absurd to leave general practitioners to work in isolation. They should be encouraged to work in health centres.

Medical Organization

Mr. A. R. HOWIE, clerk to Renfrew County Executive Council and former secretary of the Scottish Association of Executive Councils, said that the sense of frustration among general practitioners arose less from the changed attitudes of patients than from the knowledge that patients must be aware that this was the one branch of the Service which, because of a lack of forward planning, could not join fully in the general surge forward in the practice of modern scientific medicine.

There was urgent need to change the existing organizational structure to create a sense of unity of purpose within the profession and an interchange of personnel within the Service that would stimulate the maintenance of skills at the highest level. It was doubtful whether the proper answer had yet been produced, and the profession must do some serious self-questioning and define the place of the general practitioner in a unified National Health Service. The most suitable organizational arrangements would then be apparent.

Dr. E. R. C. WALKER, former Scottish Secretary of the B.M.A., said that ignorance of the history of medical organization was one of the main reasons why there was so much confusion and so many conflicting ideas about the future. For generations doctors had taken an active part in promoting measures to improve the medical care of the people. They were, however, increasingly coming to realize that changes in the conditions under which medicine was practised, no matter how necessary and desirable they might appear to be, could carry with them the risk of defeating the very ends for which they were made. Others beside doctors were also coming to realize that.

Any experiment that had been in operation for nearly 20 years and had not obviously proved successful ought to be the subject of a thorough and dispassionate evaluation, said Dr. Walker. An inquiry by a Royal Commission or by some other procedure into the N.H.S. was clearly the first step towards better medical care.

Financing Medical Care

Opening the last session of the conference, on "The Financing and Administration of Medical Care," Mr. ARTHUR SELDON, editorial director of the Institute of Economic Affairs, said that, despite rising living standards, politicians had failed to raise the percentage of national income apportioned to the Health Service. In 1950 it was 4%, in 1961 4.1%, and in 1966 again 4.1%.

As a method of financing medical care the experiment of the Health Service had failed, and after 20 years it was time the failure was recognized. There had been little hospital building before 1962. Hospital staffing had changed so much that in the main categories there were 6,800 home-born and 5,300 overseas-born doctors. To reach the 5 to 6% of the national product spent by other countries £350m. to £550m. more would have to be raised in taxes. Even if that could be done it was childish to suppose that all that vast sum could go on the N.H.S. and none on education, on housing, or on other social services. To increase expenditure on the N.H.S. by 25% something like £2,000m. in taxation would have to be raised. No one in his right mind would give that solution a second thought.

Professor JACK WISEMAN, director of the Institute of Social and Economic Research at York University, said that the proposition that if those willing to pay more were allowed to they would attract the services of "too many" doctors and that the standards of service provided for others must inevitably fall was a blinkered view of society and the nature of the economic problem. If the Government's present position as the sole purchaser of general-practitioner services

enabled it to exploit them in the short term, then its longer-term consequences must be to reduce the supply of doctors more efficiently than any consumer-oriented scheme would.

Dr. IVOR M. JONES, chairman of the B.M.A.'s Private Practice Committee, said that health insurance should become compul-

sory in the foreseeable future. But in return for their premiums patients should be free to avail themselves of all or any of the relevant benefits and to supplement such benefits if they choose to do so. Administratively there should be some decentralization of the existing structure. The establishment of regional

or area health boards, along the lines advocated by Sir Arthur Porritt, would not only assist the integration of medical services and eliminate unnecessary duplication but could promote healthy competition between the regions and permit some degree of flexibility between them in their financial arrangements.

Committee on Overseas Affairs

There are to be discussions with the Ministry of Overseas Development on how retired British doctors might help developing countries by serving for short periods in some capacity. The value of service overseas by young British doctors is said to be beginning to be recognized by appointment committees in Britain, but not universally so. The Ministry of Overseas Development wants to know of any cases in which a doctor has been resettled at a disadvantage after temporary service abroad, and the Committee is pointing out to the Ministry that it is advisable for young doctors to go overseas on secondment rather than to take an appointment. Sir John Bruce, Regius Professor of Clinical Surgery, Edinburgh University, has been appointed to the first travelling fellowship of the Commonwealth Medical Association.

The Committee on Overseas Affairs held its first meeting of the session on 6 October. Professor D. E. C. MEKIE was re-elected to the chair.

World Medical Association

The Committee considered a letter from the Secretary-General of the World Medical Association asking for the support and co-operation of member national medical associations in its drive for individual associate members. Among the advantages of individual associate membership was the receipt of the *World Medical Journal*.

Dr. M. WARE, Editor of the *British Medical Journal*, said that the W.M.A. was asking national medical associations to distribute to their members for a period of two to three years the English-language edition of the *World Medical Journal* and to pay the cost. Some national medical associations were already doing this. The matter was being looked into in Britain, but if it were done one of the advantages of associate membership of the W.M.A. would go, because every member of the B.M.A. would get the *World Medical Journal*.

Mr. J. R. NICHOLSON-LAILEY said that in 1966 the W.M.A. had managed to balance its budget and produce a small surplus of about \$20,000, but this had been possible only because the American Medical Association was providing \$40,000 a year for five years to tide the W.M.A. over the loss of revenue caused by the dissolution of the American Supporting Group. It was only by increasing individual associate membership that this loss could be made up. The operation of the tax laws in the U.S.A. made associate membership more attractive there than in Britain.

Sir CLEMENT PRICE THOMAS said that numerous associate members would provide a better solution to the financial problems of the W.M.A. than the distribution of the *World Medical Journal*.

The Committee agreed to consider the matter again when there was more information available on the implications of the W.M.A.'s request.

Report on Assembly

Dr. D. P. STEVENSON, Secretary of the B.M.A., reported on the 21st World

Medical Assembly, at which he had been elected to the W.M.A. Council. He said that for the first time there had been a substantial surplus on the year's accounts. He thought there might still be financial difficulties in the future, but support had been received from the American Medical Association.

Dr. Stevenson said that consideration was being given to the problem of national medical associations that did not pay their dues to the W.M.A. It must be recognized, he said, that some associations were poorer than others, and it was for the privileged to try to look after the underprivileged. However, it was hoped that a solution to this problem would be found.

Another of the decisions taken at the Assembly had been that the Swiss Medical Association should in future act as the liaison between the W.M.A. and other international organizations. Since many of these were based on Geneva, this would be convenient and economical.

The Assembly, said Dr. Stevenson, spent much time debating the medico-legal aspects of the "moment of death." The Council of the W.M.A. was going to study the matter and would be asking national medical associations to co-operate. Another major decision of the Assembly had been that the W.M.A. should organize a fourth conference on medical education. The subject would be "Medical Education: A Collective Responsibility," and it would be held in Europe in 1972. The Council of the W.M.A. was anxious that national medical associations should support the conference, and they would be asked shortly to nominate a member to serve on the organizing committee and to put forward the names of speakers.

Supporting Group

It was reported that the British Supporting Group of the World Medical Association had made certain changes in its constitution. An important part of the work of the group consisted in sending used medical journals to hospitals or individual doctors in developing countries. The group wished to carry on this work.

The Overseas Committee supported the continuance of the Supporting Group and the changes in its constitution.

Overseas Conference

Dr. D. L. GULLICK, Under-Secretary, said that at the overseas conference in Bristol (*Supplement*, 29 July, p. 101) the difficulties sometimes encountered by postgraduates coming to the United Kingdom from overseas had been discussed. Since then a letter had been sent to all B.M.A. Branches and independent national medical associations in the Commonwealth drawing their attention to this matter and asking them to inform B.M.A. headquarters of any difficulties their members might have experienced.

Dr. C. B. VAUGHAN pointed out that probably doctors from overseas who were already working in this country were in a better position to report on the problems they had encountered than those still in the Commonwealth.

Service Overseas After Retirement

The Committee discussed a resolution of the Annual Representative Meeting 1967 proposing that the Council should inquire into the desirability of setting up a scheme in which retired doctors could offer their services to work for a period in one of the developing countries.

Dr. J. M. LISTON, medical adviser to the Ministry of Overseas Development, said that the idea that older doctors could offer something to countries overseas was a good one. However, there were difficulties. One was the period for which they could work. If it was, say, for two years that would be useful to the country concerned. If for three months it would neither be useful nor economically feasible.

The sort of vacancies the Ministry was asked to fill, said Dr. Liston, included a number for so-called general-duty medical officers, and it was unlikely that a doctor aged 60 to 65 who had retired from practice in Britain would be fitted for that type of work. But there were other posts—in hospitals, for instance—in which there was a shortage of doctors in the middle and lower grades. The opportunities in the specialist fields were limited. Dr. Liston suggested that members of the Committee and of the Ministry should meet to work out a scheme.

The CHAIRMAN agreed that it would be useful to discuss a scheme with Dr. Liston's department. The B.M.A. could also, through

the Commonwealth Medical Association, inform doctors overseas of the type of help available to them if they required it.

Dr. R. L. LUFFINGHAM said that Dr. Liston had talked about sending doctors to salaried posts overseas. But surely that was not what the Committee envisaged. He believed that its suggestion was that doctors should go out to supplement the existing services, for which they would receive some sort of honorarium plus expenses. Such posts would not be found in Dr. Liston's list. It should be made known in the developing countries that there were various specialists willing to give their services for an honorarium and expenses. Dr. Luffingham said the Committee was not interested in career posts. Three months was perhaps too short a time, but two years for a doctor aged 60 to 65 might be too long. There should be close links with overseas medical associations to find out what posts there were which were outside the category the Ministry of Overseas Development had in mind.

Dr. VAUGHAN suggested that the doctors the Committee had in mind could be particularly useful in public health, port health, school, and mental health work.

Mr. R. V. COOKE, the President, suggested that fewer senior men were now required in the developing countries, because posts in those countries were being filled by their own nationals.

Dr. LISTON said that there was no evidence of a lessening of the overall demand in the overseas territories. The demand always kept ahead of the available resources.

The Committee agreed with Dr. Liston's proposal that its representatives should meet those of the Ministry of Overseas Development.

Secondment Overseas

The Committee considered a letter from the Ministry of Overseas Development which stated that it had always been concerned that doctors who served temporarily in the developing countries should not suffer any setback in their careers on their return to Britain. The letter continued, "At present we have little evidence that doctors are resettled at a disadvantage, and if any has come to your notice we should be very grateful indeed to have the details—not with a view to tackling any individual case, which I think would be beyond our powers at the moment, but in order to try to prevent similar occurrences in the future."

Dr. MARY ESSLEMONT said that she knew from experience that appointment committees turned down young men who had spent time in posts overseas and who had had much experience—far more than any young registrar could get in this country. They were turned down on the ground that they had not had "effective supervision." This was quite wrong, said Dr. Esslemont.

Mr. COOKE said that the Royal Colleges had sent out directives to all appointing bodies and to consultants that they should take account of service overseas when making appointments. He also emphasized that young doctors should go overseas only on secondment, because that ensured that a continuing interest was taken in their progress.

Professor F. E. STOCK said that it was now realized that there was considerable ex-

perience to be gained overseas, and in his own region there was no opposition to appointing to vacant posts doctors who had been employed overseas.

The CHAIRMAN suggested that in replying to the Ministry of Overseas Development the Committee should state that it was not persuaded that it was advisable for a young doctor to go overseas unless he was seconded to a post.

Commonwealth Medical Association

Dr. GÜLLICK reminded the Committee that the Commonwealth Medical Association had established a travelling fellowship (*Supplement*, 22 April, p. 21). It had now been agreed that Sir John Bruce, Regius Professor of Clinical Surgery, Edinburgh University, should visit certain African countries. A second fellowship was already being considered.

Overseas Undergraduates

The Committee received a report that the Committee on Medical Science, Education, and Research had suggested that in order to ensure that the principle of reserved places for overseas undergraduate students was implemented the matter might be referred to the deans of medical schools.

The CHAIRMAN said the number of overseas undergraduates in Britain had been cut down on the false assumption that the universities in their own countries would be able to give them a more appropriate education. But it was highly advantageous to have a certain number of foreign students in a university, and he thought that there should be places reserved for overseas students in British medical schools.

Dr. GÜLLICK said that there were certain Commonwealth countries, such as Sierra Leone and Cyprus, which had no undergraduate medical schools, and the result was that some of their undergraduates went to Moscow, because they could not get places in the United Kingdom.

Professor STOCK was uncertain about the wisdom of earmarking a certain percentage of places at the universities for overseas students. It would be better to make the needs of these students a reason for increasing the number of places and providing new medical schools.

Sir CLEMENT PRICE THOMAS said that that was shelving the problem until there were more medical schools. Britain should show its responsibility to those countries in the Commonwealth that did not have their own medical schools by providing a certain number of places for overseas students. It would then follow from that that it was the Government's responsibility to provide more medical schools.

Dr. VAUGHAN thought the Committee should recommend that some places should be kept for overseas undergraduates without committing itself to a percentage. Mr. COOKE said it should not be suggested that that had not been done. Some schools had kept places for overseas undergraduates as a matter of routine.

The Committee agreed that it was strongly of the opinion that there was great value in having a certain number of overseas students from Commonwealth countries, particularly those who had no medical school of their

own, but it appreciated the difficulty at the present time of implementing this policy.

Postgraduate Education

The Committee on Medical Science, Education, and Research had also suggested that in order to ensure that the principle of reserved training posts for overseas postgraduate candidates was put into effect the matter might be referred to the Committee of Postgraduate Deans.

The CHAIRMAN pointed out that any really serious postgraduate student could usually be accommodated. The idea of the reserved post would not work because each individual student came with a different requirement, and there could not be reserved posts in all departments.

Among the matters discussed at the Overseas Conference was the difficulty experienced under the Commonwealth Immigrants Act by some Commonwealth doctors wishing to enter the United Kingdom for postgraduate education.

Dr. R. A. PALLISTER, medical director, Commonwealth and International Medical Advisory Bureaux, explained that there was no problem for those students who were sponsored by universities. But many came independently. If they were Commonwealth doctors and they had an employment voucher they could be admitted to this country without difficulty and stay so long as they wished. The demand for these vouchers had increased, and there was a waiting list of more than a year.

A doctor who came without a voucher must come as a student or as a "working holiday-maker." He must have sufficient funds, like any other visitor, and his stay in the country was limited. If he wished to stay longer he had to obtain permission from the Home Office.

Dr. A. N. MATHIAS, Chairman of the Representative Body, asked why doctors had such a long wait for employment vouchers if their qualifications were acceptable to the General Medical Council. Dr. PALLISTER replied that the voucher was supplied by the Ministry of Labour. There were only a certain number for all skilled people, such as doctors and teachers, and they had to wait their turn. Dr. MATHIAS suggested that there might be a medical advisory committee which could be consulted in cases of difficulty.

It was agreed that Dr. Pallister should report to the Committee any cases of difficulty which came to his attention.

Fees for Colliery Emergencies

The B.M.A. has agreed with the National Coal Board that general practitioners who attend colliery emergencies should be paid £1 11s. 6d. for a single attendance not exceeding one hour between 8 a.m. and 8 p.m., and £3 3s. between 8 p.m. and 8 a.m. The fees for an "underground visit" will be £5 5s. for the first hour, with £2 2s. for each subsequent hour or part of an hour.

In the past the fees varied considerably in each area, and in some areas no fees were paid at all.

Opinions on Consultant Distinction Awards

The Representative Body of the B.M.A. resolved in 1966 that there should be a postal ballot of all consultants, senior hospital medical staff, and senior registrars to ascertain their views on merit awards for consultants.

On 1 June the B.M.A. sent out some 14,000 ballot papers to consultants, S.H.M.O.s, and senior registrars in the United Kingdom together with a covering letter, a memorandum of information on consultant distinction awards, and a business reply envelope. Subsequently any of these doctors who had not received the papers were asked to inform the Secretary (*Supplement*, 17 June, p. 176; 29 July, p. 108). The ballot paper invited answers to the following questions:

(1) What is your present grade in the hospital service?

(2) What is your specialty?

(3) What is your age?

(4) If eligible, are you the holder of a special distinction award?

(5) Do you support the continuation of special distinction awards (whether on the present or on some revised system)?

(6) Do you consider that the present system requires any change?

Answers of "Yes" or "No" were asked for to Questions 4 and 5, and "Yes," "No," or "Don't know" to Question 6. Those who answered "Yes" to Question 6 were asked (Question 7) to state briefly the change or changes they considered desirable.

The ballot papers did not require to be signed, and on receipt were separated from the enclosing envelopes which bore the names of the senders, so that when they came to be examined the identity of the voter was not available.

Results

The ballot closed on 30 September, and the Scottish Office and the Scottish Secretary of the B.M.A., who acted as returning officer, has issued the following information on the results.

The number of replies received was 7,349.

Valid replies were received from:

Consultants	5,889
Senior hospital medical officers	226
Senior registrars	940
	7,055

The remainder of the replies were invalid for the following reasons:

Not in above grades	22
No grading given	3
Retired	141
No identification on envelope	120
Spoilt	8
	294
	7,349

Of the 5,889 forms returned by consultants 2,066 were from consultants with distinction awards, 3,803 were from consultants without distinction awards, and 20 were from con-

sultants who omitted or refused to disclose whether or not they held an award.

Changes Considered Desirable

In an analysis of the comments of those who answered Question 7 Dr. Hadfield emphasizes that the information coming from the answers had no statistical validity and could show only trends of thought and a wide variety of ideas. Out of the valid replies 2,486 (35%) contained no comment. In

TABLE IV.—Analysis of Senior Registrars' Replies to Questions 5 and 6

Senior Registrars	General Medicine, General Surgery, Obstetrics and Gynaecology	Other Specialties	Total
Question 5 { Yes ..	212	488	700
{ No ..	65	175	240
Question 6 { Yes ..	189	474	663
{ No ..	48	87	135
{ Don't know	23	67	90

TABLE III.—Analysis of S.H.M.O.s' Replies to Questions 5 and 6

S.H.M.O.s	General Medicine, General Surgery, Obstetrics and Gynaecology	Other Specialties	Total
Question 5 { Yes ..	7	121	128
{ No ..	4	94	98
Question 6 { Yes ..	8	144	152
{ No ..	3	32	35
{ Don't know	—	22	22

TABLE I.—Replies by Consultants, S.H.M.O.s, and Senior Registrars to Questions 5 and 6

		Consultants	S.H.M.O.s	Senior Registrars	Totals
Question 5					
Do you support the continuation of special distinction awards (whether on the present or on some revised system)?	Yes	4,444	128	700	5,272
	No	1,445	98	240	1,783
Question 6					
Do you consider that the present system requires any change?	Yes	3,824	152	663	4,639
	No	1,500	35	135	1,670
	Don't know	421	22	90	533

TABLE II.—Analysis of Consultants' Replies to Questions 5 and 6

		Aged 50 and Over			Aged Under 50			Age not Stated			Grand Total
		Gen. Med., Gen. Surg., Obst. and Gyn.	Others	Total	Gen. Med., Gen. Surg., Obst. and Gyn.	Others	Total	Gen. Med., Gen. Surg., Obst. and Gyn.	Others	Total	
Consultants with Distinction Awards											
Question 5	{ Yes	559	794	1,353	174	343	517	25	57	82	1,952
	{ No	29	52	81	7	18	25	4	4	8	114
" 6	{ Yes	225	391	616	78	161	239	16	34	50	905
	{ No	310	375	685	89	154	243	8	25	33	961
	{ Don't know ..	49	78	127	11	44	55	5	2	7	189
Consultants without Distinction Awards											
Question 5	{ Yes	169	754	923	333	1,149	1,482	16	55	71	2,476
	{ No	125	434	559	126	602	728	7	33	40	1,327
" 6	{ Yes	221	907	1,128	344	1,348	1,692	19	69	88	2,908
	{ No	44	157	201	79	237	316	4	11	15	532
	{ Don't know ..	14	80	94	26	107	133	—	4	4	231
Consultants who did not disclose Award status											
Question 5	{ Yes	3	4	7	2	5	7	—	2	2	16
	{ No	—	1	1	—	3	3	—	—	—	4
" 6	{ Yes	1	3	4	—	7	7	—	—	—	11
	{ No	2	1	3	2	—	2	—	2	2	7
	{ Don't know ..	—	1	1	—	—	—	—	—	—	1

British Medical Association

Proceedings of Council

A special meeting of the Council was held on 14 October to consider: (1) a report by the Secretary on discussions with Medical Management Services Limited since October 1964; (2) reports from the Association's advisers; and (3) a report of the General Medical Services Committee.

Dr. RONALD GIBSON was in the chair.

G.M.S. Committee's Report

Dr. J. C. CAMERON presented the following report and recommendations of a meeting of the G.M.S. Committee held in B.M.A. House, Edinburgh, on 12 October.

Medical Management Services Ltd.

The G.M.S. Committee considered a report on the B.M.A.'s dealings with Medical Management Services Ltd. since 1964.

The Committee also considered the following resolutions passed by the Representative Body in July 1967, which had been referred to it by Council:

Resolved (as an instruction to Council): That this Meeting instructs our negotiating team to reopen negotiations immediately with the Ministry for the reimbursement of payments made to wives or dependants actually working as ancillary help; particularly in the case of those

who have secretarial or nursing qualifications.

Resolved: That this Meeting instructs Council to determine the commercial value of the work done in general practice by dependent relatives.

Resolved: That this Meeting instructs Council to determine immediately the number of dependent relatives working in general practice, their qualifications, and their geographical distribution.

Resolved: That this Meeting considers that any pension contributions paid on behalf of ancillary staff should be partially reimbursed by the Government, and further that these pension rights should be transferable to any Government employment.

The Committee decided to take the highest expert advice so that it could itself undertake a fact-finding survey into the employment of related and unrelated ancillary staff to be followed by a proper commercial evaluation of the services of the former.

The Committee is quite clear, however, that whatever action might be taken at this stage in this way it could have no beneficial effect on the outcome of the review upon which the Review Body is about to embark.

The Committee is confident that the Council will lend its full support to the way in which it has decided to give effect to the appropriate resolutions of the A.R.M. It has also had most careful regard to the considered views of counsel, and therefore recommends:

(1) That if M.M.S. proceeds with its stated intention of issuing a questionnaire to all general practitioners, and if as a result doctors inquire of the B.M.A. what their attitude should be to it, they should be advised to consult their own accountants and also be informed that their

answers can have no effect on the current deliberations of the Review Body.

(2) If M.M.S. in their circular should give the impression that their inquiry has B.M.A. backing steps should be taken at once to send a suitable letter to all general practitioners disclaiming any such support.

Resolutions of Council

After a lengthy debate in private the Council approved the report of the G.M.S. Committee, and it endorsed the Committee's decision to undertake a fact-finding survey into the employment of related and unrelated ancillary staff and a commercial evaluation of the services of related staff.

The Council also resolved as follows:

(1) That if Medical Management Services proceeds with its stated intention of issuing a questionnaire to all general practitioners, and if as a result doctors inquire of the B.M.A. what their attitude should be to it, they should be advised to consult their own accountants and also be informed that their answers can have no effect on the current deliberations of the Review Body.

(2) If Medical Management Services in their circular should give the impression that their inquiry has B.M.A. backing a suitable letter should be sent to all general practitioners disclaiming any connexion between that circular and the questionnaire to be issued by the British Medical Association.

(3) That the B.M.A. should not support Medical Management Services Ltd. at the present time.

Inner London Executive Council

In a foreword to the Annual Report of the Inner London Executive Council for the year ended 31 March 1967 Mr. G. F. Rowe, the chairman, writes that the council's services had undergone a major upheaval in recent months as a result of the new remuneration system for general practitioners. He thought the new methods of payment seemed to provide "a very satisfactory outcome for the doctors." In addition to an increase in their gross receipts they should derive considerable advantages from the arrangements for direct reimbursement of rent and rates on their practice accommodation. Mr. Rowe pointed out that doctors had often said money was not their first concern, and he thought this contention might be supported by the fact that several months after the new arrangements had been introduced 200 doctors out of some 1,500 whose main practices were in the council's area had failed to ask for reimbursement of their rent and rates.

London doctors were now showing "a keen interest in health centres." New health centres in Camden, Hackney, and Hammersmith had reached an advanced stage of planning, and the Grove Centre, Hammersmith, had been approved by the Ministry of Health. Twenty-three other possible projects were being considered. The planning of the health services in Thamesmead, the area of the Woolwich and Erith marshes to be developed by the Greater London Council for 60,000 people, had continued, and Mr.

Rowe paid special tribute to the work done on it by the General Practice Research Unit of Guy's Hospital.

Some Figures

The report states that the number of general practitioners on the Inner London Executive Council's medical list decreased during 1966-7 by 50 to 2,212. The number of patients included on general practitioners' lists during the year decreased from 3,465,685 to 3,445,379. Many people were said to have had difficulty in finding a doctor willing to accept them. At 31 March 1967 the average number of patients on a doctor's list, whether resident within or without the council's area, was 2,342. That compared with 2,238 in 1964, 2,290 in 1965, and 2,329 in 1966.

The council had inspected all proposed new surgeries, and the inspection was normally done by an officer of the council accompanied by an officer or member of the local medical committee. The Ministry of Health's standards of practice accommodation were applied as a guide, but with "considerable latitude" in view of the difficulties of finding accommodation in London.

By the end of March 716 claims for rent and rates for 853 surgeries amounting to £55,819 had been paid for the December quarter. Most of the claims were on an interim basis, but for 72 premises the district

valuer's assessment of a notional current market rent was received in time to pay on a permanent basis. Reminders were sent to 151 doctors who had not claimed their payment for the December quarter. By the end of the year 1,138 applications had gone to district valuers, and in 436 instances the current market rent, notional rent, or apportionment of the gross rateable value had been determined.

During the year there were 173 cases of attempts to obtain drugs by irregular means. There were 190 cases in the previous year. In 28 cases prescription forms were stolen from doctors' cars or surgeries.

Journal Committee Chairman

Professor Sir Alan Moncrieff was elected chairman of the Association's Journal Committee at its first meeting of the session on 11 October, in succession to Dr. J. G. M. Hamilton. Dr. Hamilton retired from the Committee at the end of last session. He had been 13 years in the chair.

Sir Alan Moncrieff has been a member of the Journal Committee since 1952, and before that he had been a member of its Publishing Subcommittee for many years, and chairman from 1950.

Armed Forces Committee

The Armed Forces Committee held its first meeting of the session on 9 October. Major-General J. C. BARNETSON was re-elected Chairman.

Dispute with Ministry

The CHAIRMAN reminded the Committee that since March the Association had withheld from the B.M.F. all advertisements for medical posts in the armed Forces, and that deans of medical schools had been informed that the B.M.A. could no longer recommend a career for doctors in the Services (*Supplement*, 1 April, p. 5).

These sanctions had been applied by the Association after the breakdown of the negotiations between the Government and representatives of the profession on the pay of doctors in the armed Forces.

Surgeon Commodore N. S. HEPBURN said that there was an overall shortage of doctors in the Navy, and it was worst among those with short-service commissions. Direct entry to short service, as opposed to ex-cadet entry, was falling off. The number of doctors transferring from the short-service list to the permanent list had also fallen off badly, and if this continued the position would become acute. The cadet entry continued to be satisfactory.

Surgeon Captain R. W. DUNCAN, also said that the problem had been that there were too few short-service officers. How-

ever, the Navy was now losing doctors from the regular corps. The short-service, non-specialist medical officers provided the majority of sea-going doctors, particularly in the smaller ships, and this was where sacrifices were now having to be made.

Colonel A. D. YOUNG said that the Army was facing the most serious situation in its history. A deficiency in medical officers had been increasing since 1962, and since then the number of medical officers who had voluntarily retired had also increased. The specialist services were generally at full strength, but a shortage of general-duty officers meant that the medical service was unable to meet all its commitments.

Air Vice-Marshal E. S. SIDNEY said that there was a current deficiency of 60 doctors in the Air Force, though the position was alleviated by the employment of civilian doctors. Air Force doctors thought there was no longer a rewarding career in the Services, at least financially. However, at present the Air Force was able to fulfil all its commitments. Surgeon Captain P. G. BURGESS wondered whether pay was the most important factor in recruitment. Air Vice-Marshal SIDNEY suggested that the uncertainty caused by the run-down in the armed Forces influenced the situation, and there was also loss of confidence in the present Government as an employer.

Colonel YOUNG, asked what doctors leaving the armed Forces did, replied that most

stayed in Britain and took jobs in the National Health Service with salaries equivalent to those they received in the Forces, and they also took their Service pension with them.

Reserve Army

Mr. R. MYLES GIBSON said that there was a serious lowering of morale in the Territorial Army and Army Volunteer Reserve. It was not a question of pay. There had been changes such as the reorganization of units and a consequent reduction in the number of senior appointments, and the rank and promotion structure had been adjusted.

The week-end training schemes, continued Mr. Myles Gibson, which were implicit in the new regulations for the reserve Army, occupying two week-ends a year, had not been entirely successful this year. Many busy general practitioners and hospital doctors had asked whether it was essential for them to attend the training camps. There was also the question of uniform, said Mr. Myles Gibson. The reserve Army still wore battle-dress, and as a result they felt "second-rate citizens" by comparison with their colleagues in the regular Army. He hoped those matters could be investigated.

Colonel YOUNG said that the next annual conference of the Territorial and Army Volunteer Reserve would be held in January 1968, when these points could be discussed.

Association Notices

Diary of Central Meetings

OCTOBER

- | | | |
|----|--------|--|
| 21 | Sat. | Central Committee for Hospital Medical Services, 10 a.m. |
| 24 | Tues. | Joint Consultants Committee (at Royal College of Physicians and Surgeons of Glasgow, 242 St. Vincent Street, Glasgow), 10 a.m. |
| 25 | Wed. | Council, 9 a.m. |
| 26 | Thurs. | G.M.S. Committee, 10.30 a.m. |
| 26 | Thurs. | S.H.M.O. Group Council, 2 p.m. |
| 31 | Tues. | G.M.S. Committee Hospitals Working Group, 12 noon. |

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

ABERYSTWYTH DIVISION.—At Old Maternity Hospital, Saturday, 21 October, 7.30 for 8 p.m., Dr. L. Davies: "Modern Methods of Investigating Heart Disease."

ASHTON, HYDE, AND GLOSSOP DIVISIONS.—At Deanwater Hotel, Woodford, Thursday, 26 October, 8 for 8.30 p.m., joint annual dinner and dance.●

BIRMINGHAM DIVISION.—At 36 Harborne Road, Edgbaston, Tuesday, 24 October, 8.30 p.m., jointly with A.B.P.I., symposium by Sir Derrick Dunlop (chairman), Professor O. L. Wade, Dr. S. Wand: "Prescribing Today."

BOURNEMOUTH DIVISION.—At Postgraduate Medical Centre, Friday, 27 October, 7.30 for 8 p.m., jointly with Bournemouth and District Law Society, buffet supper, Dr. C. T. Brown: "Antarctic Expedition."●

BROMLEY DIVISION.—At Bull Hotel, Chislehurst, Wednesday, 25 October, 7 for 7.30 p.m., jointly with Bromley and District Law Society, annual medical-legal dinner.●

BURNLEY DIVISION.—At Mackenzie Medical Centre, General Hospital, Friday, 27 October, 8.30 p.m., Dr. J. D. N. Nabarro: "Recent Trends in Diabetes Mellitus."

BURTON-ON-TRENT DIVISION.—At Stanhope Arms, Tuesday, 24 October, 7 for 7.30 p.m., jointly with B.D.A., dinner followed at 8.45 p.m. by Mr. P. Doherty: "Close Suppl. Dentistry."●

CITY DIVISION.—At Moorfields Hospital, City Road Branch, Tuesday, 24 October, 8.15 p.m., programme of illustrated lectures followed by discussion. (Preceded by buffet supper, 7.30 p.m.)

EALING DIVISION.—At Skyway Hotel, Thursday, 26 October, 8.30 for 9 p.m., annual dinner dance.●

EASTBOURNE DIVISION.—At Mansion Hotel, Tuesday, 24 October, 8.30 p.m., jointly with Eastbourne Law Society. Miss Celia Hensman and Mrs. Ann Hawker: "New Thinking on Alcoholism."

MAIDSTONE DIVISION.—At Medway Hotel, Friday, 27 October, 8 for 8.30 p.m., B.M.A. lecture by Professor A. Kekwick: "Obesity."

MEDWAY AND GRAVESEND DIVISION.—At Medway Postgraduate Medical Centre, Medway Hospital, Gillingham, Wednesday, 25 October, 8.30 p.m.; Mr. A. M. B. Tomkin: "Bleeding Peptic Ulcer."

MID-ESSEX DIVISION.—At Broomfield Hospital, Chelmsford, Saturday and Sunday, 28-29 October, 9.30 a.m., jointly with Chelmsford Medical Society, symposium: "Disabilities in Middle Age." (Applications should be made to the Secretary, Medical Academic Unit, Chelmsford and Essex Hospital.)

MID-GLAMORGAN DIVISION.—At Seabank Hotel, Porthcawl, Thursday, 26 October, 7 for 7.30 p.m., supper meeting, Chairman's address by Dr. J. Wynne Morgan, and election of representatives to Annual Representative Meeting.●

REDBRIDGE AND STRATFORD DIVISIONS.—At Forest Gate Hospital, 28-29 October, weekend postgraduate course in midwifery, gynaecology, and neonatal medicine for general practitioners. Applications should be made to the secretary of the hospital.

REIGATE DIVISION.—At Town Hall, Tuesday, 24 October, 8 p.m., short business meeting; 8.30 p.m., wine and cheese party for members and wives.

SOMERSET DIVISION.—At Board Room, Musgrove Park Hospital, Taunton, Thursday, 26 October, 8 p.m., four recent medical films and business meeting to elect representatives to Representative Body.

SOUTH BEDFORDSHIRE DIVISION.—At Luton Medical Centre, Tuesday, 24 October, 8.30 p.m., Boehringer lecture by Professor Sheila Sherlock: "Hepatic Cirrhosis."

SOUTH WALES AND MONMOUTHSHIRE BRANCH.—At Glan Ely Hospital, Cardiff, Thursday, 26 October, 3 p.m., jointly with Cardiff Division, clinical demonstrations by Dr. John Pathy: "Rehabilitative Techniques for use with the Elderly."

SOUTHAMPTON DIVISION.—At Postgraduate Medical Centre, Wednesday, 25 October, 8 for 8.30 p.m., Mr. A. Lawrence Abel: "The Life and Times of John Hunter—Medicine 200 Years Ago." Followed by wine buffet. Guests are invited.●

SUNDERLAND DIVISION.—At Medical Society Lecture Room, Sunderland General Hospital, Tuesday, 24 October, 8.15 p.m., Mr. R. M. Kalbag: "Cervical Spondylosis."

BIRMINGHAM REGIONAL HOSPITAL MEDICAL SERVICES COMMITTEE.—At Queen Elizabeth Hospital, Tuesday, 24 October, 5.15 p.m., meeting.

LEEDS REGIONAL HOSPITAL JUNIOR STAFFS GROUP.—At Clinical Lecture Theatre, General Infirmary at Leeds, Wednesday, 25 October, 7.30 p.m., annual open meeting.

WELSH REGIONAL CONSULTANTS AND SPECIALISTS.—At 195 Newport Road, Cardiff, Sunday, 29 October, 2.30 p.m., annual general meeting, followed by meeting of the Committee.

British Medical Journal Supplement

LONDON SATURDAY 28 OCTOBER 1967

CONTENTS

Joint Annual Meeting : Provisional Programme - - - - -	25	H.M. Forces - - - - -	28
Retirement Pensions - - - - -	26	Diary of Central Meetings - - - - -	28
Public Health Committee - - - - -	27	Branch and Division Meetings - - - - -	28

British Medical Association

Joint Annual Meeting with the Australian Medical Association, Associated with the Third Australian Medical Congress, Sydney, 12-16 August 1968

President-Elect: C. O. F. RIEGER, C.B.E., M.B., B.S., F.R.C.S.ED., F.R.A.C.S.

President of Congress: R. H. MACDONALD, O.B.E., M.B., M.S., F.R.A.C.S., F.R.C.O.G.

Chairman of Scientific Committee: Professor JOHN LOEWENTHAL, M.B., M.S., F.R.C.S., F.R.A.C.S., F.A.C.S.

Secretary of Congress: NICHOLAS LARKINS, M.B., B.S.

Executive Officer of Congress: E. RUSSELL BELL, M.V.O., D.F.C., A.F.C., 135 Macquarie Street, Sydney, New South Wales.

Provisional Programme

The 136th Annual Meeting of the British Medical Association will be held in Sydney jointly with the Australian Medical Association and in association with the Third Australian Medical Congress. A cordial invitation to any B.M.A. member to attend the Congress is extended by its Executive Committee. This is only the second occasion on which the Association has met in Australia, the previous one being in Melbourne in 1935, before the formation of the Australian Medical Association.

The Joint Annual Meeting and Congress will be opened officially on Monday evening, 12 August, at the Town Hall, and it will be followed by the President's reception at the Trocadero.

It is expected that the social programme will include a civic reception, a State garden party, the President's dinner and other dinners, and a congress ball on the final evening.

The Henry Simpson Newland Oration will be given by Sir Hugh Ennor on Thursday evening, 15 August.

Church services will be held on Sunday morning, 11 August, and a Jewish service will be held on Saturday morning, 10 August.

Sporting activities have been arranged for Saturday afternoon, 10 August, and golf competitions will take place on Wednesday afternoon, 14 August.

Details of the Ladies' Programme will be announced later.

Registration

Registration for the Joint A.M.A.-B.M.A. Meeting will take place all day on Saturday, Sunday, and Monday, 10, 11, and 12 August, and the Scientific, Pharmaceutical, and Hobbies Exhibitions will be open daily from Monday, 12 August, to Friday, 16 August.

Advance registration forms together with hotel lists will be sent early in 1968 to B.M.A. members who notify the Secretary of the B.M.A. of their interest. The registration fee is £10 (sterling) for members and £4 sterling for associates (ladies or members of family aged over 18 accompanying members). The fee includes attendance at the various dinners on 13 August and at the Congress ball.

Other Meetings

The Joint Meeting will be preceded by the following meetings: Meeting of the Council of the Commonwealth Medical Association, Canberra, 1 to 2 August.

The World Medical Association, Twenty-second World Medical Assembly, Sydney, 5 to 10 August.

Hotel Accommodation

Tariffs for hotels at which reservations have been made for the Joint Meeting range from \$A4.75 (single) to \$A9.50 (double) in a private hotel and from \$A14.50 (single) to \$A18.50 (double) in a luxury hotel for room only. The "official hotel" is the New Wentworth Hotel. (Note: \$A=approximately 8s. sterling.)

Travel Arrangements

It is expected that members attending the Meeting will wish to visit places en route. The Medical Insurance Agency Travel Department has prepared an itinerary based on a round-the-world journey by air which can be offered to a group at an inclusive tour rate which is considerably less than the normal fare and cost of accommodation.

If sufficient bookings are received two groups will be arranged—one travelling to Sydney by an eastern route and the other by a western route. Starting from London, the group going by the eastern route will stay in Colombo (four nights); Singapore (two nights); Hong Kong (three nights); Sydney (nine nights); Auckland, New Zealand (four nights); Fiji (four nights); and San Francisco (three nights). The group going by the western route will take the journey in reverse. Both parties will meet in Sydney on 7-8 August. At all places to be visited, with the exception of Sydney, sightseeing tours will be organized, and whenever possible visits to medical institutions will be arranged.

The round-the-world tours will be offered at an inclusive cost to cover economy-class air travel by scheduled flights, transport to and from airports to hotels, accommodation in first-class or de luxe hotels with demi-pension, and local sightseeing tours, except in Australia.

Pending confirmation of certain local charges, the tours will be offered at an inclusive cost of approximately £600 for each person. A detailed itinerary with the exact costing will be available within the course of the next few weeks.

Those interested may write for details to the Medical Insurance Agency Travel Department, B.M.A. House, Tavistock Square, London W.C.1. (Tel.: 01-387-8486).

Provisional Scientific Programme

The theme of the Scientific Programme will be "A Review of Australian Medicine as at 1968," and the topics for the morning plenary sessions will be "The Advantages of Modern Technology," "Research—The Growing Edge," "How Many Doctors?," and "Back to Work." On three afternoons there will be group or section meetings arising out of the plenary sessions, but the meetings on Wednesday afternoon will be given to a free choice of subjects by sections.

There will be scientific and pharmaceutical exhibitions and daily showings of medical films. Closed circuit television will be shown on Monday and Thursday afternoons, 12 and 15 August.

Provisional Time-table

Saturday, 10 August

9 a.m. to 5 p.m.—Registration office and social centre open.
9.45 a.m.—Jewish religious service.
Afternoon.—Golf, racing, bowls, etc.
Evening.—Private arrangements.

Sunday, 11 August

9 a.m. to 5 p.m.—Registration office and social centre open.
10.30 a.m.—Robing for church services.
11 a.m.—Church services (Anglican, Presbyterian/Methodist, Roman Catholic).
Afternoon.—Private arrangements.

Monday, 12 August

9 a.m. to 5 p.m.—Congress office opens, registration office and social centre, Museum and Scientific Exhibitions, Photographic and Hobbies Exhibitions open.
10 a.m.—Opening of Trade Exhibition.
10.30 a.m. to 1 p.m.—Film Festival.
2 p.m. to 3 p.m.—Film Festival.
3.30 p.m. to 5 p.m.—Closed circuit colour television.
8.15 p.m. for 8.30 p.m.—Inaugural Meeting B.M.A.—A.M.A. and Congress. Joint Annual Meeting, opening of Congress, and Adjourned Annual General Meeting of the B.M.A., followed by reception.

Tuesday, 13 August

9 a.m. to 5 p.m.—Congress office and social centre open. Trade Exhibition, Museum and Scientific Exhibitions, Photographic and Hobbies Exhibitions open.
9.15 a.m. to 1 p.m.—Film Festival.
2 p.m. to 4.30 p.m.—Film Festival.
9.15 a.m. to 12.45 p.m.—Plenary Session: "Research—the Growing Edge." (1) Immunity: (a) "Basic Theory of Immunity," (b) "Application to Organ Transplantation," (c) "Application to

Autoimmune Diseases," (d) "Application to Cancer." (2) Panel Discussion on Immunity. (3) "Prophylaxis of Foetal Damage." (4) "Kuru."

2.15 p.m. to 4.45 p.m.—Group and section meetings.

7.30 p.m.—President's dinner (by invitation only).

7.30 p.m.—Other dinners.

Wednesday, 14 August

9 a.m. to 5 p.m.—Congress office and social centre open. Trade Exhibition, Museum and Scientific Exhibitions, Photographic and Hobbies Exhibitions open.

9.15 a.m. to 1 p.m.—Film Festival.

2 p.m. to 3.30 p.m.—Film Festival.

9.15 a.m. to 12.45 p.m.—Plenary Session: "How Many Doctors?" (1) "The Educational Challenge." (2) "Community Demand for Doctors in the Next Decade." (3) "Student Selection." (4) "Student Training." (5) "General Practice Training and Distribution." (6) "Specialist Training and Distribution." (7) Panel Discussion—"Does Present Training Meet the Need?"

Afternoon.—Golf competitions. Combined and individual sectional meetings.

Evening.—Private arrangements.

Thursday, 15 August

9 a.m. to 5 p.m.—Congress office and social centre open. Trade Exhibition, Museum and Scientific Exhibitions, Photographic and Hobbies Exhibitions open.

9.15 a.m. to 1 p.m.—Film Festival.

2 p.m. to 4.30 p.m.—Film Festival.

9.15 a.m. to 12.45 p.m.—Plenary Session: "Advantages of Modern Technology." (1) "Diagnostic Use of Isotopes." (2) "The Use of the Heart-lung Respirator." (3) "Dialysis." (4) "Heart Valves." (5) "Corneas." (6) "Biomedics." (7) "New X-ray Techniques."

2.15 p.m. to 4.45 p.m.—Groups and sections.

3.30 p.m. to 5 p.m.—Closed circuit colour television.

5 p.m.—Reception.

8.30 p.m.—Henry Simpson Newland Oration by Sir Hugh Ennor.

Friday, 16 August

9 a.m. to 5 p.m.—Congress office and social centre open. Trade Exhibition, Museum and Scientific Exhibitions, Photographic and Hobbies Exhibitions open.

9.15 a.m. to 1 p.m.—Film Festival.

2 p.m. to 4.30 p.m.—Film Festival.

9.15 a.m. to 12.45 p.m.—Plenary Session: "Back to Work." (1) "Legal Impediment." (2) "Government Responsibility." (3) "Psychiatric Impediment." (4) "Spinal Injuries." (5) "Cardiac Disorders." (6) "Industrial Action." (7) "Appliances."

2.15 p.m. to 4.45 p.m.—Groups and sections.

9 p.m.—Congress Ball.

Retirement Pensions

A revised Ministry of Health leaflet (S.D.M., 1967) published in April aimed to explain in more detail the special provisions of the N.H.S. Superannuation Scheme (England and Wales) for doctors and dentists in general practice set out in the National Health Service (Superannuation) (Amendment) Regulations, 1966 (*Supplement*, 10 December 1966, p. 222).

Paragraph 24 of the leaflet read: "The retirement pension is calculated as in the following Table, subject to a reduction to take account of the National Insurance pension."

Financial Years (i.e., years ended 31 March) During Which There was some Service as a Practitioner	Percentage of Remuneration Paid in Those Years
The first 10 such years	1½ per cent.
The second 10 such years	1½ per cent.
The third 10 such years	2 per cent.
The fourth 10 such years	2½ per cent.
Any such years after the fortieth	2½ per cent.

"For a practitioner with service before 15 December 1966 the pension will be 1½ per cent. of superannuable remuneration paid before 1 September 1962, and 1½ per cent. of that paid subsequently, if that would be to his advantage."

The Superannuation Division of the Ministry of Health has now issued a statement to clarify the words "subject to a reduction to take account of the National Insurance pension" in paragraph 24. The statement is as follows:

"The retirement pension payable to, and the contributions payable by, contributors to the National Health Service Superannuation Scheme are reduced (modified) to take account of retirement benefits payable under the National Insurance Acts. Practitioners who joined the scheme on 5 July 1948 have no reduction in their contributions or benefits. With a very few exceptions, all prac-

tioners who joined the scheme after 5 July 1948 will have their contributions and benefits reduced as follows: Contributions are reduced by £3 0s. 8d. a year for men and £3 5s. a year for women, except that these reductions are doubled in the case of practitioners who are regarded for National Insurance purposes as self-employed. Pensions are reduced from age 65 (men) or age 60 (women) by £1 14s. for each year of service. For the extremely small number of practitioners who participate in the graduated pension scheme there is a further reduction of superannuation contributions and pensions to take into account any graduated pension earned. If a practitioner has a payment in lieu of graduated National Insurance contributions made on his behalf he receives from the Ministry of Health's Superannuation Division a letter explaining the further reduction in his pension which this will entail."

Public Health Committee

An offer from the Management Side of Whitley Committee C in response to the public health medical officers' salary claim was considered to be unacceptable. Negotiations are to continue.

The eradication of brucellosis was once again discussed by the Public Health Committee. The Committee believes that the Ministry of Agriculture, Fisheries and Food's voluntary system of registration will not work and that there should be a phased slaughter scheme, and it doubts whether the cost of that would be prohibitive. Discussion is to continue on this and on the provision of lavatories on main roads. The B.M.A. wants the cost of providing main-road sanitary accommodation to fall more on central rather than local government.

The Public Health Committee held its first regular meeting of the session on 11 October. Dr. C. METCALFE BROWN was re-elected Chairman of the Committee, and Dr. C. D. L. LYCETT was elected Deputy Chairman.

Salary Claim

The Committee considered an offer from the Management Side of Committee C of the Medical and (Hospital) Dental Whitley Council in response to the public health medical officers' salary claim (*Supplement*, 23 September, p. 136). The Committee was informed of the views of the Staff Side of Committee C on the offer.

After a long debate the Committee agreed that the offer was unacceptable as it stood, and that negotiations should be continued.

Employment of Children

The Committee considered correspondence between the Education Welfare Officers National Association and the B.M.A. about the employment of children, and a memorandum on the subject by Dr. J. D. Kershaw.

It was recommended in the memorandum that children under the age of 14 should be medically examined if they were doing morning work, such as paper rounds. Dr. KERSHAW explained that that applied to morning and not to evening work, because the danger in morning work was that children might miss their breakfast.

Dr. A. MACARA pointed out that the children who did not have a breakfast were probably also those who did not go to bed early, because they came from badly organized homes. Many children aged 12 to 13 in good homes could do a morning or evening job without any ill effects.

The Committee decided to recommend the setting up of a joint committee with the Society of Medical Officers of Health to consider the matter of the employment of children.

Tees-side

Dr. J. T. A. GEORGE explained to the Committee that the regional constituencies of the Public Health Committee were based on the regional offices of the Association, but those members in the Tees-side Branch, and covered by the Tees-side Branch office of the Association, did not for Public Health Committee electoral purposes come within the Leeds or the North of England constituencies.

The Committee decided that members in this area could choose to be in whichever constituency they wished.

Sanitary Accommodation

The Committee discussed a letter from the Ministry of Health concerning sanitary accommodation on main roads.

The Association had drawn the attention of the Ministry of Health to what the B.M.A. considered to be the Ministry's lack of appreciation of the extent of the problem of providing enough lavatories on main roads. Much more money was needed from central Government for these facilities, the cost of which now fell heavily on local authorities. A figure of £61,000 had been estimated as the cost of providing two lavatories at each end of one main road. The Ministry had been prepared to grant only £3,000.

The letter from the Ministry stated that the Ministry of Housing and Local Government and the Ministry of Transport had been "puzzled" because £61,000 seemed to be an exceptional amount for two lavatories in a lay-by.

Dr. LYCETT explained that that figure included all the facilities, including access roads and half an acre of parking, and buying the land, etc. Unless it was done properly the job was not worth doing. There must be ways of disposing of refuse and satisfactory water points. Dr. Lycett hoped that the Association's policy would be to continue to press for more sanitary accommodation on main roads.

The Committee agreed that it should discuss the matter again in six months.

Brucellosis

The Committee considered an extract from the minutes of a meeting of the joint committee of the British Medical Association and the British Veterinary Association which discussed the eradication of brucellosis.

Gratification was expressed that the Ministry of Agriculture had made a start towards the eradication of brucellosis, and the joint committee had carried unanimously the following resolutions:

(1) That until brucellosis is eradicated from cattle measures should be taken to protect the human population. The most effective one would be the compulsory pasteurization of all milk from infected herds, and the prohibition of the sale of raw milk from any but accredited herds.

(2) That a financial incentive to farmers should be introduced in the form of a differential payment for milk from herds known by the Ministry of Agriculture, Fisheries and Food to be free from brucella infection.

These views had been forwarded to the Ministry of Health and to the Ministry of Agriculture, Fisheries and Food. The Ministry of Health had indicated that it had "no doubt that all milk should be heat treated before consumption." There were, however, certain practical difficulties in requiring the compulsory heat treatment of milk before sale. The Ministry had stated that "geographical difficulties in some parts of the country have made it impossible to achieve at an economic price the redistribution of heat-treated milk to remote areas. Some of

the difficulties may now be resolvable by the development of longer-keeping milks, and with this in mind we are taking a new look at the problems involved. Whether or not legislative action is found to be feasible we should like the public to be more aware of the potential dangers involved in drinking raw milk."

The Committee also considered a letter from Dr. George setting out the reasons why he believed this problem was being tackled in the wrong way. He said that the Government scheme was a voluntary scheme of registration. He did not think any voluntary scheme would work, because only a minority of farmers and not all veterinary surgeons appreciated the problems associated with eradication of the disease. On 26 July the Minister of Agriculture, Fisheries and Food had reaffirmed his faith in a voluntary scheme to begin with.

In Dr. George's view the Minister's concept of islands of brucellosis-free herds in a sea of infection was quite unrealistic. The spread of infection in cattle was extremely easy but often difficult to trace, and the Minister did not say how he would prevent the spread of infection at agricultural shows, in cattle transport, etc. Dr. George said that he doubted whether these infection-free islands would exist for long, let alone get bigger and coalesce.

Wrong Approach

The other reasons Dr. George gave for believing that the problem was being wrongly tackled were as follows. (1) There was no ban on the sale of infected beasts, and he doubted whether without such a ban any scheme would work. (2) There were no plans to circularize farmers with an explanatory brochure about brucellosis. The state of ignorance of many farmers was surprising, said Dr. George, and he saw no reason why a brochure should not be issued by the Ministry of Agriculture, Fisheries and Food. (3) Strain 19 vaccine was still the linchpin of veterinary control in spite of serious doubts about it. He knew of no reason why vaccine could not be purchased from Holland.

Dr. George stated in his letter that in his opinion the Ministry of Agriculture, which had at last accepted in principle the need for eradication of brucellosis, was so alarmed by the alleged cost of a slaughter scheme that it was mistakenly embarking on a lengthy voluntary scheme of registration. This might never work, said Dr. George, and would ultimately prove more costly than the obvious alternative of a phased slaughter scheme by areas with compulsory registration and a ban on the sale or movement of infected beasts. The amount of money available would dictate the speed of the area eradication scheme.

The Committee agreed to consider the matter further at its next meeting in the light of a memorandum from Dr. George.

H.M. Forces

Major-General J. A. D. Johnston, O.B.E., M.C., late R.A.M.C., has been appointed Honorary Physician to the Queen, in succession to Major-General M. H. P. Sayers, O.B.E., late R.A.M.C., retired.

Colonel C. Weymes, T.D., R.A.M.C., T. & A.V.R. has been appointed Honorary Surgeon to the Queen, T. & A.V.R., in succession to Colonel R. Barraclough, M.B.E., T.D., tenure expired.

Surgeon Commander A. I. MacDougall and Surgeon Lieutenant-Commander M. MacLean, R.N.R., have been awarded the Royal Naval and Royal Marine Forces Reserve Decoration.

Appointments.—Wing Commander T. C. Dobie, O.B.E. (deputy director of aviation medicine, Ministry of Defence, with acting rank of Group Captain); Wing Commander W. T. Fothergill (anaesthetic duties, R.A.F. Hospital, Cosford); Wing Commander I. M. Ogilvie (senior medical officer, R.A.F. Changi, Singapore); Wing Commander D. I. Fryer, O.B.E. (liaison duties with U.S.A.F., British Defence Staffs, Washington, U.S.A.).

ROYAL NAVY

Surgeon Captains E. H. Murchison, O.B.E., E. B. Martin and P. O'Brien have been placed on the Retired List.

Surgeon Lieutenant-Commander J. E. D. MacLaren has been placed on the Emergency List.

Surgeon Lieutenant A. M. Ashby to be Surgeon Lieutenant-Commander.

ARMY

Surgeon Colonel E. W. Hayward, O.B.E., late Royal Horse Guards, has retired.

Colonel A. L. J. Webb, late R.A.M.C., has retired on retired pay.

ROYAL ARMY MEDICAL CORPS

Major J. S. Templeton has relinquished his commission, and receives a gratuity.

REGULAR ARMY RESERVE OF OFFICERS

Major-General J. C. Barnetson, C.B., O.B.E., late R.A.M.C., having attained the age limit, ceases to belong to the Reserve of Officers, retaining the rank of Major-General.

ROYAL ARMY MEDICAL CORPS

Colonel J. R. Horler, T.D., from T.A., to be Colonel.

Major K. J. Dalgliesh has resigned his commission.

Major P. Esmonde, M.C., from Active List, to be Major.

Major D. L. Nicholls, T.D., from T.A., to be Major.

Short Service Commission.—Major J. D. Garry, from Active List, to be Major.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

ROYAL ARMY MEDICAL CORPS

Majors J. S. G. Blair, T.D., and B. Devlin, O.B.E., have been granted the acting rank of Lieutenant-Colonel.

Major D. L. Hamblen, from T.A., to be Major.

Captain P. Hudgson has been granted the acting rank of Major.

TERRITORIAL ARMY

ROYAL ARMY MEDICAL CORPS

Major J. E. Dann Charles-Jones has resigned his commission.

TERRITORIAL ARMY RESERVE OF OFFICERS:

ROYAL ARMY MEDICAL CORPS

Major E. D. Edmondson has resigned his commission and has been granted the honorary rank of Lieutenant-Colonel.

Major H. J. Bell, M.B.E., T.D., has resigned his commission, retaining the rank of Major.

Majors G. R. Fryers and H. J. Fisher have resigned their commissions.

Captain (Honorary Major) J. C. Fletcher, T.D., has resigned his commission, retaining the honorary rank of Major.

ROYAL AIR FORCE

Group Captain E. W. R. Fairley has retired. Wing Commanders A. B. Goorney, A. M. Kingon, M.B.E., and E. R. Griffiths, O.B.E., have retired.

Wing Commanders P. J. Grant and W. A. Crawford, O.B.E., have retired at their own request.

Squadron Leaders A. C. MacLachlan, C. C. G. Rawll, D. A. V. Bearblock, I. G. Currie, J. Cottam, A. F. Hignell, and M. H. Rogers to be Wing Commanders.

Squadron Leaders S. B. Lydon, R. J. Wrighton, R. P. Christian, and G. Mackie have been transferred to the Reserve.

Flight Lieutenants G. L. Smith, J. G. Paterson, and I. Chorlton to be Squadron Leaders.

M. S. Hughes to be Squadron Leader.

Association Notices

Diary of Central Meetings

OCTOBER

- 31 Tues. G.M.S. Committee Hospitals Working Group, 12 noon.

NOVEMBER

- 1 Wed. Chairman's Subcommittee (Full-time Medical Teachers and Research Workers Committee), 10 a.m.
1 Wed. Annual Meetings Committee, 12 noon.
1 Wed. Liaison Committee with the Royal College of General Practitioners (at Royal College of General Practitioners, 14 Princes Gate, London S.W.7), 4.30 p.m.
2 Thurs. G.M.S. Planning Working Group on Medical Care in Rural Areas, 2 p.m.
3 Fri. Ophthalmic Qualifications Committee, 1 p.m.
3 Fri. Assistants and Young Practitioners Subcommittee (G.M.S. Committee), 2 p.m.
3 Fri. Common Market Committee, 2 p.m.
3 Fri. Ophthalmic Group Committee, 2 p.m.
7 Tues. G.M.S. Committee (Scotland) (at 9 Lynedoch Crescent, Glasgow), 10.30 a.m.
7 Tues. Forensic Medicine Subcommittee (Private Practice Committee), 2 p.m.
8 Wed. Joint Formulary Committee, 10.30 a.m.
8 Wed. Charities Committee, 2.15 p.m.
14 Tues. Standing Subcommittee (Central Ethical Committee), 11 a.m.
14 Tues. G.M.S. Disciplinary Machinery Working Group, 2 p.m.
15 Wed. Committee on the Mental Health Act, 10.30 a.m.
15 Wed. Rural Practices Subcommittee (G.M.S. Committee), 2 p.m.

DECEMBER

- 13 Wed. Journal Committee, 2 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

CHESTERFIELD DIVISION.—At Grosvenor Rooms, Friday, 3 November, 8.30 p.m., Mr. P. D. Trevor-Roper: "Influence of Eye Diseases on the Artist" (illustrated). Followed by buffet supper.●
CITY OF EDINBURGH DIVISION.—At 7 Drumsheugh Gardens, Thursday, 2 November, 7.30 for 8 p.m., dinner. Guest of honour, Mr. Ludovic Kennedy.

CREWE DIVISION.—At Crewe Arms Hotel, Wednesday, 1 November, 8 p.m., annual general meeting.

DUMFRIES AND GALLOWAY DIVISION.—At Cresswell Maternity Hospital, Dumfries, Sunday, 5 November, 3 p.m., B.M.A. lecture by Professor Thomas McKeown: "The Redesign of Medical Services."

DARTFORD DIVISION.—At Joyce Green Hospital Study Centre, Tuesday, 31 October, 8 for 8.30 p.m., B.M.A. lecture by Wing Commander P. Howard: "Space Medicine." Guests are invited.

EAST HERTS DIVISION.—At Recreation Hall, Queen Elizabeth II Hospital, Welwyn Garden City, Thursday, 2 November, 8 for 8.15 p.m., clinical meeting by Mr. D. Bedford.

GREENWICH AND DEPTFORD DIVISION.—At Miller General Hospital, Wednesday, 1 November, 7.30 p.m., clinical meeting.

HAVERING DIVISION.—At Nurses' Lecture Room, Oldchurch Hospital, Romford, Friday, 3 November, 8.30 for 9 p.m., Dr. J. Horder: "What General Practice Can Be."

HEREFORD DIVISION.—At Board Room, Hereford County Hospital, Wednesday, 1 November, 8.15 p.m., meeting to discuss lengthening time-lapse for outpatient appointments.

LANCASTER DIVISION.—At Postgraduate Medical Centre, Monday, 30 October, 7.30 p.m., residents' evening.●

LEWISHAM DIVISION.—At Medical Centre, Lewisham Hospital, Friday, 3 November, 8.30 p.m., The Forward Edge of Research I lecture by Dr. A. Macrae: "Viruses and Virus Disease."

LONDON DERRY DIVISION.—At Board Room, Altnagelvin Hospital, Derry, Friday, 27 October, 8.15 p.m., Mr. D. Baird: "Rheumatoid Arthritis."

MORPETH DIVISION.—At Queen's Head Hotel, Morpeth, Wednesday, 1 November, 7.45 for 8 p.m., dinner followed at 9.15 p.m. by B.M.A. lecture by Mr. N. Leigh-Taylor: "In Defence of Doctors."

PERTH BRANCH.—At Station Hotel, Wednesday, 1 November, 8 p.m., B.M.A. lecture by Professor Henry Miller: "Accident Neurosis."

RENFREWSHIRE DIVISION.—At Brablock Hotel, Paisley, Wednesday, 1 November, 8 p.m., B.M.A. lecture by Professor W. Gissane: "Road Accidents—their Prevention and Disposal."

SOCIETY OF MEDICAL OFFICERS OF HEALTH: WELSH BRANCH.—At B.M.A. House, Newport Road, Cardiff, Friday, 3 November, 6.30 p.m., inaugural meeting followed at 7.30 p.m. (approximately) by extraordinary general meeting.

SOUTH STAFFS DIVISION.—At Park Hall Hotel, Wolverhampton, Thursday, 2 November, 8.45 for 9 p.m., annual supper dance.●

SWANSEA DIVISION.—At Langland Bay Hotel, Friday, 3 November, annual dinner. Guest of honour, Dr. Ronald Gibson (Chairman of Council, B.M.A.).

TUNBRIDGE WELLS DIVISION.—At Spa Hotel, Thursday, 2 November, 8 for 8.30 p.m., annual dinner-dance.●

WALSALL DIVISION.—At the Hollies Club, Cannock, Thursday, 2 November, joint supper meeting with Cannock Medical Society, Dr. B. L. Pentecost: "Acute Coronary Care."

Correction

The statement in the report of the Armed Forces Committee (*Supplement*, 21 October, p. 24) that there was "loss of confidence [among potential recruits to the armed Forces] in the present Government as an employer" was wrongly attributed to Air Vice-Marshal E. S. Sidey. We apologize to Air Vice-Marshal Sidey for any inconvenience that may have been caused to him.

British Medical Journal Supplement

LONDON SATURDAY 4 NOVEMBER 1967

CONTENTS

Proceedings of Council - - - - -	29	Surrey Public Health Appointment - - - - -	41
H.M. Forces - - - - -	35	Tuberculosis and Diseases of Chest - - - - -	41
Central Committee for Hospital Medical Services - - - - -	36	B.M.A. Nuffield Library - - - - -	41
General Practice Finance Corporation - - - - -	41	Association Notices - - - - -	42

British Medical Association Proceedings of Council

Preparation of evidence for the next review of doctors' pay by the Review Body is well in hand. The B.M.A. has lost some 2,000 members owing to the New Zealand Branch becoming independent. What the Private Practice Committee regarded as the Association's lack of support for private practice and for Independent Medical Services Ltd. was criticized by the Chairman of the Private Practice Committee. The Council recognized that the policy of extending private practice and of giving all practicable support to I.M.S. had been approved by the Representative Body, and it resolved to urge "resolute and continuous action in this respect by all concerned." The action to be taken will be considered in the light of a memorandum to be provided by the Private Practice Committee. Negotiations on the public health medical officers' salary claim are continuing. A motion that the B.M.A. should not assist Independent Medical Services Ltd. in respect of those aspects of its discount trading scheme that overlap existing activities which it is already Association policy to support was lost.

A meeting of the Council of the Association was held on 25 October. Dr. RONALD GIBSON was in the chair.

The CHAIRMAN announced that the Harrogate Division had accepted the nomination of Sir John Richardson, Bt., as President of the Association for 1971.

The Chairman reported that all past-presidents, with the exception of one or two who were unable to attend, had given a dinner to Sir Arthur Porritt, Bt., to celebrate his appointment as Governor-General of New Zealand, and to wish him well (*B.M.J.*, 21 October, p. 181).

The Chairman said that Mr. J. R. Nicholson-Lailey, the Editor, the Secretary, and himself had attended the XX1st World Medical Assembly in Madrid (*B.M.J.*, 23 September, p. 795). Dr. Stevenson had been elected to the Council of the World Medical Association.

Annual Representative Meeting

The Council received protests from the Cornwall, North Bedfordshire, and Liverpool Divisions about the manner in which the Agenda had been dealt with at the Annual Representative Meeting at Bristol.

The first two Divisions complained that not all sections of the profession had received a fair proportion of the time available for debate, and speaking for the Liverpool Division Dr. G. E. CRAWFORD referred to the waste of time in the Representative Body discussing matters which had also been referred to the Conference of Representatives of Local Medical Committees. He thought that if the Conference were held at about Easter time there would be more time for Divisions to make themselves aware of what the Conference had decided, and they might not need to send up similar motions.

Dr. J. S. NOBLE, Chairman of the Organization Committee, stated that his Committee was seized of the problem. The duplication of debate was a waste of time, and every effort would be made to deal with the problem when the Committee made its report on procedure.

Dr. A. SKENE suggested that it was not the duplication of debate that was the problem but rather the sense of unreality at the A.R.M. when matters were debated in the knowledge that they had already been debated by the Conference.

Dr. R. B. L. RIDGE pointed out that it would be impracticable to hold the Conference as early as Easter, because it would make the active part of the session far too short.

Dr. D. P. STEVENSON, Secretary, said that in future before the A.R.M. met every representative would receive a paper showing what action had been taken by the Conference.

Emigration

The CHAIRMAN reported that a letter had been received from the Ministry of Health informing the Association officially that the Department had decided to send a medical team to North America to encourage British doctors to return to work in this country.

Dr. J. E. MILLER said there was some misgiving among doctors that favourable treatment might be given to induce the doctors who had emigrated to return. The interests of those doctors who had stayed at home must be safeguarded.

Dr. A. N. MATTHIAS, Chairman of the Medical Practices Committee, gave Dr. Miller an unqualified assurance that general practitioners were appointed to practices on their merits, wherever they came from.

Helicopter Ambulance Service

As the result of a letter from Dr. A. J. MACLEOD (Outer Isles Division) calling for the establishment of a helicopter ambulance service, the Council decided to refer the matter to the Central Committee for Hospital Medical Services with a strong recommendation that it should press for the establishment of such a service.

Welsh Committee

The Council agreed that the Welsh Committee be renamed the Welsh Council, and that it should function on the same basis as the Scottish Council, provided that the Association was not involved in extra expenditure.

The proposal was passed to the Organization Committee for the necessary arrangements to be made, including amendment of the by-laws.

Gifts

The Council received with gratitude the following gifts to the Association:

A silver tray, presented by the Immediate Past-President, Professor Hamid Ali M. Khan.

A silver porringer, originally presented to the late Sir Kaye le Fleming by the doctors of Dorset, and presented to the Association by his son, Mr. Christopher le Fleming.

A silver condiment set from Sir Arthur Porritt.

Sainsbury Report

The Council received the *Report of the Committee of Enquiry into the Relationship of the Pharmaceutical Industry with the National Health Service* (Sainsbury Committee).

Dr. STEVENSON said that much of the report was a matter for the industry, but there were some items to which the attention of doctors should be drawn. For instance, there was a recommendation that the Minister of Health should consider bringing the general medical and pharmaceutical services within the definition of "services of the Crown" for purposes of Section 46 of the Patents Act, 1949. Secondly, the report recommended that in future brand names should disappear. Drugs would be known by their approved name. Another recommendation dealt with the appointment of a Medicines Commission. There was a difference between the recommendation of the Sainsbury Committee and the Government's intended legislation. The Sainsbury Committee recommended a Medicines Commission which should be independent, and should be plainly seen to be independent. But according to the Government's White Paper on forthcoming legislation on the safety, quality, and description of drugs the Medicines Commission was to be appointed by the Minister of Health. Further, the Minister reserved the right to make regulations, and the Medicines Commission would be an advisory body and not necessarily an executive body.

The Association, said Dr. Stevenson, had been invited to comment on the legislation now proposed in the light of the recommendations of the Sainsbury Committee.

Dr. RIDGE drew attention to paragraph 53 of the White Paper, which referred to the Ministers having power by statutory instrument to prohibit the supply or sale of a drug. "Before we know where we are drugs that we want to use for our patients will be denied to us by statutory instrument," he said. "This is a serious threat to the clinical freedom of the clinician, and I ask Council to take note of it."

Dr. I. M. JONES said it should be made clear to the Government that the Council deplored the unseemly haste with which a Bill was being introduced before proper consultation on the Sainsbury Report with the profession. Furthermore, serious consideration should be given to the threats to clinical freedom contained in the Sainsbury Report and in the proposed legislation.

The Council agreed to ask the *ad hoc* Committee, set up under the chairmanship of Dr. A. Skene to prepare evidence to the Sainsbury Committee, to look into the matter, in consultation with representatives of the Joint Consultants Committee, and to report back to the Council at its next meeting.

Resolutions of A.R.M. 1967

The Council dealt with a number of resolutions adopted by the Annual Representative Meeting in 1967, and not referred to elsewhere in the agenda, and motions not considered by the A.R.M.

Review Body

The CHAIRMAN reported that the Review Body had requested the submission of evidence for the next review of remuneration by the end of October, and the preparation of evidence was well in hand. The Joint Evidence Committee was meeting in November.

In reply to Dr. D. J. PEREIRA GRAY, Dr. J. C. CAMERON, Chairman of the G.M.S. Committee, said that the G.M.S. Committee was finding out the position in relation to the employment of non-related staff by general practitioners.

Deputation to G.M.C.

The CHAIRMAN said that a deputation consisting of Dr. J. C. Cameron, the Secretary, and Dr. R. A. Pallister had had a useful meeting with the General Medical Council

to discuss the implications of the case of a Polish medical practitioner whose temporary registration on the Foreign List of the *Medical Register* had been withdrawn upon her marriage to a British citizen.

The President of the G.M.C. had made it clear that his council was under an obligation to implement the provisions of the Medical Acts and could not depart from them. Any departure from the present procedure would require amending legislation. The deputation obtained an assurance that when legislation was imminent the B.M.A. would be asked to join in further discussions.

Reports of Committees

The Council then proceeded to consider the reports of the Standing Committees.

Hospital Medical Services

Mr. H. H. LANGSTON presented the report of the Central Committee for Hospital Medical Services (C.C.H.M.S.). Mr. Langston said that it had given further consideration, at the request of the Council, to the representation of the special Groups on the Committee. It had examined the possibility of an alternative method of representation, but it had come to the conclusion that the only acceptable solution was to continue the direct representation of the Groups as it at present existed.

The Committee was not prepared to reduce the number of seats reserved for representatives of regional committees, and there was no other section of the Committee in which more than marginal reductions could be made.

Mr. Langston said there were a number of items in the hospital doctors' "Charter" on which it had been found possible to reach satisfactory agreement with the Ministry. There remained the important question of the structure of hospital medical staffing. Discussions on that matter were proceeding. There was no intention of putting anything into effect without a document being circulated to all interested parties and a full discussion taking place. It was hoped that a report would be issued before the end of the year.

Referring to the appointment of medical assistants, Mr. Langston drew attention to a recommendation of the Committee that a working party should be set up, consisting of Dr. G. E. Owen Williams (chairman), Dr. A. Allison, Dr. D. Lloyd Griffiths, and Dr. E. A. Harvey-Smith, to consider (1) the particular problems of the medical assistant grade at the present time, and (2) the representation of the grade within the Central Committee for Hospital Medical Services and associated bodies.

The Committee had agreed to a proposal of the Joint Consultants Committee "Group of Nine" and of the health departments that in future the medical assistant grade should be known as the "assistant grade" and that individual doctors in the grade should be known as "assistant surgeon," "assistant physician," etc.

The report was approved and the recommendation adopted.

Organization

Dr. J. S. NOBLE presented the report of the Organization Committee. He said that it had been digesting the enormous meal of the constitution debate at the A.R.M., and there was little to add. The Committee was considering with the Agenda Committee the procedure at the Annual Representative Meeting, and was about to consider, in conjunction with its representatives, the resolutions and memorandum from the East Yorkshire Branch which were referred to the Organization Committee.

Membership

Dr. Noble said that current membership was 66,573, which compared with 69,676 at the same period last year. The loss of some 2,000 owing to the New Zealand Branch becoming independent had to be taken into account.

Dr. CRAWFORD drew attention to a recommendation of the Organization Committee concerning deputations to Council. The Committee recommended that after the reception of the deputation its members should be invited to make a statement, and members of Council, at the discretion of the Chairman, might put questions to the deputation. The Chairman of Council, or at his invitation a member of Council, should reply to the points raised by the deputation, but if it appeared to the Chairman of Council that the matter should first be debated the deputation should be asked to withdraw until the debate was concluded.

Dr. Crawford suggested that the fact that a deputation needed to come to the Council rather indicated a lack of communication between the Council and the periphery, and it would be impossible to get improved communication in an exercise which looked like a monologue rather than a dialogue. In his view its whole purpose would be wasted if the deputation were not allowed to ask questions. He accordingly moved the reference back of the recommendation.

Dr. H. G. DOWLER seconded the reference back.

Dr. NOBLE said he could not conceive of an occasion when the Council would not give a fair hearing to a deputation, and it would be unlikely that Council would not give a deputation an opportunity of replying to points raised.

Dr. H. FIDLER opposed the reference back. The Council must make a stand about what

it would do. If the deputation wanted answers to its questions it would doubtless get them, and the Council should not go beyond that.

Dr. CRAWFORD said that if a deputation had taken the trouble to come to the Council there was something desperately wrong somewhere in communications, and it was very important to get the communications put right.

The motion to refer back the recommendation was lost.

The Council unanimously accepted a recommendation of the Organization Committee that Dr. D. Stenhouse Stewart, of the East Yorkshire Branch, should be admitted to the Roll of Fellows of the Association.

The report was approved and the recommendation adopted.

Private Practice

Dr. I. M. JONES presented the report of the Private Practice Committee.

He recalled that it was more than a year ago that the Council passed the following resolutions:

(a) That, as a matter of urgency, Council impress upon the profession the gravity of the present crisis facing the medical services of this country and the serious danger of the establishment of a complete Government monopoly in the provision of these services; In addition, Council strongly supports and urges, by all means at the Association's disposal, continuing and increasing practicable support of the profession for Independent Medical Services Ltd. to ensure its consolidation and expansion as a viable alternative medical service available to the whole community.

(b) That, as a matter of urgency, honorary secretaries of branches and divisions be invited to call meetings to publicize the scheme produced by Independent Medical Services Ltd.

Dr. Jones added that no doubt members of Council had read the report of the recent meeting of the Private Practice Committee (*Supplement*, 7 October, p. 9). It was an accurate report which truly reflected the attitude unanimously adopted by that Committee. Its members were dismayed that action had fallen short of what it should have been.

Resolution (a) of the Council was really divided into two parts, said Dr. Jones. The first part was concerned with the dangers of a Government monopoly in medical services being created and with the need to do everything possible to encourage private practice. Resolution (b) was concerned specifically with Independent Medical Services Ltd. (I.M.S.), of which he was the chairman. It must be recorded with regret that, though a number of Divisions did call meetings to publicize I.M.S., and though on some occasions the Council was represented by a speaker other than himself, nevertheless there were many meetings at which no member of Council was present.

It was also sad to recall, continued Dr. Jones, that, though I.M.S. was set up with the support of the Representative Body and the Council, he had never been able to find a single letter to the profession as a whole, other than those written by himself, asking the profession to give the financial support to I.M.S. which it needed if the B.M.A.'s policy in respect of private practice was to be implemented.

The CHAIRMAN intervened to say that Divisions had been asked to assist, and he wondered how many had responded.

Dr. JONES replied that approximately 40 Divisions had done so.

The CHAIRMAN said that that was 40 out of some 300 Divisions. Referring to the Private Practice Committee's recommendation on the Council's agenda, he pointed out that it urged "resolute and continuous action" by all concerned. He asked Dr. Jones what more the Council or anyone could do.

Dr. JONES replied that, though the Council had accepted that to ensure the success of I.M.S. a fund of not less than £200,000 was needed, there had never been one official letter of appeal from the Association to the membership. A phrase which had been used to describe the project was "Ivor Jones's private army," and that was how it had been viewed by too many, but it was doubtful whether it would have been viewed in that way had there been a letter from the Association in support of its declared policy. "All I am asking is that the Council should be consistent," said Dr. Jones. "It is pointless to enunciate a policy and then fail to do what is necessary to carry it out."

Reference Back Moved

Dr. R. L. LUFFINGHAM moved the reference back of the following paragraph in the Private Practice Committee's report which preceded its recommendation:

The policy was affirmed by the Representative Body in July 1967. The Committee is dissatisfied with the action taken up to date to encourage private practice and to assist Independent Medical Services Ltd. It deplores the lack of support for this aspect of the policy of the Association.

Dr. G. R. OUTWIN seconded the motion.

Dr. LUFFINGHAM said the reason he asked for the reference back of the paragraph was that it was a vote of censure on the Council. There must be a fair amount of feeling—quite rightly—in the Private Practice Committee that the success of I.M.S. had not been so great as had been hoped. His feeling was that the Committee was raging at the wrong body and had inserted what he regarded as offensive words into its report to the Council. It deplored the lack of support for what was the policy of the Association.

Dr. Jones had made it clear that it was the Council which was in the dock, but he had not much of a case. The Council traditionally laid down principles and it remitted to the Committees the day-to-day work. Council gave I.M.S. the go-ahead at the appropriate time, and it had a board of management. So far as Dr. Luffingham was aware there had never been an occasion when Dr. Jones had asked for anything of the Council on behalf of I.M.S. when the Council had not done what was asked of it. "I submit that, far from Council having to set the pace and tell us how I.M.S. should be publicized and how money should be raised, it is for the Private Practice Committee with the information it has from I.M.S. to come before this Council to recommend specific action."

The Private Practice Committee was disturbed at the lack of support for I.M.S., and in Dr. Luffingham's view it was that which had led to the intemperate language. "Many of us are disturbed about I.M.S. because it

has not fulfilled what was hoped," he added, "but we are prepared to look for more radical reasons why it has not been satisfactory." Dr. Luffingham said that his branch had recently commissioned a questionnaire to be sent to all its members asking what support there was not only for I.M.S. but for a return to private practice in general practice. It was thought that there would be little support for the restoration of private general practice, and if that was the case it would explain why only 40 divisions out of 300 had called a meeting about I.M.S. "I think it is time that the Private Practice Committee had a careful look at the whole concept of I.M.S. and decided whether in fact its original remit was the right one," Dr. Luffingham concluded.

Dr. OUTWIN said he took the gravest possible exception to criticisms of the Council by the Chairman of I.M.S. (Dr. Jones) in his role as Chairman of the Private Practice Committee. In Dr. Outwin's view the Council must review its support of I.M.S. in the light of its changing appearance.

Dr. C. M. SCOTT said the Council was witnessing a somewhat curious attack on I.M.S. He was not particularly interested in defending all the ramifications of I.M.S. Indeed, there were one or two aspects of it with which he would personally disagree. But I.M.S. was the only possible solution, which the Council had backed, for producing an alternative medical service. Dr. Scott said he was not at all convinced that the root cause of the trouble lay with the Representative Body or with the Council. He thought it lay in the medical profession generally. The lack of increase in private practice was more due to lack of interest by doctors than to lack of demand by the public. With one notable exception, there was not only a complete disinterest in private practice but almost a disinclination to see it return in any shape or form. Until the idea of private practice could be sold to the medical profession it would be impossible to persuade the public, though a number were asking for the return of private practice and were experiencing difficulty in finding a doctor to attend them privately.

Evangelical Mission

Dr. WALLACE said that Dr. Jones had pointed out that I.M.S. was not getting the support it required if it was to become a success. Dr. Jones had suggested something in the way of mounting "an evangelical mission," which would have the support of the Council, to make doctors realize that, though there might be no immediate gain in joining I.M.S., the ultimate gain was infinite. At the moment many doctors were wallowing in wealth when compared with the poverty of some doctors a few years ago, continued Dr. Wallace, but wallowing in comparative wealth had never been a good atmosphere in which to conduct a mission. He hoped the Council would not take umbrage at the paragraph in the Private Practice Committee report, and would not read into it things that were not there.

Dr. C. C. LUTTON said that I.M.S. had been supported fairly well, but not by the patients, and that surely was one of the main reasons why the results were disappointing. He suggested that I.M.S. should be considered rather like the Territorial Army and held in

reserve. Some day an alternative health service would be needed. The crisis had died away at the moment.

Dr. J. E. MILLER said there was an unfortunate tendency for the matter under discussion to be regarded as a private battle between Ivor Jones's private army and the Council. Dr. Miller asked the Council to realize that it was not a private controversy at all. It was a unanimous recommendation of the Private Practice Committee that reference to the lack of support for I.M.S. should be made in its report to the Council.

The Council should not allow the debate to blow the matter up out of all recognition. It should be kept in its proper perspective. There had been from the start an unfortunate feeling that I.M.S. did not have the whole-hearted support of the Association through the Council. He had been told on several occasions that there was lukewarm support from the Council for I.M.S. It was all very well to say that the root cause of the failure of I.M.S. to attract support appeared to be among doctors at the periphery. There had been lukewarm interest in many aspects of B.M.A. activity in the past on the part of doctors at the periphery. They were, however, subject to changes of mind provided they recognized that they were getting a lead from the top. It was a lead from the top that Dr. Miller said he pleaded for, and was the reason for the insertion of the paragraph in the Committee's report.

He was delighted to hear that Dr. Luffingham's Branch was interested enough to go to the expense of sending out a questionnaire to its members drawing their attention to I.M.S. and asking for their views on private practice. If more Branches and Divisions took similar action, and if members of the Council recognized the importance of I.M.S., even as an insurance for the future, perhaps more interest would be stimulated at the periphery.

Dr. Miller suggested that not only had there not been sufficient stimulus from members of the Council, but Divisional and Branch secretaries should have constantly been stimulating their members to take action in the matter. Whether the fact that only 40 Divisions had held meetings to discuss I.M.S. reflected lack of interest on the part of doctors at the periphery or reflected lack of activity on the part of members of Council and Divisional secretaries was for the Council to judge. But there could be no doubt in the mind of the Council that failure on the part of any section of the B.M.A. reflected failure on the part of the Association as a whole, and the Association in the future would be blamed by doctors at the periphery for not having taken a stronger line in stimulating further interest in I.M.S.

A motion that the question be now put, proposed by Dr. A. M. RANKIN and seconded by Mr. G. E. MOLONEY, was carried.

Dr. JONES, in reply, asked the Council to look again at the paragraph which it was being urged should be referred back. He quoted from it. The first sentence was "The policy was affirmed by the Representative Body in July 1967." There was no doubt about that. Policy had been enunciated fully at the Annual Representative Meeting in Bristol and had been approved by the Representative Body. "The Committee is dissatisfied with the action taken up to date to encourage private practice and to assist

Independent Medical Services Ltd." The Council, said Dr. Jones, now knew why the Private Practice Committee was dissatisfied with what had been done up to date to support that policy. "It [the Private Practice Committee] deplores the lack of support for this aspect of the policy of the Association." That, said Dr. Jones, was an expression of opinion on the part of the Committee.

In moving the reference back Dr. Luffingham had suggested that he (Dr. Jones) had been intemperate in submitting the report to the Council. Dr. Jones assured the Council that if it had listened to the debate in the Private Practice Committee it would think that he had been very temperate indeed in putting the Committee's recommendation to the Council.

Dr. LUFFINGHAM, in reply, said he hastened to point out that he had not attacked Dr. Jones personally. Secondly, he had suggested that it was the Private Practice Committee which had been intemperate and not Dr. Jones. He assured Dr. Scott that he was not against private practice. What he was unhappy about was that the product being offered was unacceptable to the customers—that was, the doctors. In Dr. Luffingham's view the Council was being censured, and Dr. Jones had not suggested that it was not a vote of censure.

The motion to refer back the paragraph was lost.

Committee's Recommendations

The CHAIRMAN then drew the Council's attention to the recommendation of the Private Practice Committee:

That the Council, recognizing that the policy of extending private practice and of giving all practicable support to Independent Medical Services Ltd. has been approved by the Representative Body, urges resolute and continuous action in this respect by all concerned.

Dr. RIDGE said he was unable to support the recommendation, because it was far too imprecise. For example, what was meant by "continuous action"? Did it mean that those concerned had to ensure the encouragement of I.M.S. all day and every day to the exclusion of everything else? Secondly, the implication of what was said in the presentation of the report was that "all concerned" included all members of Council. But if it was accepted that every member of Council had to take action on every policy decision of the Council then manifestly they were being asked to do something that was impossible. Therefore, why should a particular policy decision of the Council be singled out? If "all concerned" meant subscribers to I.M.S. that was a different matter, but it was not clear.

Dr. J. HENNEMAN said it was clear what the Private Practice Committee meant. It asked that the Council should do everything in its power to implement what was the policy of the Association. There were many ways in which the Council could do more along the lines outlined by Dr. Jones. One was to get the public interested in I.M.S. At the moment many doctors did not join I.M.S. because the public did not know about it until they were ill and visited the doctor's surgery and saw the notice about I.M.S.

Dr. WALLACE urged the Council not to read into the recommendation things which

were not there. "If we want to support the decisions of the Representative Body and Council let us adopt this recommendation," he said.

Dr. JONES said he had had to deal with hundreds of letters and phone calls from members of the public who wished to find a doctor who would provide services under the I.M.S. scheme but who had been unable to do so. "I cannot believe that such a situation would continue if all of us were doing all we could to promote a scheme which was twice supported and twice approved by the Representative Body," he concluded.

Dr. R. E. W. OLIVER said he thought that the character of I.M.S. had changed, and he asked Dr. Jones for an assurance that it had not changed since it was last discussed. Dr. JONES gave an assurance that the primary objects of I.M.S. remained what they had been at the outset—to further private practice in this country and to enable the profession and the community to participate in it.

The recommendation was adopted.

The CHAIRMAN said that both he and the Secretary were worried about the wording of the recommendation, because they did not know what the Private Practice Committee wanted them to do. He asked whether the Committee could submit a memorandum indicating exactly what it wanted done.

Dr. JONES replied that now that Council had adopted the recommendation his Committee would of course submit a memorandum setting out specifically what it wanted done.

It was agreed that any further action should await the Council's consideration of the memorandum.

The Committee's report was approved.

Occupational Health Committee

Dr. R. E. W. FISHER, chairman of the Occupational Health Committee, attended by invitation to present its report.

He referred to negotiations with the British Railways Board and the National Coal Board on the pay of medical officers employed by those boards, and he said that the Committee was pleased with the results.

Dr. J. M. DUNLOP asked why the claim in respect of British Railways was backdated to 1 July 1967, whereas the claim in respect of the National Coal Board was backdated to October 1966.

Dr. FISHER replied that the National Coal Board had been prepared to accept that there had been an existing commitment to review pay before the freeze started on 20 July. British Railways had not been prepared to accept that it had a commitment.

Dr. DUNLOP asked whether the claim to British Railways had been put in before the freeze started. Dr. FISHER said that the detailed claim was not put in to the Coal Board or the Railways Board before 20 July, but because the Committee had been in continuous negotiations with the National Coal Board the Board was prepared to accept that continuing discussion implied a commitment to review.

Asked whether doctors employed by British Railways were happy with the settlement, Dr. Fisher replied that naturally they would have liked more, but they were prepared to accept what was obtained.

The report was approved.

Committee on Medical Science, Education, and Research

Mr. A. LAWRENCE ABEL presented the report of the Committee.

He said the Committee would like the Council's advice on how the following recommendation in the Committee's report should be implemented: "That Council take whatever steps necessary to draw Resolution 461† to the attention of Parliament. In this connexion the matter might be ventilated through the Parliamentary and Scientific Committee, of which the Association has recently become a member."

Mr. Abel said that a working party had been set up to explore the pros and cons of the use of amphetamine drugs.

The CHAIRMAN said that he was a member of the Home Office Committee on Drug Dependence, and it was sympathetic towards the B.M.A. and had been most helpful and co-operative. He asked whether Resolution 461 should be sent to that Committee.

The Council agreed with the suggestion.

Dr. SKENE said that the Ministry of Health already had a draft memorandum which covered a good deal of the recommendation contained in Resolution 461. It had been seen by the Joint Consultants Committee.

The Council agreed to make a grant not exceeding £250 towards the cost of a half-day symposium on the subject of the structural design of operating-theatres, with specific reference to the control of infection. The symposium, which was to commemorate the Lister Centenary, would be held at B.M.A. House on 8 December in the afternoon.

The report of the Committee on Medical Science, Education, and Research was approved.

Central Ethical Committee

Dr. J. S. HAPPEL presented the report of the Central Ethical Committee on behalf of its chairman, Dr. W. Woolley.

He said that Dr. Woolley had been appointed Chairman of the Committee on the retirement of Dr. S. Noy Scott. The Committee had placed on record its warm appreciation of the outstanding manner in which Dr. Noy Scott had conducted the proceedings of the Committee for the past ten years.

The report of the Central Ethical Committee was approved, and the Council endorsed the expression of appreciation by the Committee of the work which Dr. Noy Scott had done during the years in which he had been its Chairman.

Welsh Committee

Dr. A. WESLEY HILL presented the report of the Welsh Committee in the absence of its chairman, Dr. Rowland J. Williams.

He reported that the Committee had completed its study of the second report of its Subcommittee on Area Health Boards, which had been drawn up in the light of the criticism received on the progress report of

1966. The second report was submitted to the Council with the recommendation that its circularization as a report of the Welsh Committee of the Association should be approved.

The Council expressed gratitude to the Welsh Committee for producing an excellent report, and it was agreed that it be referred to the Association's major standing committees for consideration and report at the meeting of the Council in January.

The report of the Welsh Committee was approved.

Journal Committee

The CHAIRMAN welcomed Sir Alan Moncrieff, the newly elected Chairman of the

Journal Committee (*Supplement*, 21 October, p. 23).

Sir ALAN MONCRIEFF, in presenting the Committee's report, referred to the retirement from the chair and from the Committee of Dr. J. G. M. Hamilton, and said that he would be very much missed.

Sir Alan Moncrieff called attention to the Committee's proposal that within the next two years the printing of the *B.M.J.* should be changed from flat-bed letterpress to web-offset. With new methods of printing it should be possible to speed up the process and to ensure that every member of the Association received his *B.M.J.* by the Saturday morning.

The report of the Committee was approved

Public Health Committee

Dr. C. METCALFE BROWN presented the report of the Public Health Committee.

Salary Claim

Dr. Metcalfe Brown reported that since the sanctions on local authority public health appointments were introduced in May two emergency meetings of the Committee had been held to discuss proposals from the Management Side of Committee C in response to the salary claim on behalf of public health medical officers.

A further meeting of the Committee had been held on 11 October to discuss the latest offer. Though it contained the elements of a possible settlement, the Committee had been unable to accept certain of the conditions proposed by the Management Side.

The Council heard *in camera* a report from Dr. Metcalfe Brown on the nature of the Management Side's offer.

Appointment in Surrey

Dr. Metcalfe Brown said that the post of county medical officer of health of Surrey had been advertised and filled during the summer. After a meeting called by the British Medical Guild of all doctors in contract with Surrey County Council representations had been made to the chairman of the County Council about the action of his authority in filling the vacancy during the period when the British Medical Guild had recommended all doctors not to apply for public health medical appointments. It was known that a number of distinguished medical officers of health had abstained from applying for the post as a result of the Guild's recommendation, and it was believed that no county medical officer of health had applied.

A deputation had seen the chairman of the Surrey County Council and had put the profession's case. It was pointed out that the number of applicants must have been seriously reduced by the operation of the Guild's recommendation, and that the action of the authority in filling the appointment would have the most serious consequences on the local health authority services in the country. [A report of a British Medical Guild meeting on 26 October appears at p. 41.]

County Borough of Tees-side

Dr. METCALFE BROWN reported that an advertisement published in *The Medical Officer* and in the *Lancet* for a medical officer of health for the newly created County Borough of Tees-side in September 1967 contained the sentence, "This advertisement is made with the agreement of Committee C of the Medical and Dental Council." The Public Health Committee considered the statement to be misleading, and a notice to that effect was published in the *British Medical Journal* and in *The Medical Officer* of 23 September.

Dr. G. N. MARSH said that when the post was advertised the local public health medical officers who were in order in applying for it wrote to the Association to see whether they should do so. Other medical officers of health withdrew their applications when they heard of the B.M.A.'s embargo. Nevertheless, the post had now been filled.

Expectation of Life

Dr. R. P. HENDRY protested about the way in which the Public Health Committee was handling the question of career earnings. He referred to a statement in the Committee's report that consideration had been given to a resolution of the A.R.M. 1966 requesting that the Council should publish the average expectation of life of the various branches of the medical profession and compare and contrast those with those of certain other professions mentioned in the Report of the Royal Commission on Doctors' and Dentists' Remuneration. "The Committee," stated its report, "is of the opinion that no useful purpose would be served by attempting to compare the average expectation of life in the various branches of medicine with that of other professions."

Dr. Hendry suggested that the A.R.M. resolution was being handled in a slipshod manner. Indeed, it had been quietly sat upon for fifteen months, and was then grossly misquoted and rejected in an unconstitutional way. The A.R.M. resolution was a straightforward instruction to the Council that it should publish the average expectation of life of those in the various branches of the medical profession and compare and contrast them with those of the professions mentioned in the Royal Commission's report, thus finally to

† Resolution 461 of the A.R.M. 1967 reads as follows: "(i) That this Meeting recommends that when a patient has completed treatment for drug addiction there should be adequate provision for his rehabilitation and follow-up on a long-term basis, such rehabilitation should be directed by a person with proper skill and experience in this field and (ii) that the Government be urged to implement all the other recommendations of the Brain Committee report of 31 July 1965."

explode the myth of career earnings. Dr. Hendry submitted that statistics were needed and not opinions. He accordingly moved that the part of the Public Health Committee's report dealing with career earnings should be referred back. • Dr. OUTWIN seconded the motion.

Dr. METCALFE BROWN said he would have appreciated some notice of the charge which Dr. Hendry had made. He would be willing to look at the point if he could be furnished with the information. What the resolution asked for was a big research job which might or might not be worth while. However, he was certain that it would cost the Association a great deal of money.

The motion was carried, and the Public Health Committee's report, duly amended, approved.

General Purposes Committee

The CHAIRMAN presented the report of the General Purposes Committee.

I.M.S. Discount Scheme

Dr. OUTWIN moved the following motion: "That this Council is opposed to the assistance of Independent Medical Services Ltd. by the B.M.A. in respect of aspects of the trade discount scheme activities which overlap existing activities for which Association support is already policy, and thereby rejects the section of the Private Practice Committee's report dealing with the discount scheme."

Dr. DOWLER seconded the motion.

Dr. OUTWIN said he wanted to make it clear at the outset that the motion was not intended as an attack upon I.M.S. or a personal attack on any member of its board of management, or on Dr. Jones in particular. He wanted to point out that the Association's business sense would seem to be in grave doubt if the proposal outlined in the General Purposes Committee's report was adopted.

It was apparent that the trade discount scheme had territorial ambitions which knew no boundaries. It was the avowed intention of I.M.S. to spread its ubiquitous net over insurance, travel, and wines and spirits among other things. That raised some important issues. The Association had its own Hastings Wine Club. Members might or might not regard the club as a successful project in what was a highly competitive field, but it was one which was launched some years ago with a fanfare of Association trumpets, and in the minds of all members the Hastings Wine Club was part of the B.M.A. and it should not be lightly jeopardized.

So far as the Medical Insurance Agency (M.I.A.) was concerned, the B.M.A. had no direct control over M.I.A., but for some 60 years there had been a close connexion between the B.M.A. and the M.I.A. and the profits of the M.I.A. went to medical charities. That relationship with the M.I.A. must be regarded as an Association asset.

I.M.S. was a commercial organization over which the Association had no control. According to the report of the General Purposes Committee, M.I.A. would be willing to co-operate with I.M.S. "on the assumption that its scheme had the Association's approval." M.I.A. was "over a barrel,"

because it was in no position to express opposition to anything which was Association policy. Nevertheless, if I.M.S. appeared to be a competitor in the field of insurance relationships with M.I.A. would doubtless suffer. Dr. Outwin asked the Council seriously to consider whether it would be wise for the Association to hand over its assets in the form of the Hastings Wine Club and help to medical charities to an organization over which it had no control whatever.

B.M.A. Organization

Dr. DOWLER, speaking as chairman of the Hastings Wine Club, said that it was founded 8 to 9 years ago, and it could be said to have been successful. It had some 5,500 members, and it was under the control of a committee which was appointed and controlled by the Organization Committee. It was an Association organization completely.

Some time ago Dr. Jones had arranged for the manager of the I.M.S. trading scheme to see the secretary of the Hastings Wine Club to discuss the question of selling wines and spirits. The question was whether the new I.M.S. service and the Hastings Wine Club could co-operate. It was explained that there was no possible way in which the I.M.S. service and the Club could co-operate. It was further explained that the Club was run entirely by the Association, and it was thought that the I.M.S. service should desist from offering wines and spirits. Dr. Jones had agreed, and it was rather surprising to read in the report of the General Purposes Committee that wines and spirits should be sold through the facilities division of I.M.S.

Dr. Dowler suggested it was wrong in principle for a service sponsored by the B.M.A. to set up in direct competition with a service already given by the B.M.A. I.M.S. was independent and could do what it liked, but the Association had sponsored it. It was an irrational and undesirable situation.

Dr. LUTTON said that the mail order business was always a dangerous one. Discount trading would always have its problems. When he learnt of the facilities being offered by I.M.S. he put the matter to his three partners, and all of them agreed that if I.M.S. went into the wine and spirit business they would ask for their £10 subscription back. They pointed out that they were not in medicine to put up a shop in the Association. Furthermore, if money were lost who would stand that loss?

Dr. J. S. ROSS said that in his view there was much to be said for the scheme in attracting membership to the Association. At the same time, however, he agreed that it was unwise, unfair, and unkind to tread on the feet of the M.I.A., who had been good friends of the Association for many years. Whatever was done it was bound to jeopardize friends in the Medical Insurance Agency. The Hastings Wine Club was part of the Association, and it would be ridiculous to put up a rival organization within the aegis of the B.M.A.

Dr. J. COTTRELL said he thought that the introduction of the proposed scheme would probably help to undermine the good image which the Association had always endeavoured to put before the public.

Dr. HAPPEL thought that everyone was being a little hard on Dr. Jones. After all, the Council was under an instruction to pro-

vide such a service, which was now possible through I.M.S. When members wrote in and asked for goods on discount there was no need to draw any distinction between electrical goods and wines and spirits.

Interests of Profession

Dr. D. J. PEREIRA GRAY said that one of the objects in the Memorandum and Articles of Association of the B.M.A. was to promote the interests of the profession, and he submitted that the proposed scheme did promote those interests. Speaking for younger doctors, a pound saved was more valuable than a pound earned, because tax was not paid on it. As a result of the trade discount scheme new money would be brought into I.M.S. at no cost to the Association, and it would be an attraction to membership of the B.M.A.

Dr. JONES, in reply, outlined the history of the I.M.S. discount trading scheme, which had become policy of the Association in July. Far from rendering any disservice to M.I.A., far from depriving it of any custom, the activities of I.M.S. were already channelling to M.I.A. custom which it might not otherwise have received. Dr. Jones said he had letters from the M.I.A. welcoming the arrangements which had been made between the two bodies. No commission on insurance business was taken by I.M.S. except in respect of arrangements which were sometimes made in connexion with hire purchase. In that case he did ask for a modest commission on the transaction to meet the costs of what was being done. It was a service to M.I.A. that in respect of all motor cars obtained on hire purchase through the I.M.S. scheme at least the purchasers' attention was directed to the facilities which the M.I.A. offered. There was already evidence of an increased volume of business going to M.I.A.

Among the things which Dr. Jones's manager reported to him as part of his general remit to make the best arrangements he could were arrangements in respect of wine and spirits. Dr. Jones said he was aware of the Hastings Wine Club. He had found that it was bound hand and foot to one particular firm. He was further amazed to find on a preliminary survey that it was possible for the I.M.S. discount scheme to arrange for wine and spirits to be available to doctors on better terms than the Hastings Wine Club could offer.

However, I.M.S. was still anxious to help the Hastings Wine Club to the maximum possible extent, and his manager had met Dr. Dowler and Dr. Potter. The manager had reported back that there was no prospect of agreement, because the Club was bound hand and foot to one particular firm. Dr. Jones said he had made it clear to the secretary of the Wine Club that I.M.S. would be prepared to supply it with wines and spirits which the Club could disburse if it wanted to on better terms than were currently available, "but they did not want that."

Go Ahead

Dr. Jones said he had agreed to defer decision on all the outstanding matters until the General Purposes Committee had considered them and to abide by whatever decision it reached. It had, however, been necessary to indicate at the time that once

the Committee's decision had been reached I.M.S. would go ahead with its discount scheme. The General Purposes Committee had debated all the matters and had voted in favour of the I.M.S. discount scheme. Even then, so far as wines and spirits were concerned, Dr. Jones said he made a further endeavour to reach agreement with the Hastings Wine Club, but it had not proved possible. Dr. Jones said he had arranged, despite the vote of the General Purposes Committee, not to issue a catalogue of wines and spirits to anyone who did not specifically inquire whether he could be provided with wines and spirits.

Dr. Jones said he was somewhat puzzled by the motion, because he did not know what Dr. Outwin thought I.M.S. had been receiving in the way of financial support from the Association. I.M.S. had paid for the letter and application form that went out with "B.M.A. News," and it had paid for its advertisements in the *B.M.J.* He was therefore at a loss to understand what Dr. Outwin thought should be withdrawn from I.M.S. and which he believed, erroneously, that I.M.S. had received.

Dr. OUTWIN said he had not suggested that I.M.S. was proposing to do anything that would in any way jeopardize M.I.A. He had merely pointed out that I.M.S. was an organization over which the B.M.A. had no control. He agreed that certain members of Council were on the board of management of I.M.S., but that did not mean that the Association had ultimate control over the organization. However well intentioned I.M.S. might be now there could be no guarantee of the ultimate outcome of the relationship.

In the case of the Hastings Wine Club, the chairman and secretary of the club found I.M.S. an unacceptable bed-fellow, so the two bodies were in open competition. Why was Dr. Jones's organization so altruistic in channelling so much new custom into M.I.A. and taking no profit? Obviously it would not lose anything if the motion were carried by Council.

The motion was lost.

Different Policy

Dr. RIDGE then read a letter from a Division expressing disquiet that the I.M.S. discount service was not now in the form approved by the Representative Body.

Dr. JONES said that Dr. Ridge had asked for an explanation of the change from a policy of charging one or two guineas as a subscription to the I.M.S. discount service to one of making it freely available to members of the B.M.A. and to I.M.S. subscribers, whether or not they were members of the Association, and also to members of the British Medical Students Association.

Dr. Jones said that when the original project was placed before the Council in 1966 it had been a confidential document. He was well aware then that anything being offered would very likely be copied, if the opportunity presented itself, by certain other organizations. Council might like to consider whether in fact there was any leak of the intentions of the Association. The fact remained that the position had changed very much in that by the time the Representative Body had approved the I.M.S. discount scheme there was in existence, available without subscrip-

tion to doctors, whether members of the B.M.A. or not, a discount trading service of a kind. It had been necessary therefore to consider whether I.M.S. should proceed along the lines originally intended. He discussed the matter with his Committee and with the Chairman of Council, the Secretary, and others, and they agreed that if it were possible I.M.S. should offer the service to members without any additional subscriptions.

Dr. Jones said he had disclosed all the facts to the General Purposes Committee. He had not taken any final decision until he had known the views of that Committee, and there had not been one dissentient.

Dr. RIDGE said he would be satisfied if the explanation for the change in policy on subscriptions to the I.M.S. discount service were given to the Representative Body in the Annual Report of Council for 1967-8. It would then be for the Representative Body to decide whether it accepted the change that had been made in its policy without it being consulted.

Dr. HAPPEL suggested that, in view of what Dr. Jones had told the Council, the General Purposes Committee should again consider whether it was best for the Hastings Wine Club to remain restricted to one supplier when there were better terms available through the trade.

Dr. DOWLER pointed out that the Hastings Wine Club was not set up merely for the purpose of buying wines and spirits cheaply. It was also set up to help doctors to become interested in and learn about wines. The club organized tours of wine-growing areas and suchlike.

The report of the General Purposes Committee was approved.

B.M.A. and Magistrates

Dr. G. S. R. LITTLE presented the report of the Joint Committee of the B.M.A. and Magistrates' Association.

The CHAIRMAN congratulated the Adoption Subcommittee of the Joint Committee on the Memorandum on Adoption that was before the Council for approval.

The Council adopted a recommendation that, subject to its approval by the Council of the Magistrates' Association, the memorandum should be submitted to the Home Office and any other appropriate bodies.

The Council also adopted a further recommendation that the Home Office be urged to consider: (a) extending the facilities provided for the treatment of drunken offenders to drug offenders; (b) making disorderly behaviour while under the influence of drugs an offence, so that opportunities would become available to the Courts to order treatment; (c) empowering the Courts to confiscate all drugs and addicts' gear in the possession of persons convicted of drug offences; (d) better priority for outpatient psychiatric reports.

The report of the Joint Committee was approved.

Breathalyser Tests

Dr. HAPPEL referred to the Breathalyser test, and asked Council to support all efforts to standardize unofficial apparatus and to encourage their use in every way possible, because they were helpful to the public. He further pointed out that nothing had been done to try to alter the whole pattern of social drinking in private houses. He understood that in Canada it was customary for the host to present his guest with a bottle and a glass and ask him to help himself. That might be usefully adopted in this country with a special measure.

Council agreed to submit the points raised by Dr. Happel to the B.M.A.'s Expert Committee.

Other Committees

The reports of the following Committees were approved without discussion: Annual Meetings Committee, Scottish Council, Full-time Medical Teachers and Research Workers' Committee, Committee on Overseas Affairs, Finance Committee, Armed Forces Committee, Film Committee, G.M.S. Committee, and Family Doctor Committee.

The meeting terminated at 6.30 p.m.

H.M. Forces

ROYAL NAVY

ROYAL NAVAL RESERVE

Surgeon Commander H. R. Gray, V.R.D., has been placed on the Retired List.
Surgeon Lieutenant R. C. Clark to be Surgeon Lieutenant-Commander.

ROYAL ARMY MEDICAL CORPS

Major J. C. Wilson to be Lieutenant-Colonel.
Major J. H. Taylor has resigned his commission.

REGULAR ARMY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel S. Ward, having attained the age limit, ceases to belong to the Reserve of Officers.

Major (Honorary Colonel) W. H. Valentine, O.B.E., E.R.D., having exceeded the age limit, ceases to belong to the Reserve of Officers, and has been restored to the rank of Colonel.

Major W. N. L. Haynes, having exceeded the age limit, ceases to belong to the Reserve of Officers.

Major E. J. Ewell, O.B.E., T.D., from T.A., to be Major.

Major R. L. Jillett, T.D., has relinquished his commission on appointment to a commission in the Royal Auxiliary Air Force with the rank of Squadron Leader.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel A. A. Shivas, T.D., has reverted to the rank of Major.

Captain (Acting Major) J. Grier, from T.A., to be Captain, retaining the acting rank of Major. (Substituted for the notification in a *Supplement* to the *London Gazette* dated 4 April 1967.)

Captain I. D. Walters to be Major.

ROYAL AIR FORCE

Squadron Leader E. D. Colterjohn has retired at his own request.

Flight Lieutenant D. J. Clarke to be Squadron Leader.

ROYAL AIR FORCE RESERVE OF OFFICERS

Flight Lieutenants I. W. Geere and D. C. Prior to be Squadron Leaders.

Central Committee for Hospital Medical Services

The existing Interim Negotiating Subcommittee for hospital medical staff—the “Committee of Fifteen” appointed early in the year—is to remain in office to finish the preparation of evidence for the Review Body. The Negotiating Subcommittee for 1967–8 will be elected in December. Three out of the nine members elected to the Executive Subcommittee of twelve were representatives of hospital junior staff. The three ex officio members are the chairman and the two deputy chairmen. The C.C.H.M.S. did not take exception to the Sainsbury Committee’s report in general but emphasized the importance of the proposed Medicines Commission being independent. The Committee thought ambulances going to accidents should carry pain-relieving drugs for the use of any doctor who might be on the scene but unequipped. The value to the B.M.A. of the statistical group set up jointly by the profession and the Ministry of Health was explained by the Secretary. The Committee dealt with a number of resolutions referred to the Council from the Annual Representative Meeting 1967 and also A.R.M. motions which had not been debated by the A.R.M. and had been referred en bloc to the Council. A subcommittee is to be appointed to study the question of the medical staffing of the casualty service in hospitals.

A meeting of the Central Committee for Hospital Medical Services was held on 20 and 21 October. Mr. H. H. LANGSTON was in the chair.

Negotiating Subcommittee

The Committee considered the appointment of the Negotiating Subcommittee.

The CHAIRMAN reminded the meeting that an interim negotiating subcommittee of 15 members (the “Committee of 15”) had been set up in the middle of the last session. It had met three times, and it had been almost entirely occupied in preparing evidence for the Review Body. He thought it would be a great mistake to change the subcommittee’s membership at this stage: it should be allowed to finish its task. He suggested that the election of the Negotiating Subcommittee for the session 1967–8 should be postponed until early next year.

Dr. E. A. HARVEY-SMITH, chairman of the Hospital Junior Staffs Group Council, agreed that the existing membership should remain for the present, but he hoped it would be reviewed at the meeting of the Central Committee for Hospital Medical Services (C.C.H.M.S.) in December.

The Committee agreed with Dr. Harvey-Smith’s proposal.

Executive Subcommittee

The Committee considered the appointment of its Executive Subcommittee, which had consisted of the chairman, the two deputy chairmen, two members nominated by the C.C. and S. Committee (Scotland), one member nominated by the Hospital Junior Staffs Group Executive Committee, and six members elected by ballot.

Dr. HARVEY-SMITH proposed that the Executive Subcommittee should be increased by two members, and that three places on it should be reserved for members of the hospital junior staff.

Dr. H. GLYN JONES was disturbed that the Executive should be split into groups. Dr. N. STRANG (chairman of the Senior Hospital Medical Officers Group Council) proposed that there should be a place on the Executive reserved for S.H.M.O.s. Dr. H. L. LEAMING hoped that at least seven places would be reserved for non-teaching staff.

The CHAIRMAN said he hoped he would not have to put these proposals as formal motions. The Committee could nominate whom it wished. It was unfortunate that

there should be talk about teachers and non-teachers when the regional peripheral hospitals were all trying to do more and more teaching.

Mr. H. A. KIDD said that the regional hospitals were badly represented, and they had got a raw deal in the last review. There was still a division between the teaching and the non-teaching hospitals. The teaching hospitals took what they could out of the cake and what was left had to be shared out among the non-teaching hospitals. Every committee was heavily weighted in favour of the teaching hospitals’ views. It was time the consultants in the regions were better represented.

Dr. GLYN JONES pointed out that if the Central Committee was heavily weighted in favour of teaching staff then that tendency was bound to be spread through its subcommittees. Mr. J. R. BLACKBURN said that, as a non-teaching hospital consultant, he would be sorry to see the composition of the Executive tied to a particular proportional representation. It was up to the Committee to choose the best men.

The CHAIRMAN believed that any sort of division would be unhelpful. He suggested that members of the Executive should be elected as individuals and not as members of particular groups.

Dr. R. M. MAYON-WHITE proposed that the Hospital Junior Staffs Group should nominate three members, but that it would be still open to members of the C.C.H.M.S. to propose other names. When it came to the vote the top six of the senior members nominated would be elected and the top three of the juniors. Dr. HARVEY-SMITH agreed that the H.J.S. Group should nominate three members, but others were at liberty to put forward other names.

The Committee agreed to that proposal.

The following were elected: Mr. J. R. Blackburne, Mr. R. Myles Gibson, Dr. R. M. Mayon-White, Professor Ian Rennie, Dr. A. Skene, and Dr. G. E. Owen Williams (representing senior hospital staff), and Dr. D. Guttman, Dr. E. A. Harvey-Smith, and Dr. W. P. U. Kennedy (representing hospital junior staff).

Sainsbury Committee

Dr. A. SKENE reported to the Committee on the *Report of the Committee of Enquiry into the Relationship of the Pharmaceutical Industry with the National Health Service, 1965–7* (the Sainsbury Committee).

He said that the B.M.A. had submitted evidence to the Sainsbury Committee. There

had been a fear that the Committee might be prejudiced in favour of the nationalization of the pharmaceutical industry. These fears had been allayed by the committee’s specific statement that it did not recommend nationalization.

The first two-thirds of the report dealt with marketing procedures, advertising, and the profitability of the industry. Dr. Skene thought there was nothing in the recommendations which called for any action on the part of the medical profession at the present time. The Association of the British Pharmaceutical Industry was well able to speak for itself. Dr. Skene said that the part of the report which concerned the medical profession was the proposal for a Medicines Commission. The Sainsbury Committee considered that the Medicines Commission should have an independent constitution and should be plainly seen to be independent. It would have certain functions with regard to licensing, and it would also deal with standards of advertising and keep watch on the accuracy of claims. After outlining some of the other proposed functions of the Medicines Commission Dr. Skene concluded that there was no immediate danger to the freedom of practice of doctors, particularly in general practice, or any likelihood of limitations being placed on the industry which would diminish its research potential. He recommended that the C.C.H.M.S. should inform the Joint Consultants Committee that it did not disagree with the findings of the Sainsbury Committee, and that it supported the recommendation for an independent Medicines Commission, with the proviso that the matter should be kept under observation.

Dr. OWEN WILLIAMS said that the view of the B.M.A. was that the Medicines Commission should be completely independent, and that it should be the authority issuing and revoking the licences. The Ministry was the major, although not the exclusive, customer of the pharmaceutical industry. That was one of the reasons why the membership of the Commission should preferably be appointed by the various interested bodies.

Clinical Trials

Dr. R. MAGGS commented on the paragraph in the Sainsbury Report about clinical trials, in which it was recommended that in addition to satisfying the requirements of safety a new pharmaceutical product should, before being granted a licence, be shown in evidence produced to the Medicines Commission to have the efficacy claimed for it by the manufacturer. The evidence would in

most cases be expected to be in the form of reports of approved clinical trials. Dr. Maggs wondered what kind of "approval" was meant. The Committee did not seem to have made any recommendation that could help doctors to check more easily the basis upon which manufacturers made their claims. So often postal advertising material was full of names and references which doctors did not have time to check.

Dr. SKENE said that there was a limit to what an advertisement could carry, but the Sainsbury Committee had stressed the desirability of advertisements giving references to valid research. The Sainsbury Committee was concerned about the standard of clinical trials. They would need to be supervised.

Dr. D. P. STEVENSON, Secretary, pointed out that the Government's White Paper on forthcoming legislation on the safety, quality, and description of drugs and medicines

(*B.M.J.*, 16 September, p. 734) had stated that the appointments to the Medicines Commission would be made by the Minister of Health. The Sainsbury Report had stated that the Medicines Commission should be plainly seen to be independent. Had the Government produced its White Paper knowing what the recommendations of the Sainsbury Committee would be, or was it just coincidence? The B.M.A., he thought, should align itself with the clear recommendation in paragraph 335 of the Sainsbury Committee's report that the Medicines Commission should have an independent constitution and should be plainly seen to be independent.

The Committee, while finding the Sainsbury Report generally acceptable, and emphasizing strongly the importance of paragraph 335, considered that the matter should be kept under close review.

Ambulance Training and Equipment

The Committee considered Part II of the report of the Working Party on Ambulance Training and Equipment, set up in 1963 by the Minister of Health and the Secretary of State for Scotland. The Ministry of Health had asked for the Committee's comments on (1) the suggested role of the Central Ambulance Services Council in relation to equipment (including vehicles); (2) the standardization of equipment; (3) the interchange of equipment (for example, blankets) between hospitals and visiting ambulance vehicles; (4) the carriage and use of pain-relieving drugs and surgical instruments; and (5) the provision of clothing against radiation hazards.

Mr. WALPOLE S. LEWIN, a member of the working party, said that ambulances tended to be thought of in terms of their use in cases of accidents. Only 5% of those carried in ambulances were accident cases. It was for that reason that the working party had advised that there should not be separate training courses for accident work as distinct from the other duties of ambulance men, and that there should be one training programme for everyone. Similarly, the working party had set out what it believed to be reasonable equipment for all ambulances and had stated what should be available at ambulance stations for major accidents, and that it should be able to be got to the scene of an accident within half an hour. He did not think any comment could be made on the suggested role of the Central Ambulance Services Council until there was a central administrative body which would do for the ambulance service what had been done for the nursing services.

Standardization of equipment was important. Some things such as blankets were interchangeable, and there should be no need for ambulance men to take patients off stretchers in order to get their equipment back. Every ambulance should be equipped with oxygen and with suction apparatus.

Drugs and Instruments

The questions of the carriage and use of pain-relieving drugs and surgical instruments

had caused the working party more difficulty than any others. There were about six ambulance authorities whose vehicles carried morphine, and they all reported that it was rarely used. Mr. Walpole Lewin excluded from that special aspects of ambulance work such as that carried out by mountain- and sea-rescue parties. They carried pain-relieving drugs. But the majority of the medical advice on the working party had been that the risk of giving these drugs in circumstances when they would do more harm than good was greater than the benefit which undoubtedly resulted for the few. Two members of the working party had thought that pain-relieving drugs should be carried in ambulances, and they signed a minority report to that effect. In the final report it was recommended that at present such drugs should not be carried as a general routine, although certain circumstances when they should be carried were suggested. It was not thought that the provision of clothing against radiation hazards was necessary. Every ambulance depot had equipment which could be sent for in special circumstances.

The CHAIRMAN said that the Ministry of Health had asked all regional hospital boards for their comments on the minority report of the working party. There was some opinion in favour of pain-relieving drugs being carried, and to that had been tied the suggestion that ambulance men should have some training in hospitals to gain experience in using the drugs.

Mr. WALPOLE LEWIN, in reply to a question by Dr. J. D. Whiteside, said that when he had mentioned ambulances carrying oxygen he had been referring to ambulances used for accidents.

Mr. R. MYLES GIBSON thought that carrying pain-relieving drugs in ambulances should be given a trial in one or two areas, and the result should be reported on after two to three years.

The Committee agreed to recommend that that should be done.

Dr. GLYN JONES proposed that it should be recommended that ambulances should carry pain-relieving drugs only for the use of a doctor who might come upon the scene of an accident unequipped to deal with it.

Dr. Glyn Jones's proposal was carried by 21 votes to 20.

Ballot on Distinction Awards

The CHAIRMAN reported that on the instructions of a resolution of the Annual Representative Meeting 1966 a postal ballot had been undertaken of all senior hospital medical staff and senior registrars to ascertain their views on distinction awards. The results (*Supplement*, 21 October, p. 22) had indicated that there was support for the continuance of the awards but that some doctors wished to see certain changes. However, a substantial number made no comment at all, and there was no one subject other than secrecy that seemed to worry many doctors. He suggested that a copy of the report be sent to the Council, to the Joint Consultants Committee, and to the chairman of the Advisory Committee on Distinction Awards, Lord Platt.

Dr. S. J. HADFIELD, Scottish Secretary, who prepared the report on the ballot, said that some of the comments made, though striking, were made by only a few, and they might not therefore represent a wide section of opinion. Even those who commented on secrecy represented only 21.7% of the total returns.

Report on Negotiations

The CHAIRMAN reported that the Interim Negotiating Subcommittee had met twice since the last meeting of the parent committee. Both meetings had been mainly devoted to the preparation of evidence for the Review Body, which was now in the hands of the legal advisers. Negotiations between representatives of the Negotiating Subcommittee and of the Health Departments on the revision of Categories I and II of the Schedule to paragraph 167 of the Terms and Conditions of Service of Hospital Medical and Dental Staff were progressing satisfactorily.*

The Subcommittee was pressing the Ministry of Health on the payment of removal expenses of doctors moving from Northern Ireland to Britain. The Northern Ireland Government had agreed to pay removal expenses for doctors moving to Northern Ireland, but so far the Ministry of Health had been unwilling to make a reciprocal arrangement.

Mr. H. M. BENNETT, Northern Ireland, pointed out that the British Minister of Health did not recognize for seniority the years a young man might have spent as a registrar in Northern Ireland. This attitude might have had some validity some years ago, when the situation was different in Northern Ireland from Britain and a registrar became a senior registrar on getting certain qualifications, but now the system was the same in both countries.

The CHAIRMAN reported that the Negotiating Subcommittee had noted the following resolution of the Hospital Junior Staff Group Council: "That in future the Hospital Junior Staffs Group Council shall, when seeking evidence for the Review Body, brief the appropriate experts about the facts and figures to be discovered, so that these experts

* Paragraph 167 of the Terms of Service defines what work comes within the scope of the services provided under the N.H.S. and what does not.

may advise and devise the best means of discovering those facts."

Dr. S. CAMPBELL SMITH, a member of the H.J.S. Group Council, explained that it wanted to get independent evidence and not rely on Ministry sources, which might be accurate, but which were not always complete.

Dr. D. G. FAGAN, also a member of the H.J.S. Group Council, said that the intention was to find out what figures were needed and then to follow them through for perhaps five to ten years. At present figures were collected and then the experts gave their opinion on them. That was the wrong way round. The experts should decide what figures were needed, and then they should be collected and kept constantly up to date.

Statistical Information

Dr. STEVENSON said that for the B.M.A. to set up a department of statistics would require a large staff. The main source of any Association's statistical information must inevitably be Governmental. The Government could go direct to statutory authorities and require them to provide information. The Association could only make requests. A busy regional hospital board would be unlikely to provide the Association with statistics which could compete with the Government's. Therefore a year ago, by arrangement with the Ministry of Health, the B.M.A. agreed to take part in the joint statistical group. This group was never involved in policy. Its chairman was a statistician, and the Ministry of Health's representatives on it were the statisticians in the Department. On the Association side there were Sir Roy Allen, accountants, and economists. The result was that it got up-to-date and authoritative statistics. Another advantage was that such agreed statistics were not likely to be disputed by the Review Body. This was important, because in the past each side had put figures in evidence to the Review Body. The area of disagreement was now much narrower, and on matters such as emigration, work load, the number of doctors looking for jobs in general practice, and the number of vacancies the B.M.A. now had as much evidence as it was possible to obtain.

Dr. HARVEY-SMITH said that the negotiators did not have detailed figures of work load, though they might have global figures.

Dr. E. GREY-TURNER, Deputy Secretary, said he had been disappointed at what little help had been obtained from the profession itself. On three occasions he had written to regional consultants and specialists committees asking for material for evidence to the Review Body. There were 21 regional committees, and on the first occasion there was only one reply. On reminders being sent out he had received about 20 extremely good accounts from individual members of the position in particular units.

Consultant Staffing

The Committee considered the following resolution of the H.J.S. Group Council: "That the Group Council is of the opinion that, in order to make a thorough assessment of the ideal number of consultant posts in each specialty, the specialist groups of the B.M.A. should each determine a suitable and ideal work load (in all its aspects) for a consultant in their specialty."

Dr. HARVEY-SMITH said that consultant establishments should be based on objective studies independent of local vested interest and independent of what a particular regional hospital board might think. An establishment should be based on the work to be done in a particular hospital. The H.J.S. Group Council thought that the right way would be for the specialist groups to study the work load that they considered was right for a typical consultant to carry.

Dr. GREY-TURNER said that the profession had always been hostile to a time-and-motion study. It could be done on a time basis, but most people felt it was useless to establish criteria for highly specialized work, because time schedules did not measure the quality of the work or the weight of responsibility.

A decision on the matter was deferred to a subsequent meeting.

Mileage Allowance

The Committee considered a resolution from the H.J.S. Group Council asking for the support of the C.C.H.M.S. in bringing pressure to bear on the Ministry of Health by ceasing to use their private cars for a limited period in certain selected hospital groups.

The Committee rejected the resolution.

Resolutions of the A.R.M.

At the resumption of the meeting of the Central Committee for Hospital Medical Services on 21 October a number of resolutions of the Annual Representative Meeting 1967 which had been referred to the Committee were considered, together with a number of motions which, owing to lack of time, had not been debated by the Representative Body but had been referred en bloc to the Council. Representatives of the Divisions putting forward motions, or amendments to them, had been invited to attend the C.C.H.M.S. meeting so that they might have an opportunity of speaking to the motions.

Medical Services in Developing Areas

The Committee considered a resolution by Worcester and Bromsgrove: "That this Representative Body urges the Ministry of Health and its regional hospital boards to take note of proposals in certain areas to increase population densities, by redistribution, redevelopment, or formation of new towns, and to provide in good time appropriate hospital services for these areas."

Mr. F. S. A. DORAN, speaking to it, said that Birmingham intended to transfer 52,500 of its surplus population to Bromsgrove in about three years' time. Bromsgrove at present contained 43,990 people, so that the overspill would more than double its size to 96,490. The Bromsgrove General Hospital consisted of hatted units which had been scheduled to be demolished and rebuilt in 1960. Its total waiting list had risen in the last five years from 670 to 981, or by 47%. Increasing at that rate, the waiting list would have reached 1,229 by the time the first new house was occupied. There was no question of a new hospital being built at Bromsgrove, and even if there was there would be no nurses to staff it.

Hospital Pharmacists

The Committee considered a resolution from the N.E. Metropolitan Regional Committee for Hospital Medical Services drawing attention to the grave shortage of hospital pharmacists and to the need to pay them higher salaries.

The CHAIRMAN pointed out that it was not the policy of the Committee to negotiate salaries for ancillary staff but to recommend that they should negotiate their claims for themselves.

Dr. MAYON-WHITE said that this was the Committee's concern in so far as it brought about a curtailment of the hospital service owing to a shortage of staff. This was an occasion to press the pharmacists' difficulties on the Ministry.

Dr. GREY-TURNER said that the Ministry knew that hospitals were finding difficulty in getting ancillary staff, and it had set up a committee to examine the matter. Its terms of reference were to consider the future organization and development of hospital scientific and technical services in National Health Service hospitals, and the broad pattern of staffing required, and to make recommendations.

The Committee agreed that the matter should be taken up with the Ministry of Health.

The Bromsgrove General Hospital also supported Redditch, continued Mr. Doran. Redditch had a population of 35,960, and was being converted into a new town of approximately 90,000 people. That would take place at the rate of 3,500 people a year over the next 15 years. The regional board had stated that it could not build a new hospital for the new town in the next ten years, by which time the population of Redditch would have risen by 35,000 to 70,960. Therefore, in ten years' time the population relying on the hospital at Bromsgrove would have risen to 167,450.

Dr. MAGGS supported the resolution and suggested that consultation should take place at national level to see that adequate hospital accommodation was available in areas where redevelopment was contemplated. Dr. OWEN WILLIAMS said that if population growth was necessary in certain areas it was equally necessary for services to be established in these areas.

The committee supported the resolution.

Contract of Service

Dr. D. L. D. LAMONT spoke to the following motion by Mid-Hertfordshire which was among those not discussed by the Representative Body and referred to the Council: "That this Representative Body rejects the concept of 'whole-time' service defined in the third sentence of para. 22 of Appendix III of Annual Report of Council." All con-

† The third sentence of para. 22 of Appendix III of the Annual Report of Council read as follows: "'Whole-time' service means continuous availability, with unlimited hours of work, upon a fixed salary." The last sentence of the same paragraph read: "The maximum contractual week might then be defined as one of 10 notional half-days, and any service provided over and above this would require a separate (additional) contract."

tracts should be based on the criteria of the last sentence of that paragraph."

Dr. Lamont said that Mid-Hertfordshire rejected the present concept of full-time service.

The CHAIRMAN informed the Committee that the ten-tenths system was still being examined. Dr. H. L. LEAMING said there was a danger of approving the ten-tenths system by adopting the motion. He moved as an amendment "that further urgent consideration be given to the feasibility of the ten-tenths payments system."

Dr. LAMONT accepted the amendment, and the motion, as amended, was carried.

Review of Hospital Medical Staffing

Mr. R. COWLEY moved the following motion by Cleveland and Middlesbrough which had not been discussed at the A.R.M.: "That this Representative Body demands that the figures arising from the review of hospital medical staffing as modified and brought up to date following the Platt Committee report be published."

He suggested that the Minister of Health should concentrate on keeping doctors in this country, but that he would not be successful unless they could see that there were jobs for them.

Dr. HARVEY-SMITH said that the motion did not go far enough. It was all very well having figures published, but action was needed to implement them.

The CHAIRMAN drew attention to an amendment in the name of Redbridge which read: "Delete all words after 'brought up to date' and add: '... bearing in mind the urgent need to reduce waiting lists, and also to take into account the inpatient and outpatient work load, and, where necessary, to institute an immediate increase in consultant establishment.'"

The amendment, he said, seemed to strengthen the motion appreciably.

Mr. COWLEY agreed, and the motion, as amended, was carried.

Staffing of Accident and Emergency Departments

Dr. R. M. WARREN moved the following motion by Southampton that had not been discussed by the A.R.M.: "That this Representative Meeting, while appreciating the efforts of the Central Consultants and Specialists Committee and the Joint Consultants Committee, instructs Council to press vigorously for the implementation of a career structure in the 'casualty (emergency) service' in hospitals recommended in the memorandum submitted to the Central Consultants and Specialists Committee by the Senior Casualty Officers Subcommittee."

Dr. Warren said that the variety of skill required in the casualty service warranted a special study, and in order to obtain doctors of the right calibre it was necessary to offer those specializing in this field the prospect of reaching the top of the tree. An advantage in having consultant posts in the casualty service would be that the standard of treatment of minor injuries would be raised. Secondly, there would be uniformity of approach to a wide variety of specialized subjects, and the doctor in charge of the casualty department could negotiate with other specialized units on an equal footing.

Mr. J. C. WATTS (North Bedfordshire) supported the motion. Accidents, he said, were the commonest cause of death up to the fifth decade, the commonest cause of admission of males to hospital, and the commonest cause of emergency attendance at provincial hospitals and in suburban general practices, though not at teaching hospitals.

Mr. Watts said that at present undergraduates received one lecture on trauma during the elementary clinical period. In the surgical revision lectures there were three lectures on orthopaedics, including one on trauma. In postgraduate education in 1967 there were 69 lectures and courses, of which one was on accident and emergencies. Trauma was the only branch of surgery which embraced the whole body, yet there was very little known about it. Mr. Watts suggested that accident surgery would provide a satisfactory career for a consultant, and if consultants were appointed to work whole-time in accident departments able graduates would be attracted to fill the junior posts, as there would be prospects of advancement.

Mr. MYLES GIBSON suggested that the Committee would be unwise to rush into any major policy decision on this matter. He proposed that a small subcommittee should be appointed to assess the existing position in relation to the Platt Committee recommendations.

Mr. T. M. HENNEBRY said he thought a proposal for full-time consultants in casualty work should be viewed with suspicion. Some years ago there had been a plethora of senior registrars trained in orthopaedics, and for a short time they had been appointed as consultants to accident departments, but by and large it had not been a success. Though he would support anything which would strengthen the accident service, Mr. Hennebry said he was not convinced that this suggestion was the right way to go about it.

Mr. WATTS referred to what he described as a curious paradox in the Platt Report on medical staffing. It suggested that care of trauma was too big a subject for one man to tackle, yet it should be the part-time hobby of a surgeon. The two suggestions were incompatible. In his view there was a place for a specialist in trauma.

Dr. GLYN JONES supported the motion. The accident and emergency service was the most important part of the hospital service, he said, and should be recognized as a specialty in its own right. Dr. OWEN WILLIAMS thought there was a strong case for setting up a subcommittee to look at the problem. The need for a doctor of consultant status to look after casualties was self-evident. Dr. MAYON-WHITE said that he also was in favour of a career grade for casualty surgeons.

The CHAIRMAN said he did not think that the Committee had ever really studied the problem, and he asked the mover and seconder of the motion if they would agree to the suggestion that a subcommittee should be set up to study the matter.

Dr. WARREN and Mr. WATTS agreed, and Mr. Watts emphasized the urgency of the problem, because, he said, those currently in charge of accident departments received their training in trauma during the war. There were no replacements in the line.

The Committee agreed to appoint a subcommittee to study the question as a matter of urgency and to report.

Consultant Training

Dr. K. C. ROBINSON moved the following West Hertfordshire motion that had not been discussed at the A.R.M.: "That this Meeting regrets the omission from Appendix IV of the Annual Report of Council of any mention that some experience in general practice should be a requirement of the training of a consultant."

Appendix IV, Dr. Robinson said, examined the existing system of postgraduate education in relation to consultants, medical teachers, research workers, general practitioners, and public health medical officers. Referring to the training of consultants, Dr. Robinson said that it was well known that a trainee was expected to hold a series of posts, including possibly some time in a research post, before he applied for a consultant vacancy. The West Hertfordshire Division thought that time should be allowed for some work in general practice.

Dr. R. C. GREENBERG said it was deplorable that a doctor could become a consultant without ever having set foot in a patient's home. It was an important motion in relation to improving communication between doctor and patient.

Mr. W. DRUMMOND said that the concept of every consultant doing a period in general practice was excellent, but it was very doubtful whether there was time for it during training. A young man had to do many other things in climbing up the ladder in the hope of becoming a consultant. Mr. Drummond suggested that time in general practice might be better spent at student level.

Dr. ASTLEY opposed the motion. He said that he had always believed that the alleged benefits of a consultant doing a few weeks in general practice were emotionally exaggerated. Mr. MYLES GIBSON agreed with Mr. Drummond. While he sympathized with the content of the motion, it was a matter that was increasingly being taken into account in the undergraduate curriculum.

Dr. J. B. S. MORGAN said it was difficult to insist on a period in general practice. There were many factors which determined a man's career. It was true that those who had had general practice experience and who had become consultants usually held the view that it was of great value. Dr. RIDGE said that a period of training in general practice could serve a vital function. General practitioners derived more help from consultants who had gained practical knowledge of general practice problems than they obtained from consultants who had not had this experience. The patients' interests would be improved by a closer understanding by consultants of the problems which general practitioners faced. Dr. MAYON-WHITE said it was becoming increasingly impossible during the postgraduate training years for consultants to spare time for other things. Valuable as experience in general practice was it must be gained by the student before qualification.

The motion was lost.

Care of Young Chronic Sick

Dr. GREENBERG moved an A.R.M. motion by East Herts: "That urgent attention should be given to the provision of special centres for the care of the young chronic sick."

There was an amendment by Finchley and Sheffield to add the words: "which should take into account their need to live as full a life as possible in close contact with their own families."

Dr. Greenberg said it was necessary to deal with the problem of the young chronic sick in a more humane way than in the past. It was quite wrong to take them away from their family setting. They were human beings who should not be excluded from the community.

Dr. WEDGWOOD said that everyone must be sympathetic with the idea put forward, but the trouble with the motion was that it referred to the provision of "special centres" for the care of the young chronic sick. The problem was already being dealt with in most centres. Geriatricians were aware of the problem. In his view many of the young chronic sick fitted in quite well to geriatric hospitals.

Dr. MAGGS supported the motion. He thought the number of young chronic sick would increase in the future, particularly as a result of road accidents. Head injuries in young people were more frequently encountered. Unfortunately, general hospitals were often unable to go on caring for these people, and a number of them were sent inappropriately to a psychiatric hospital.

Dr. A. T. FORD supported the motion, particularly bearing in mind young patients suffering from malignant disease. They were often unsuitable for admission to geriatric units.

Dr. ASTLEY asked what the mover of the motion had in mind by "young chronic sick." Dr. GREENBERG replied that he had in mind those with congenital disorders, but he thought that the Sheffield Division, who were joined in the amendment, had in mind "lame brains." There was, he suggested, a need for special provision to meet the problem, but he emphasized that such special provision need not inevitably mean hospital beds.

The motion was carried.

Preregistration Posts

Dr. I. MCKIM THOMPSON moved a motion by Birmingham that had not been discussed at the A.R.M.: "That this meeting is of the opinion that any provisionally registered practitioner shall be allowed to take his preregistration posts in any hospital approved for the purpose, regardless of its geographical location."

He said that in March the following notice was posted in Birmingham University: "After a recommendation from the General Medical Council that universities should supervise preregistration appointments of their medical graduates much more closely than in the past, the Board of the Faculty has passed the following resolution: 'That medical graduates of this university are normally required to complete their preregistration service in approved posts at hospitals under the jurisdiction of the United Birmingham Hospitals and the Birmingham Regional Hospital Board, or in Salisbury, Rhodesia.' The notice had concluded: 'Exceptions from this rule will be few and will require the personal approval of the Dean.'"

An immediate protest had been made by local members of the B.M.A. at this direction of labour and unheralded reduction of per-

sonal freedom. After that protest a press statement was made by a senior member of the faculty which stated that posts existed which could never be filled. Furthermore, "many students leave the area for extraneous reasons such as married quarters. The more remote areas have been able to entice married men away with the offer of a nice little love nest."

Two extremely important points arose from those statements, continued Dr. Thompson. Firstly, any attempt to direct labour on any grounds must be resisted. If preregistration jobs were once allowed to be filled by compulsory drafting it would be only a matter of time before more senior posts were filled on the same basis. Secondly, it was probably significant that hospitals with poor amenities for resident staff (and he included married quarters) were finding it increasingly difficult to fill junior hospital posts. "Let them correct these faults and they will have a much easier time in filling their posts," he added.

Dr. Thompson agreed with the General Medical Council that adequate postgraduate supervision was long overdue, and, while in no way advocating broodiness, the preregistration doctor must be able to choose the place where he decided to nest.

Dr. GREY-TURNER said that the attention of the Medico-Legal Subcommittee had already been drawn to the notice. Legal opinion had been taken, which was that the notice was *ultra vires*.

The motion was carried, and the Committee agreed that a statement making the position quite clear should be drawn up and published.

Accepted Motion

The CHAIRMAN drew attention to the following motion, standing in the name of Mid-Essex, that had been an accepted A.R.M. motion: "That the consultant selection committees should be balanced, in order to ensure that the application of the registrar with regional experience is always considered equitably."

Mr. ALEX LYALL moved an amendment in the name of Renfrewshire to add at the beginning of the motion: "When consultant appointments are being made in the teaching hospitals, the consultant selection committees . . ."

Mr. D. BROWN urged the Committee to reject the amendment. He thought the motion should stand, so that registrars with regional experience were given a fair chance, whether applying for teaching hospital appointments or other hospital appointments.

The Committee agreed to allow the original motion to stand, and to consider as a separate motion the motion by Mid-Essex as amended by Renfrewshire—namely, "When consultant appointments are being made in the teaching hospitals, the consultant selection committees should be balanced in order to ensure that the application of the registrar with regional experience is always considered equitably."

The motion was carried.

Dr. A. N. MATHIAS, Chairman of the Representative Body, said he greatly regretted the truncation of hospital business at the Annual Representative Meeting in Bristol. The new procedure for the conduct of business at the meeting would prevent that sort of thing happening again. In addition to constitutional suggestions which had been

approved the Agenda Committee had already met and had suggested certain changes in Standing Orders which would facilitate matters. If the Standing Orders were agreed by the Representative Body what occurred at Bristol would be most unlikely ever to happen again. Subject to there being no major medico-political crisis to be considered, he had promised the Chairman of the Committee that hospital business would be taken after the preliminary business on the first day of the A.R.M. in 1968.

The Committee agreed that the following motion in the name of Brighton and Mid-Sussex be submitted to the Hospital Junior Staff Group Council for consideration: "That, in view of the unsatisfactory career structure of Junior Hospital Staff, it is proposed that in future 75% of the appointments to the ranks of registrar and senior registrar should be linked to major centres."

The following amendment to the motion, standing in the name of Renfrewshire, was sent to the Regional Committee for Hospital Medical Services for comment and report to the Central Committee: "Add at the end of motion: ' . . . but that there be no diminution in size of the total registrar establishment of the area, without prior agreement with the district hospitals, and that there should be rotation of registrars between the teaching and district hospitals.'"

A motion in the name of Winchester, urging the B.M.A. to take steps to persuade the Ministry of Health to permit independent work studies to be carried out within all branches of the National Health Service, was carried.

Hospital Building

The Committee considered the following motion by St. Marylebone that had not been discussed by the A.R.M.: "That this Meeting deprecates the present practice of money obtained from the sale of valuable hospital sites being put directly into the Treasury, and strongly recommends that these monies should be credited to the funds of the hospital or hospital services concerned."

Mr. ALAN SMALL said that he had always thought that if some arrangement could be made with the Treasury for compensation to be paid to the group when a hospital was disposed of it would encourage hospital management committees to be more efficient. Dr. WHITESIDE supported the motion.

Dr. SKENE pointed out that a hospital was not owned by a group. It was Crown property, and if it was not required for Crown purposes the Treasury deployed the resources for other Crown purposes.

The motion was carried.

Other A.R.M. Motions

The following motion by South Staffs was considered: "That whole-time senior hospital staff be granted tax incentives equivalent to their part-time colleagues."

The CHAIRMAN said that if the Committee supported the motion it would be asking the negotiators to undertake an almost impossible task.

The motion was lost.

A motion by Brighton and Mid-Sussex, noting that the value of conferences such as the Hospital Medical Staff Conference was

largely vitiated by the absence of previously notified specific motions for debate, was referred to the Arrangements Subcommittee for consideration.

The Committee agreed to look at the following motion in the name of St. Marylebone in association with the report of the Royal Commission on Medical Education: "That this Meeting recommends that non-teaching or peripheral hospitals should be used much more than they are for the teaching of medical students, and it would be desirable for all medical students to spend part of their curriculum outside a teaching hospital where they would obtain wider experience of medicine and surgery than is available at the overspecialized teaching hospitals of the present day."

A motion on the same subject in the name of Tower Hamlets, "That this Meeting considers that where it is proposed that a

non-teaching hospital should be designated to a teaching hospital there, should be adequate consultations with local practitioners before any action is taken," was accepted, provided "local practitioners" meant all local members of the profession concerned.

A motion by Morpeth and Blyth, expressing concern at the deplorable lack of geriatric beds in the County of Northumberland, particularly in the Wansbeck area, and censuring the Ministry of Health for failing to make adequate provision over a period of 18 years, was submitted to the regional committee for consideration.

The CHAIRMAN reported that a recommendation in a motion by Havering, that a standard discharge summary form giving details of the diagnosis, treatment, and follow-up recommendations be used, was being dealt with.

Similarly, he said that action was being taken on a motion by Liverpool that completion of cremation certificates Parts B and C should attract a fee for all doctors.

The Committee gave general support to the following motion by Dunbartonshire in the sense that it referred to emergency calls: "That there should be an investigation into a proper method of recognition for the services of a consultant who undertakes work in a general-practitioner unit."

The Committee also supported the general principle contained in a motion by Greenwich and Deptford asking the Minister of Health to make post-auricular hearing aids prescribable by consultants in the N.H.S., and referred the motion to the Otolaryngologists Group Committee for comment.

The remaining motions were submitted to the Executive Subcommittee for consideration and report back to the Committee.

General Practice Finance Corporation

The Ministry of Health has stated that since the General Practice Finance Corporation began to consider applications from general practitioners in May it has made 141 loans totalling £683,000. It has also agreed to make loans totalling nearly £800,000 which had been approved under the Group Practice Loans Scheme but had not been issued when that scheme was wound up in May. About 10 new applications for loans are received by the Corporation each week.

The first report of the General Practice Finance Corporation* was published on 23 October. It covers only the first few months of the Corporation's existence, before it had made any loans.

The Corporation was established by the Government to implement the agreement between the Minister of Health and the general practitioners' representatives in their discussions on the family doctor service (*Supplement*, 5 June 1965, p. 238) that an independent corporation should be established with powers to make loans to doctors for the purchase, erection, and improvement of practice premises, and with a reserve power to make loans for the purchase of equipment.

The members of the Corporation are Sir Frederick A. Hoare, Bt. (Chairman), Sir William Mullens (Deputy Chairman), Lord Crook, Dr. F. Lishman, Sir William Murrie, Mr. A. E. Orchard-Lisle, Dr. S. Wand. The Corporation operates within a scheme

approved by the Health Ministers and the main purposes for which it makes loans are (1) to provide, or to acquire a share in, practice premises; (2) to alter, enlarge, improve, or repair practice premises; (3) to acquire land required for the erection of, or in connexion with the use of, practice premises; and (4) to repay a loan raised earlier for any of these purposes.

Security

The report states that one of the Corporation's important functions will be to make loans on security which might not be considered adequate when judged by normal commercial standards. At the same time the Corporation had to bear in mind the requirement of the relevant section of the N.H.S. Act 1966 that it should so discharge its functions "that, taking one year with another, its revenue shall be sufficient to meet its expenses including allocations to reserve." The Corporation has decided therefore that, while it "would be willing to consider loans of up to 100% of the valuation of the premises or land and would, if required, add approved costs to this amount, it would, wherever possible, require the security of a legal mortgage."

Loans will, nevertheless, be made in suitable cases, even though little security can be given other than the borrowing doctor's covenant to pay coupled with a guarantee from a third party and, possibly, the assignment of an endowment policy.

* *Report of the General Practice Finance Corporation for the period 21st November 1966 to 31st March 1967.* H.M.S.O., London, 1s. 6d.

Surrey Public Health Appointment

After a meeting called by the British Medical Guild on 26 October, to which all medical officers of the Surrey County Council were invited, a letter was sent by the Guild to the County Council criticizing the circumstances in which the appointment of the new county medical officer of health was made. "Any appointment of a chief officer by an authority in such circumstances and from a restricted field of applicants could scarcely be expected to inspire confidence in the staff of the department concerned," it said.

The letter went on to state that the medical officers of the Surrey County Council had

asked that an immediate request be made by the British Medical Association to the Minister of Health and to the Secretary of State for Education and Science for an inquiry into all aspects of the appointment.

Owing to the British Medical Guild's appeal to doctors not to apply for public health service posts until an acceptable offer has been made in response to the profession's pay claim, it is known (the Guild's letter states) that many medical officers "admirably fitted" for the Surrey appointment refrained from replying.

Tuberculosis and Diseases of Chest

A meeting of the Tuberculosis and Diseases of the Chest Group Committee of the B.M.A. was held on 17 October. Dr. T. W. Davies, who had been chairman of the Group Committee for many years, did not seek re-election.

Dr. G. F. EDWARDS, Harrogate, was appointed Chairman, and Dr. W. D. GRAY, Liverpool, Deputy Chairman. The Chairman and Deputy Chairman were appointed to represent the Committee on the Central Committee for Hospital Medical Services.

The Group Committee paid tribute to Dr. Davies's services during his tenure of the chair.

B.M.A. Nuffield Library

The Library Service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

- Bell, E. T., and Loraine, J. A.: *Recent Research in Gonadotrophic Hormones.* 1967.
- Bernstein, N.: *The Co-ordination and Regulation of Movements.* 1967.
- Cargill, D.: *Accidents in the Home.* 1967.
- Cargill, D.: *How to Avoid a Coronary Thrombosis.* 1967.
- Carter, G. S.: *Structure and Habit in Vertebrate Evolution.* 1967.
- Cartwright, A.: *Patients and their Doctors.* 1967.
- Croll, N. A.: *Ecology of Parasites.* 1966.
- Edeiken, J., and Hodes, P. J.: *Roentgen Diagnoses of Diseases of Bone.* 1967.
- Elkes, A., and Thorpe, J. G.: *A Summary of Psychiatry.* 1967.
- Feinstein, A. R.: *Clinical Judgement.* 1967.
- Fishlock, D.: *The New Materials.* 1967.
- Fripp, A. T., and Shaw, N. E.: *Club-foot.* 1967.
- Gibson, J., and French, T.: *Nursing the Mentally Retarded.* 1967.
- Goldman, M.: *A Nurse's Guide to the X-ray Department.* 1967.
- Gray, C. H. (Editor): *Laboratory Handbook of Toxic Agents*, 2nd. edition. 1966.
- Grieve, J. M.: *Cancer in the Cape Division, South Africa.* 1967.

Association Notices

Armed Forces Committee
Nomination of Members for Co-option

The constitution of the Armed Forces Committee was amended at the Annual Representative Meeting of the Association in July 1967 to allow greater representation of serving medical officers, especially younger members, by means of co-option to the Committee. The Committee may now co-opt two representatives of the rank of major or equivalent (lieutenant-commander or squadron leader) or below, one of whom should preferably be of specialist status, from the medical branch of each of the Services.

Notices appeared in the *B.M.J.* (Supplement, 26 August and 16 September, pp. 124 and 130 respectively) inviting serving medical officers to nominate members of the Association in the armed Forces in these ranks for co-option to the Committee.

At its meeting in October the Armed Forces Committee considered the nominations received and the following have been co-opted to the Committee:

Army.—Major T. R. Austin, specialist in anaesthetics at the Cambridge Military Hospital, Aldershot.

Navy.—Surgeon Lieutenant-Commander J. A. M. Wright, medical specialist at the Royal Naval Hospital, Plymouth; Surgeon Lieutenant-Commander D. S. Wright, G.D.O., H.M.S. *President*.

R.A.F.—Squadron Leader J. B. Crowe, Consultant Radiologist, P.M.R.A.F. Hospital, Halton, Bucks.

The Committee thought it was most important that non-specialists should be represented from each of the Services, and it decided to seek further nominations for the non-specialist vacancy in the Army and in the R.A.F. representation.

Serving medical officers in the Army and the R.A.F. are therefore invited to nominate members of the Association in the rank of major, squadron leader, or below of non-specialist status for co-option to the Committee. It is hoped that those nominated would have a reasonable expectation of being available to attend meetings in London in the foreseeable future.

Nominations should be sent to the Secretary of the Association by 23 December 1967 for subsequent consideration by the Armed Forces Committee.

DEREK STEVENSON, *Secretary*.

Diary of Central Meetings

NOVEMBER

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|-----------|--|
| 7 Tues. | G.M.S. Committee (Scotland) (at 9 Lynedoch Crescent, Glasgow), 10.30 a.m. |
| 7 Tues. | Consultant Pathologists Group Committee, 2 p.m. |
| 7 Tues. | Forensic Medicine Subcommittee (Private Practice Committee), 2 p.m. |
| 8 Wed. | Joint Formulary Committee, 10.30 a.m. |
| 8 Wed. | Working Group on the Instruction of Expectant Mothers by Unqualified Teachers, 11.30 a.m. |
| 8 Wed. | Charities Committee, 2.15 p.m. |
| 14 Tues. | Standing Subcommittee (Central Ethical Committee), 11 a.m. |
| 14 Tues. | G.M.S. Disciplinary Machinery Working Group, 2 p.m. |
| 15 Wed. | Committee on the Mental Health Act, 10.30 a.m. |
| 15 Wed. | Rural Practices Subcommittee (G.M.S. Committee), 2 p.m. |
| 16 Thurs. | Chairman's Subcommittee (Organization Committee), 9.30 a.m. |
| 16 Thurs. | Film Committee, 2 p.m. |
| 16 Thurs. | Membership and Information Subcommittee (Organization Committee), 2 p.m. |
| 17 Fri. | Working Party on Postgraduate Medical Centres, 2 p.m. |
| 17 Fri. | Welsh Committee (at the Metropole Hotel, Llandrindod Wells, Radnorshire), 2.15 p.m. |
| 22 Wed. | Working Party on Amphetamine Preparations (Committee on Medical Science, Education, and Research), 9.30 a.m. |
| 22 Wed. | Journal Committee, 10.30 a.m. |
| 22 Wed. | Psychological Medicine Group Committee, 2 p.m. |
| 23 Thurs. | Compensation and Superannuation Committee, 2 p.m. |
| 23 Thurs. | Dermatologists Group Committee, 2.30 p.m. |

DECEMBER

- | | |
|---------|--|
| 4 Mon. | Scottish Committee for Hospital Medical Services (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m. |
| 13 Wed. | Journal Committee, 2 p.m. |

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

ARGYLL AND BUTE DIVISION.—At Cairnbaan Hotel, Sunday, 12 November, 11 a.m., Autumn meeting, luncheon and address by Lord Birsay: "General Medical Services in the Highlands and Islands."

Dr. S. J. Hadfield (Scottish Secretary, B.M.A.) will be present. Ladies are invited.●

BARNET DIVISION.—At Outpatients' Department, Barnet General Hospital, Tuesday, 7 November, 8 p.m., clinical meeting.

BLACKBURN DIVISION.—At Committee Room, No. 1, Town Hall, Tuesday, 7 November, 8.15 for 8.30 p.m., B.M.A. lecture by Sir Theodore Fox: "Population and Family Planning." Ladies are invited.

BRADFORD DIVISION.—At Bradford Royal Infirmary, Wednesday, 8 November, 8.15 p.m., general meeting.

BRENT DIVISION.—At St. Andrew's Hospital, Tuesday, 7 November, 8.30 p.m., clinical evening presented by hospital consultants.

BUCKINGHAMSHIRE DIVISION.—At Archery Unit, Stoke Mandeville Hospital, Friday, 10 November, 8.30 p.m., B.M.A. lecture by Professor W. J. H. Butterfield: "Community Medicine of the Future." (Preceded by election of representatives to Annual Representative Meeting, 8.25 p.m.)

BURY DIVISION.—At Bury General Hospital, Saturday, 11 November, annual dinner.

COVENTRY DIVISION.—At Outpatient Department, Coventry and Warwickshire Hospital, Tuesday, 7 November, 8.30 p.m., "spot diagnosis" evening, followed at 9.30 p.m., in Physiotherapy Department, by discussion of cases.

CUMBERLAND DIVISION.—At Cumberland Infirmary, Carlisle, Friday, 10 November, 8 p.m., annual general meeting.

DEWSBURY DIVISION.—At Three Nuns Inn, Mirfield, Thursday, 9 November, 8 for 8.30 p.m., annual dinner.

DUNBARTONSHIRE DIVISION.—Monday, 6 November, visit to Broadcasting House, Glasgow.

EAST YORKSHIRE BRANCH.—At Postgraduate Centre, Hull Royal Infirmary, Wednesday, 8 November, 8.30 p.m., B.M.A. lecture by Professor Henry Miller: "Pain in the Arm."

GLOUCESTERSHIRE BRANCH.—At Board Room, Gloucestershire Royal Hospital, Gloucester, Thursday, 9 November, 6.30 p.m., meeting, Dr. A. E. Tinkler: "The Recrudescence of Venereal Disease or the Copulation Explosion." (Followed by dinner at New Country Hotel.)●

GUILDFORD DIVISION.—At School of Nursing, St. Luke's Hospital, Tuesday, 7 November, 8 p.m., jointly with Guildford Postgraduate Medical Centre, clinical meeting, followed at 8.45 p.m., Coyle Hall, by discussion of cases.

HALIFAX AND TADMORD DIVISIONS.—At White Swan Hotel, Halifax, Thursday, 9 November, 8.30 p.m., Dr. J. Todd: "Drug Addiction."

HARROW AND HILLINGDON DIVISION.—At Whittington Hotel, Pinner, Tuesday, 7 November, 8.45 p.m., Dr. S. T. Hayward: "Motoring Through Russia" (illustrated). Guests are invited.

HOLLAND DIVISION.—At Westland Hall, Boston General Hospital, Wednesday, 8 November, 8.15 p.m., Mr. K. F. Wood: "Diseases of the Small Bowel." (Followed by buffet supper.)●

HUDDERSFIELD DIVISION.—At Rest Room (next to Chapel), South Entrance, Royal Infirmary, Lindley, Tuesday, 7 November, 8.30 p.m., general meeting followed by film: "And Then There Was One."

ISLE OF WIGHT DIVISION.—At Medical Centre, St. Mary's Hospital, Newport, Thursday, 9 November, 8.30 p.m., B.M.A. lecture by Dr. J. Cyriax: "Manipulative Medicine."

LIVERPOOL DIVISION.—At Exchange Hotel, Tuesday, 7 November, 8 for 8.30 p.m., annual general meeting, followed by videotape discussion: "Treatment of Depression in General Practice."

MID-ESSEX DIVISION.—At Academic Unit, Chelmsford and Essex Hospital, Wednesday, 8 November, 8.30 p.m., annual general meeting.

MID-GLAMORGAN DIVISION.—At York Hotel, Bridgend, Monday, 6 November, 8 p.m., at invitation of Pharmaceutical Society, taped lecture on "Diuretics" followed by discussion.●

MID-HERTS DIVISION.—At Medical Centre, St. Albans City Hospital, Friday, 10 November, 8.30 p.m., annual clinical demonstration.

NORTH BEDFORDSHIRE DIVISION.—At Medical Institute, Thursday, 9 November, 8.30 p.m., jointly with Bedford Medical Society, Wing Commander P. J. Stevens: "Medical Investigation of Aircraft Accidents."

NORTH NORTHUMBERLAND DIVISION.—At Community Centre, Berwick-upon-Tweed, Tuesday, 7 November, 8.30 p.m., film: "The Anaemias."

NUNEATON DIVISION.—At Gymnasium, Manor Hospital, Tuesday, 7 November, 8 for 8.30 p.m., symposium by Mr. A. Gourevitch, Dr. J. Howel Jones, Dr. E. E. Jones, Dr. A. W. Robinson: "Peptic Ulcer."

ROTHERHAM DIVISION.—At Brecon Hotel, Monday, 6 November, 9 p.m., B.M.A. lecture by Dr. Brian Inglis: "Fringe Medicine." (Preceded by supper, 7.45 for 8 p.m.)●

SALISBURY DIVISION.—At Pembroke Arms, Wilton, Saturday, 11 November, 7 p.m., annual dinner and lecture, Dr. K. J. Kilka: "Coma and Consciousness."●

SOUTH BEDFORDSHIRE DIVISION.—At Halfway House, Tuesday, 7 November, 8 for 8.30 p.m., annual dinner. Principal guest, Dr. Derek Stevenson (Secretary, B.M.A.). Guests are invited.●

SOUTH MIDDLESEX DIVISION.—At Skyway Hotel, Saturday, 11 November, 7 p.m., annual dinner dance.●

SOUTH SHIELDS DIVISION.—At General Hospital, Wednesday, 8 November, 8.30 p.m., Professor S. Shuster: "The Skin and Gut, Further Developments in Dermatological Mythology."

STOCKPORT DIVISION.—At Alma Lodge Hotel, Thursday, 9 November, annual dinner dance.●

WALSALL DIVISION.—At Hollies Club and Hotel, Cannock, Thursday, 9 November, 8.15 p.m., joint supper meeting with Cannock Medical Society, Dr. B. L. Pentecost: "Acute Coronary Care." Guests are invited.●

WIGAN AND LEIGH DIVISIONS.—At Haigh Hall, Haigh, Friday, 10 November, annual dinner and dance.●

WORCESTER AND BROMSGROVE DIVISION.—(1) At Board Room, Worcester Royal Infirmary, Monday, 6 November, 8.30 p.m., meeting to elect representatives and to discuss problems in hospital services in North Worcestershire. (2) At Gifford Hotel, Worcester, Saturday, 11 November, 7.45 for 8.15 p.m., annual dinner. Guest speaker, Mr. David Franklin.●

British Medical Journal Supplement

LONDON SATURDAY 11 NOVEMBER 1967

CONTENTS

General Medical Services Committee	43	Opportunities Overseas for Retired Practitioners	50
General Medical Services Committee (Scotland)	47	H.M. Forces	50
University and Armed Forces Pay for Prices and Incomes		Was it a Drug?	50
Board	48	B.M.A. Nuffield Library	51
S.H.M.O. Group Council	49	Armed Forces Committee: Nomination of Members	51
"Mediflash"	50	Association Notices	52

General Medical Services Committee

How to make local medical committees more democratic was again a matter of debate in the G.M.S. Committee. Some of the ways in which the changeover to the metric system will affect prescribing were described in a Ministry of Health memorandum which was the subject of a preliminary discussion. An inquiry of local medical committees showed that 10% would like general practitioners in their area to have better facilities for open access to hospital pathology departments and 20% would like better access to radiodiagnostic departments. More than 30% would like more access to electrocardiography and physiotherapy. The Committee did not come to a decision on a motion proposing that postgraduate education sessions should in no way be connected with general practitioners' career earnings, including seniority payments. With the support of the Public Health Committee, the G.M.S. Committee is again to ask the Ministry of Health to encourage local health authorities to provide domiciliary physiotherapy services. The Ministry is also to be pressed to provide an admissions bureau for emergency admissions to mental hospitals in Greater London. The problems for general practitioners in dealing with heroin addicts under the new legislation were discussed.

A Meeting of the General Medical Services Committee was held on 26 October. Dr. J. C. CAMERON was in the chair.

A report of the death of Dr. K. S. Maurice-Smith, of Ely, who had been a member of the Committee from 1952 to 1964, was received with deep regret. The Committee paid tribute to Dr. Maurice-Smith's services to it and to the profession.

Appointment System

The Committee considered a letter from the Inner London Local Medical Committee stating that it had received a complaint from a London doctor that general practitioners who had an appointments system were being greatly troubled by patients without appointments who wanted to be seen on the day they attended. The doctor had suggested that the Ministry of Health should tell the public that patients had no right to be seen without an appointment unless their condition was urgent.

The Inner London Local Medical Committee supported the doctor's complaint, and asked the G.M.S. Committee to consider "arranging with the Ministry of Health for the preparation of an appropriate notice for doctors' waiting-rooms, and for its eventual circularization to practitioners by executive councils, and for the position to be brought to the notice of patients by all other possible means."

Dr. D. R. COOK thought that the complaint was fully justified, and asked for the Committee's support.

The Committee agreed to draw the Ministry's attention to the matter.

Constitution of Local Medical Committees

The Committee considered the Ministry of Health's comments on the draft model scheme for the constitution of local medical committees, drawn up by the Constitution Subcommittee of the G.M.S. Committee, together with a revised draft scheme for the constitution of Liverpool Local Medical Committee.

Dr. A. SPEAKMAN said that there were certain points which he would like to have included in the model constitution to offset criticism from the electorate that it had insufficient voice in the running of the local medical committee. He referred to the question of the terms of office of members of the local medical committee and to the appointment of officers. There was often a belief among the

electorate that the chairman of the local medical committee, once elected, would remain in the chair for many years. There should, he said, be a clause in the model scheme to ensure that the electorate was free to change the chairman if it so wished. The object was to make sure that the process was democratic. It would then be up to the electorate to use it.

Dr. Speakman thought that there should be a clause in the model constitution to the effect that the local medical committee must meet regularly. He also said that there should be provision for extraordinary meetings of the committee.

Dr. A. ELLIOTT agreed that local medical committees must be run democratically and be seen to be democratic. Four years ago, he said, as a result of a decision of the Annual Conference of Representatives of Local Medical Committees, a committee had been set up to look into this, and it had met many times. Every point raised by Dr. Speakman had been considered by that committee. The G.M.S. Committee had no right to impose anything on local medical committees. It could only try to persuade all local medical committees to conduct their affairs by the highest standards. A survey had been carried out, and it appeared that many local medical committees were not elected democratically. It was up to the G.M.S. Committee to persuade local doctors to change the situation.

Dr. Elliott said he would have wished to see other things included in the model constitution, but in its existing form it was a big step forward from the practice in some areas. Attention was being drawn to the situation, and it was now rare to find doctors who did not know about their local medical committee. It was a matter of education. The model constitution was not mandatory and could be adjusted to local circumstances. Revised constitutions would have to be submitted to the Ministry for approval.

Combined Posts

Dr. R. A. KEABLE-ELLIOTT pointed out that policy varied from place to place. In some local medical committees the secretary was also the clerk to the executive council, and this often worked well, but in these circumstances there needed to be a medical public relations officer, because a doctor preferred to discuss matters with a doctor.

Dr. G. CORMACK did not agree that it was a good idea for the secretary of a local medical committee also to be the clerk of the executive council. He thought it could lead to empire-

building, and create the impression that the powers of the clerk of the executive council were unlimited.

Dr. R. B. L. RIDGE said that the Committee must bear in mind the true nature of a local medical committee. It was an autonomous local professional committee. It was vital in the interests of general practice that this autonomy should be preserved. But under the National Health Service Act there were certain statutory functions to be discharged by local medical committees, which were recognized by the Minister as being representative of general practitioners in the area. It was solely in relation to the discharge of those statutory functions that the constitution required ministerial approval.

Dr. Ridge suggested that it would be unwise to incorporate in the constitution of a local medical committee, over which the Minister of Health had control, matters which were more appropriate for the standing orders of the committee. The standing orders did not have to be approved by the Minister, and these could include the method of election of the local medical committee and its officers, and rules relating to its meetings and to the conducting of its business, and for the election of representatives on the executive council. These were all matters, said Dr. Ridge, which should be left within the autonomy of the local medical committee. If there was any doubt in an area that the local medical committee was not running its affairs democratically the electorate had its redress at election time.

Dr. SPEAKMAN agreed with Dr. Ridge's comments and suggested that the G.M.S. Committee might draw up a model list of standing orders, which could be given to local medical committees as a guide, together with the model constitution if any committee requested assistance on this matter.

The G.M.S. Committee agreed with Dr. Speakman's suggestion, and decided to consider the matter again later.

Evidence to Review Body

After a debate *in camera* the Committee decided that a statement should be issued on the subject of the submission of evidence to the Review Body. The statement was as follows:

"The Committee heard a statement from Dr. Cameron on the bases on which the evidence was being prepared and the procedure to be adopted before the Review Body. He also explained the cross-representation with those preparing the case for hospital doctors. It was resolved that the document of evidence would be published when the Review Body had reported, and it was assumed that the Ministry of Health would agree that its evidence would be similarly available for publication.

"Dr. Cameron gave an assurance that in the evidence full weight was being given to all the relevant decisions of the Conference of Representatives of local medical committees and of the Representative Body."

Prepaid Postage

The Committee considered the question of the prepayment of postage on doctors' letters referring patients to hospital.

Dr. H. J. EASTES said that the practice varied over prepayment of official postage when returning medical records to executive councils, and he asked why there could not be a uniform practice for all areas in this matter. Dr. A. J. ROWE explained that the Ministry would not take this item out of context of all other practice expenses, because postage was considered to be part of a doctor's normal practice expenses.

The Committee agreed to press the matter with the Ministry.

Dr. H. S. HOWIE WOOD pointed out that there was also a lack of uniformity in the prepayment of postage on letters referring patients to hospital.

The Committee agreed also to discuss this matter with the Ministry of Health.

Metric System

The Committee considered a memorandum from the Ministry of Health setting out the ways in which the medical and pharmaceutical professions would be affected when a change-over to the metric system for prescribing and dispensing took place. The Ministry had stated that regulations would be necessary in connexion with the completion of the change-over.

The memorandum before the Committee was the result of informal discussions between the Ministry of Health and the Pharmaceutical Society, which had been considering the practical steps necessary in a changeover to the metric system. The Ministry asked for the G.M.S. Committee's comments on any aspects which it thought might give rise to difficulty. In the meantime the Ministry was considering the legal aspects of the matter.

Dr. RIDGE called attention to the following extracts from the memorandum.

When prescribing was not done in the metric system, the memorandum stated, an accurate equivalent in metric of the order in grains, drachms, etc., would be dispensed. By using the title of the preparation the doctor would be regarded as having ordered the ingredients contained in 5 ml. or 10 ml. of the preparation to be formulated in the B.N.F., 1968, not the amount in a teaspoonful or tablespoonful, and the respective 5-ml. or 10-ml. volumes would be dispensed. Labels would bear the instruction "One 5-ml. dose to be taken . . ." and a 5-ml. dose British Standard spoon would be issued. Similar instructions would be given for the 10-ml. dose, and a measure would be supplied graduated at 10-ml. dose and permitting the necessary dilution of the stronger adult mixtures of the future.

Dr. Ridge said that it was impossible with that type of vertical measure to get a medical dose. There should be a proper measure which clearly indicated what the dose should be.

The memorandum pointed out that when the quantity ordered or the number of doses specified instead of quantity did not coincide with one of the metric bottle sizes and the round number of doses it contained it would be necessary to establish a practice acceptable to medical opinion. Either the patient could be given a partially filled bottle of medicine, or the quantity or number of doses dispensed could be adjusted by reference to the "Total Quantities Table," so that the patient received a full bottle. If the second alternative were accepted (as pharmacists and probably

patients would prefer) the quantities dispensed and received would be those which doctors would be expected to order when fully accustomed to the new system. Provision could be made for the supply of the odd quantity in essential cases when the doctor expressly indicated it.

Dr. Ridge said that doctors would be in danger of having their freedom to prescribe a predetermined course of treatment limited if courses had to be related to standard-size bottles. The Committee should state its preference for the first alternative.

Dr. Ridge said he did not understand which regulations in the terms of service were being referred to in the following statement in the memorandum, and he hoped that there would be nothing put into the terms of service requiring doctors to prescribe in metric units: "For the dispensing of prescriptions not written in metric, and, where applicable, to those written in metric, consideration is being given to the preparation of regulations under the Weights and Measures Act, 1933, and to requisite changes in the N.H.S. (General Medical and Pharmaceutical Services) Regulations (terms of service)."

The Committee decided to defer further consideration of the memorandum until its next meeting.

Open Access to Diagnostic Departments

The Committee considered a summary of replies from local medical committees to its inquiry about the availability of open access to hospital diagnostic departments.

The inquiry had shown that there was little dissatisfaction among general practitioners over access to departments of haematology, biochemistry, and bacteriology. Just over 10% of local medical committees wanted more facilities in pathology departments, and 20% wanted more facilities in x-ray departments. More than 30% wanted greater access to both electrocardiography and physiotherapy departments, though the doctors in the areas of over 60% of all the committees which had replied had no access at all to those facilities.

One point which had become apparent from the inquiry was the shortage of staff in the various departments. A number of local medical committees had indicated that, though there were sufficient laboratories and hospitals in the area with all the necessary facilities, no access was available because of the lack of staff. This applied particularly to departments of physiotherapy and electrocardiography.

Dr. T. K. COOKE said he thought the figures were too optimistic, because they were provided by those who used the services. For instance, he did not believe that 61% of general practitioners had full access to post-mortem rooms, as was stated in the memorandum. The biggest delays in the National Health Service occurred when investigations were needed. When new hospitals were being built no account was taken of the morbidity in the area. The number of beds should depend on the total number of investigations which were likely to be required in a given area.

Dr. A. ELLIOTT said that the memorandum would be useful evidence in negotiations with the Ministry, and it would also show their constituents that the G.M.S. Committee was

taking action on their behalf. If general practitioners were to work satisfactorily they had to be given the tools to do the job.

Dr. G. MURRAY JONES said that there was a shortage of technicians in Wales, and one reason for that was their low salary. Open access to hospitals would lead to the shortening of waiting-lists for hospitals. However, when a hospital had to decide which work should be curtailed because of shortage of staff it was usually open access to diagnostic departments for general practitioners which was cut down.

Local Matter

Dr. H. GLYN JONES said that if two-thirds of the replies received from local medical committees expressed satisfaction that was a significant number. It was no good saying what would happen if more people used the service: that was impossible to assess, and it was possible only to work on the existing demand. Little could be done by the Ministry to improve the situation. The provision of these services was a local matter: any complaints should be dealt with locally. When there was no access or insufficient access for general practitioners to any of the departments it was up to the local medical committees to find out the reason why. The

facile explanation of shortage of staff should not be accepted without further investigation.

Dr. Glyn Jones said that the local medical committee should immediately ask what the staff establishment was. It should ask what the deficiency in the establishment was and what measures had been taken, and with what success, to bring the establishment up to strength. In the majority of cases the excuse of staff shortage was untrue, because, as had been pointed out, the work reached the departments in one way or another. Naturally there were occasions when this excuse was genuine, and it was usually only a temporary matter, but in such times it was the inpatient work and the outpatient work of the hospital which had to be given priority. The battle should be fought on the issue of principle at local level.

Dr. C. J. WELLS pointed out that local opinion was influenced by Ministry statements. If the Ministry went on repeating that these services were inadequate hospital management committees and regional hospital boards would accept it. He hoped that the memorandum would be sent to the Ministry in an attempt to get it to change its present attitude that open access facilities for general practitioners are satisfactory.

The Committee agreed that doctors should be recommended to take up complaints through local channels.

connexion between the two, said Dr. Speakman.

Wrong Time

Dr. A. A. CLARK said that in theory all would support Dr. Speakman, but now was the wrong time. General practitioners had thrown out merit awards but they had persuaded the Government to include seniority payments as a reward for long experience in general practice. The Government had included postgraduate sessions as part of the terms of the agreement. As a long-term policy the Committee should not accept this, but this was the wrong time to go back to the Ministry. It should be brought up again at a future date.

Dr. MURRAY JONES said that the subject had been discussed before in the context of vocational training for general practice. If the Committee believed that training for general practice was a continuous process then the idea of seniority must be linked with tangible proof that the doctor was making efforts to keep up to date. Experience as a result of years in practice was good, provided it was the right experience, but at the same time the doctor must prove that he was continuing his medical education.

Dr. D. L. WILLIAMS said that there were occasions when it was wiser not to pass resolutions. He thought the negotiators should be allowed to tackle the matter in whichever way they thought fit, in an endeavour to get expenses and payments for doctors undertaking postgraduate education.

Dr. R. W. RAE said that the seniority payment was not an award but a method of payment. This was the only occasion when payment depended on a doctor doing certain courses. The Committee should make it clear that though it had accepted the condition of postgraduate sessions that did not mean it agreed with it.

Review Body's Report

Dr. RIDGE referred to paragraphs 198 and 199 of the Review Body's seventh report: "When we were asked last year to consider the introduction of seniority payments we made clear our view that, if the concept of payment for seniority were to be adopted, it would require radical changes in the present arrangements for payment to general practitioners. This condition is now in process of being satisfied. We also made it clear that our figure of average net income was based on an assessment of what total earnings should be over the whole of the practitioner's career, and therefore allowed already for differences between general practitioners and other professional men in the pattern of career earnings. It follows from this that we have not been able to regard seniority payments as new and extra remuneration."

"The new system will, however, also include additions to the basic practice allowance for vocational training before entry to practice, and for special experience and service to general practice. . . . The proposed allowances for pre-entry vocational training and for special experience and service to general practice would be very much in line with what we have envisaged [in the fifth report], and we have thought it right to regard these as truly additional allowances,

Seniority Payments

Dr. SPEAKMAN moved the following motion: "That this Committee takes the view that postgraduate education sessions should in no way be connected with a doctor's career earnings, which include seniority payments; that postgraduate education is, by virtue of our profession, desirable for all doctors, and that throughout their careers as general practitioners postgraduate education should continue; that it should be in a form suitable to the doctor's own convenience and that it should not further reduce leisure time available or increase the work load, and that there should be payments made such as to make it worth while."

Dr. RIDGE asked whether in the last part of his motion Dr. Speakman meant "payments" to be restricted to expenses. If it intended that there should be some payment in addition to expenses, as suggested in the early part of the motion, and the payment was made by the Ministry of Health through the executive council, then it inevitably became part of career earnings. Also, if the payment was made by the executive council it attracted superannuation at the appropriate rate. Was Dr. Speakman suggesting a completely new type of payment? Or was it limited to expenses only?

Dr. SPEAKMAN explained that the Review Body had indicated the need for incentives for doctors to encourage them to stay in this country, and the need to attract people to enter the profession. The Review Body had said that seniority awards would not be regarded as new and additional payments, but it had added new and additional duties for the doctor in that seniority payments were conditional on the doctor attending an unspecified number of postgraduate education

sessions. The Review Body had stated that seniority payments would be regarded as part of a doctor's career earnings.

In Dr. Speakman's view there was a difference between keeping up to date and postgraduate education. A doctor could keep up to date by reading medical journals and by contact with consultants. But postgraduate education was something which started on the day a doctor qualified and finished on the day he ceased to practise medicine, and from that point of view it was not justifiable to specify a certain number of postgraduate sessions.

Dr. Speakman said that he had specifically used the words "doctor's own convenience." Doctors had undertaken to look after the health of the nation at all times. It was possible that the number of postgraduate educational sessions could become large. Conditions varied in different parts of the country, and the way in which some doctors could organize their work to attend postgraduate sessions might not suit other doctors. The work load would inevitably be increased, and if the Ministry wished to make postgraduate sessions mandatory they should attract additional payment. The opportunities to attend postgraduate sessions would differ for all general practitioners, and for this reason Dr. Speakman thought seniority payments should be excluded from career earnings but should be superannuable.

He said that it was clear from resolutions of the Annual Conference of Representatives of Local Medical Committees and of the Annual Representative Meeting 1967 that general practitioners wanted seniority payments safeguarded, at the same time recognizing the importance of postgraduate educational sessions, but there should be no direct

covering aspects of general practice which have not been recognized in the system of remuneration until now. The Health Departments agreed that we should not on this occasion regard these as being included in career earnings, and we have regarded them as additional to the increased remuneration which we have thought it right to recommend on other grounds."

Dr. RIDGE said the implication of these paragraphs was clear: that even though the Review Body recommended that on the first occasion the seniority payments should be regarded as additional payments, subsequently these payments would inevitably become part of career earnings. Therefore, said Dr. Ridge, it was unlikely that a request to the Review Body for a payment which was not part of career earnings would be successful.

Dr. N. S. MALIMSON emphasized that what annoyed most doctors was that middle-aged general practitioners with years of experience could earn only the same money as the newcomer into general practice.

The CHAIRMAN said that the Minister must not be allowed to impose clinical standards on the profession. But whatever resolution the Committee passed, he said, it would not embarrass the negotiators so long as the term "seniority payments" was left in a broad sense.

The Committee accepted a motion to pass to the next business.

Domiciliary Physiotherapy

The Committee considered a letter from the Ministry of Health in reply to a resolution of the Annual Representative Meeting 1966 concerning domiciliary physiotherapy. The letter stated that while physiotherapy might play a useful role in domiciliary practice it was, in the Ministry's view, a limited one. "Domiciliary practice is an extravagant use of physiotherapists' time because, although physiotherapists can visit and treat six or eight patients a day in their own homes, they can treat over three times as many, and generally more effectively, in a hospital department. For this reason, while there is a widespread demand for more physiotherapists, little encouragement can be given to setting up domiciliary services which might take away physiotherapists from the hospital service and so reduce the number of patients treated at hospital, without making a comparable increase in the number treated in their own homes. We doubt (the letter continued) whether domiciliary services organized by local authorities would attract many physiotherapists who are not working in hospital, because a substantial proportion of physiotherapists employed in hospitals are in fact married women."

Dr. B. D. MORGAN WILLIAMS said that was a fallacy, because there were many married women who would be willing to do physiotherapy in domiciliary visits but who could not work in hospitals.

The letter from the Ministry continued: "You asked whether it was already open to local health authorities to set up a domiciliary physiotherapy service on the lines of the district nursing service, if they so wish. We are advised that the provision of a domiciliary physiotherapy service providing intensive skilled treatment for short periods is not something which would be proper to a local

health authority. Broadly the consideration underlying this view is that in general the intention of the National Health Service Act, 1946, seems to be that 'treatment' should be provided by the hospital service and practitioner services, and that this is to be distinguished from 'care' which a local health authority may provide under Section 28. There may be minor forms of physiotherapy which could reasonably be regarded as part of 'care,' but most physiotherapy given by a skilled physiotherapist is regarded as treatment and outside the scope of arrangements which a local health authority may make under the Section."

The Committee was informed that the Public Health Committee had considered the matter, and, while it had recognized that the existing shortage of physiotherapists might make the provision of a domiciliary service difficult, it had thought that the Ministry had "not paid enough regard to the needs of patients in remote areas and those who are recovering from such conditions as strokes who cannot reach hospitals for treatment as outpatients." The Public Health Committee had pointed out that in Scotland a domiciliary physiotherapy service had been established and was working satisfactorily. The Public Health Committee also believed that domiciliary physiotherapy would provide an invaluable service to the community, and it had recommended that the Ministry of Health should be urged to encourage local authorities to establish a service along the lines of the district nursing service.

The G.M.S. Committee agreed that the matter should be raised again with the Ministry, with the support of the Public Health Committee.

Rent and Rates

The Committee's attention was drawn to the following letter from the Ministry of Health about the two months' time limit for making representations against apportionments of gross value under the provisions of paragraph 34 of E.C.N. 569 (*Direct Payments for Rent and Rates*):

As agreed during negotiation this paragraph provides that representations to the Minister must be made within two months of the date of the [executive] council's final decision. In apportionment cases the doctor is of course in a position to appeal against the apportionment shortly after learning what the apportionment is, but it can well be argued that the date on which the council notifies the doctor about the payment he will receive under the scheme—that is, the amount that will have been calculated by reference to the apportioned figure multiplied by the factor—is the relevant date for the purpose of appeal. We have let it be known, therefore, that we would not refuse to consider any representations made within this limitation. This is not of course quite the same as your correspondent mentions, as in our view the actual date of announcement of the factor to the profession as a whole has no relevance in this context and there may have been some slight misinterpretation of words.

We think it reasonable to allow the above interpretation of paragraph 34, as to many doctors the apportionment itself without knowledge of the factor is not a meaningful figure, particularly when there is a preconceived idea of what an acceptable payment would be. It must be clearly understood, however, that any representations deferred until the amount of payment is known can still only be made against the apportionment itself. There is no individual appeal against the

factor which will be a negotiated figure common to all.

Mental Health Service

The Committee considered a letter from the Ministry of Health about a proposal to have an emergency mental health service admission bureau for Greater London. It stated that the Ministry still took the view that a catchment area system for admission was best, with its advantages of full integration of admission, care, and aftercare. When there was difficulty the Ministry was confident that the solution was to be found in the better use of existing resources on a catchment area basis rather than by setting up a further organization. From the evidence the Ministry had available it thought that the difficulties of finding a bed for cases needing hospital admission were far from being general, and it was proceeding with its review of emergency admission arrangements, and was concentrating on one or two areas where clarification of admission procedures might improve the service.

Dr. D. R. COOK said that this was completely unsatisfactory. The Committee must insist on either an emergency bed bureau or areas of district responsibility, so that the hospital concerned had to accept final responsibility for finding a bed for an emergency case.

The Committee agreed to continue to press the Ministry on this matter.

Heroin Addicts

The Committee discussed a memorandum from the Ministry on the rehabilitation and aftercare of heroin addicts.

The CHAIRMAN drew attention to the following paragraph headed, "The Provision of General Medical Services," which related particularly to general practitioners: "In all cases of discharge from hospital there should be full consultation with the general practitioner well in advance of discharge, and he should be notified in the usual way immediately a patient leaves hospital. Many of these patients, however, will have had no family doctor, and in such instances the executive council for the area to which the patient is to be discharged should be notified well in advance, so that, in consultation with the local medical committee, they may help the patient and/or his relatives to find a doctor who will undertake to be responsible for the patient's general medical care."

The Chairman pointed out that the Committee had previously considered the *Second Report of the Interdepartmental Committee on Drug Addiction (B.M.J., 27 November 1965, p. 1259)*, and one of its recommendations was that there should be powers of compulsory detention. The Government had not sought that power in the Act, largely as a result of medical opinion. The intention was that registered addicts could obtain their supplies only from certain centres, and it would be an offence for a general practitioner to treat a registered addict. In his opinion that was an impairment of the professional freedom of the doctor.

Dr. RIDGE pointed out that it was the Minister's duty to carry out the Act. The memorandum was concerned almost exclusively with hospital arrangements, and it

was not the G.M.S. Committee's business to comment on the proposed administrative arrangements within the hospital field. It would be wiser to limit observations to the paragraph, quoted by the Chairman, on the provision of general medical services.

Dr. A. ELLIOTT asked what a general practitioner was to do when an addict came to his surgery, perhaps in the middle of the night. The facilities envisaged in the Act to cover such an emergency did not yet exist. Dr. SPEAKMAN asked what would happen if an addict who was allocated to a doctor got hold of heroin: would the doctor have to appear before the service committee? What protection was there for the doctor?

The CHAIRMAN replied that it was the duty of a doctor who came across a heroin addict to notify the case, and when the patient was registered as an addict he would be able to get his supplies only through a centre. So long as the doctor acted in good faith in the interests of the patient, the Chairman said he did not think the doctor would be in breach of his terms of service.

Dr. COOK said he was surprised that there was so much anxiety about the proposals. At present doctors were faced with the appalling situation where a drug addict could be allocated to them and they had the inescapable responsibility of providing general medical care for an impossible case. Under the new Act general practitioners would be relieved of the responsibility of providing heroin for addicts, and that should be an unqualified blessing for the doctor.

Dr. T. J. CARTER referred to a passage in the paragraph mentioned by the Chairman which stated that the executive council in consultation with the local medical committee might help the patient and/or his relatives

to find a doctor who would undertake to be responsible for the patient's general medical care. Dr. Carter hoped that the Committee might suggest that the allocation scheme should not be used in these circumstances.

Dr. J. L. MCCALLUM pointed out that if an addict were allocated to a doctor the doctor would still have a primary duty to the addict as a patient, and he could not escape that by quoting an Act of Parliament; he must treat the patient if he came to the surgery.

Dr. RIDGE said that the point made by Dr. Carter was the reason for the wording of this paragraph. But the Minister was not prepared to write to executive councils to the effect that in no circumstances would patients discharged from hospital after treatment for heroin addiction ever be assigned to a doctor. Dr. Ridge proposed that no exception should be taken to the wording of the paragraph of the circular.

Dr. WELLS said that that was not the only paragraph which concerned general practitioners. There were paragraphs on the placement of drug addicts in families and the provision of hostels. The care of addicts living in hostels or with families would fall on general practitioners. It was obvious that such people would have to be allocated, because they would not be generally acceptable.

Lack of Facilities

Dr. D. L. WILLIAMS said that this was a "typical Ministry paper scheme," putting forward proposals which could not be implemented owing to lack of facilities. It was up to doctors to produce evidence for the

Minister that these facilities were non-existent, particularly in London.

Dr. I. M. JONES hoped that the Committee would reject Dr. Ridge's proposition. He thought it was a mistake to consider a document, take one paragraph of it completely out of context and pronounce upon it, and to ignore all the other paragraphs. If an addict came to a doctor's surgery the doctor had an ethical obligation to do what he could for him. The Minister was placing doctors in a position in which they might be unable, without breaking the law, to do what was necessary for the patient. Doctors should not acquiesce in an arrangement of that kind. The Minister had made regulations which he must have known he was in no position to fulfil. The result was that a doctor could have a drug addict allocated to him, he could be compelled to accept that patient, and yet he would be unable, owing to an Act of Parliament, to provide him with what he needed. The acceptance of this document would lessen the freedom of the profession, and would go against its ethical and moral principles.

Dr. W. HEDGCOCK, Secretary to the Committee, pointed out that a general practitioner could prescribe heroin in an emergency.

The Committee decided that the Minister should be informed that his proposals were premature. Grave disquiet had been expressed by the members of the Committee who were acquainted with the problem. When it was possible, with the help of the local executive council and local medical committee, to find a doctor who was willing to undertake the responsibility for an addict's general care that would be acceptable, but the Committee considered that to use the allocation procedure would be inappropriate.

General Medical Services Committee (Scotland)

The General Medical Services Committee (Scotland) met in Edinburgh on 21 September. Dr. ALISTAIR CLARK was in the Chair.

The CHAIRMAN welcomed two new representatives from the Glasgow Local Medical Committee, Dr. J. McGlone and Dr. J. S. Scobbie.

The Committee discussed the method of appointment of the two Scottish representatives on the Assistants and Young Practitioners' Subcommittee of the G.M.S. Committee. Though it had been customary for the G.M.S. Committee (Scotland) to nominate one assistant and one young practitioner to the Subcommittee (at the same time coopting them to the G.M.S. Committee (Scotland)), that procedure was now considered insufficient.

The Committee resolved that in future local medical committees should be asked to submit nominations, and that from these the G.M.S. Committee (Scotland) should choose one assistant and one general practitioner to serve on the Assistants and Young Practitioners' Subcommittee.

General Practitioners in Hospitals

Dr. C. J. SWANSON reported that a meeting of the working party, of which he was chairman, had considered the remuneration

attached to 10(a)* hospital appointments. The working party thought that the increase in the "bed fund" had been unrealistic and that it should be reassessed. The Secretary was collecting data from cottage hospitals on the numbers of 10(a) beds and the amount paid per doctor out of the "bed fund" over the past year.

Also, said Dr. Swanson, the working party had been concerned with the position of general practitioners who undertook more specialized clinical responsibilities under 10(b) appointments—for example, in anaesthetics. The working party thought that in such situations responsibility pay should be added which would recompense those doctors for their special skill and experience. It was also important that there should be security of tenure for such appointments. Dr. Swanson said that it was hoped that an early meeting could be arranged with the Scottish

* General practitioners employed part-time in hospitals are paid in one of two ways. In one they are paid from a staff fund at the rate of £40 a year per bed occupied (10(a) appointments), and in the other they are paid at the rate of £275 a year for each weekly notional half-day up to a maximum of £2,475 a year (10(b) appointments). The staff fund (10(a)) method of payment applies to work in general-practitioner hospital units, and the sessional method (10(b)) to work in convalescent homes, general-practitioner maternity hospitals, and other types of hospital where no other rate is appropriate.

Home and Health Department to make representations on this subject.

Matters for Department

The Stirling and Clackmannan Local Medical Committee reported a case of a doctor who, at the request of the police, had hurried many miles to a casualty only to find that the patient had been removed to hospital.

That circumstance was not uncommon, it was stated, and the Committee thought that doctors should be entitled to some payment. It decided to discuss the matter with the Scottish Home and Health Department.

Previously suggestions had been made by the Committee for a pad which would incorporate claim forms for (1) attendance on a temporary resident, (2) emergency treatment, and (3) a night visit. It had been agreed that the matter should be discussed further with the Scottish Home and Health Department.

Dr. W. B. PRESTON urged that this multi-purpose claim form should also include a form for treating dental haemorrhage.

Maternity Services

The Committee debated whether the Maternity Services Committee of the Scottish

Council was the appropriate body to consider general-practitioner maternity service fees. Though that Committee had a number of general practitioners among its members it seemed wrong that consultants and public health medical officers should be involved in questions of general-practitioner pay.

Dr. W. W. FULTON proposed that the G.M.S. Committee (Scotland) should appoint a Maternity Services Subcommittee to consider matters affecting remuneration, and that the Maternity Services Committee of the Scottish Council should continue to discuss clinical matters. Dr. SWANSON, however, thought that the Maternity Services Committee of the Scottish Council was competent to cover all aspects of the maternity services, and that it was advantageous to have representatives of other branches of the profession on the Committee.

Dr. Fulton's motion was seconded by Dr. W. M. WILSON, and it was resolved that a Maternity Services Subcommittee of the G.M.S. Committee (Scotland) should be appointed and that its membership should be the Chairman and Vice-Chairman (*ex officio*), Dr. J. McGlone, and the G.M.S. (Scotland) members of the Maternity Services Committee of the Scottish Council.

A memorandum from the Fife Local Medical Committee was considered which described arrangements between that committee and the medical staff of the Forth and Craigtoun hospitals for a shared maternity service.

Dr. JOAN K. SUTHERLAND suggested that this document might be available to the Maternity Services Committee of the Scottish Council. Dr. MCGLONE disagreed with Dr. Sutherland. He thought that the subject should be discussed first by the new Maternity Services Subcommittee.

The Committee agreed with Dr. McGlone.

Birsay Report

Dr. SWANSON, Chairman of the Highlands and Islands Practitioners' Subcommittee, informed the Committee that the subcommittee was examining the Report of the "Birsay Committee" on General Medical Services in the Highlands and Islands (*Supplement*, 8 July, p. 23). Its views would be presented to the next meeting of the G.M.S. Committee (Scotland) on 7 November.

Dispensing Doctors

It was reported to the Committee that the Rural Practitioners Subcommittee, at a recent meeting, had resolved that it be recommended to the G.M.S. Committee (Scotland) (a) that a small *ad hoc* subcommittee should be appointed to examine the position of dispensing doctors, and thereafter to meet the Scottish Home and Health Department for an exploratory discussion, and (b) that the members of the *ad hoc* subcommittee should be Drs. C. J. Swanson, H. B. Muir, P. A. P. Mackenzie, J. L. T. Dickie, and C. S. Sandeman.

The Committee agreed that the time was appropriate to consider the overall "dispensing situation" in Scotland, and that arrangements should be made for discussions with the Scottish Home and Health Department.

Vaccination and Immunization Fees

The Committee received a letter from the Scottish Home and Health Department about a review of immunizations scheduled as being on the ground of public policy and their evaluation by a Joint Working Party of the English and Scottish Health Services Councils. The draft revised schedule was before the Committee.

Dr. C. D. FALCONER, Assistant Scottish Secretary, read a letter from Dr. H. B. Muir which pointed out that a changeover from the existing schedule would necessarily take some time, since patients who had already been instructed to bring their children at 18 months would continue to do so for another 12 months. General practitioners carrying out these immunizations should be paid under the current schedule of fees.

Dr. S. PEACE suggested that a reference should be made in the revised schedule to measles immunization. Dr. E. V. KUENSSBERG said that the Medical Research Council was undertaking a national study on this and it would be advisable to await the result.

The Committee agreed that approval should be given to the draft revised schedule.

Open Access to Diagnostic Facilities

Dr. C. D. FALCONER reported that a second survey of diagnostic facilities open to general practitioners in Scotland had been carried out. It had shown little substantial change in circumstances since the previous inquiry three years ago, and that in fact the facilities available in Scotland were considerable.

Dr. PRESTON pointed out that access to x-ray facilities were inadequate in Fife, and the Fife Local Medical Committee was anxious to have the matter raised with the Scottish Home and Health Department. Dr. J. S. GARDINER reported a similar situation in Stirling and Clackmannan where practitioners had been informed that x-ray facilities would cease forthwith. General practitioners had been annoyed at the abruptness of the closure without any prior consultation with the doctors in the area.

University and Armed Forces Pay for Prices and Incomes Board

The National Board for Prices and Incomes has been instructed to keep under continuous review the pay of university academic staff and pay and allowances in the armed Forces. The order came into force on 1 November, and was made by the Government under Section 3 of the Prices and Incomes Act, 1966. The board will report on the subject matter of the standing references from time to time or when asked to do so by the Ministers concerned. Standing references can be varied by Ministers or withdrawn at any time.

In the past the pay of preclinical medical teachers has been settled at the same time as other university academic staff. The pay of clinical medical teachers has been fixed separately, and it has been customary for it to be related to the Review Body's awards to hospital doctors in the N.H.S. At a meet-

The Committee agreed to make representations on behalf of these two areas to the Scottish Home and Health Department.

Draft Memoranda

The Committee considered a circular to executive councils from the Scottish Home and Health Department concerning additional payments to women doctors during absence owing to pregnancy and child birth.

Dr. JOAN SUTHERLAND complained that the scheme appeared to exclude all women who were in a group or partnership, when it was assumed that their colleagues would take on the extra work without payment. She thought that the payment should be available to all married women doctors in general practice.

The Committee did not support Dr. Sutherland's view, and it was resolved to accept the draft document.

The Committee also considered another draft executive council circular concerned with the modifications in the interpretation of the remuneration arrangements for designated areas, group practice, seniority, and vocational training. The Committee was not satisfied about the position of single-handed rural practitioners, and it objected strongly to the suggestion in the document that a group of single-handed doctors could manage to operate from a common surgery.

Dangers of Tranquillizers

Dr. W. M. PATTERSON complained that the pamphlet on the dangers of tranquillizing drugs which had been sent recently to all doctors by the Committee on Safety of Drugs (the Dunlop Committee) had been quoted in the public press. This had caused much distress to patients, who were the very people who should not have access to this type of news.

The Committee agreed to write to the Medical Assessor of the Dunlop Committee to ask that in future every care should be taken to see that the Dunlop Committee's communiqués reached only the medical profession.

ing with representatives of the B.M.A. in November 1966 the Minister of State for Education and Science, Mr. Goronwy Roberts, stated that in the event of university teachers' pay being referred to the Prices and Incomes Board the B.M.A. would be able to give evidence on medical pay directly to the board.

Since 1962 the pay of doctors in the armed Forces has been fixed separately from other branches of the Forces, and has customarily been related to the Review Body's awards. Currently negotiations between the B.M.A. and the Minister of Defence on the B.M.A.'s pay-claim for doctors in the armed Forces have broken down, and the Association has refused to accept advertisements for medical posts in the three Services, and has advised deans of medical schools of the situation.

S.H.M.O.s Group Council

A meeting of the Association's Senior Hospital Medical Officers Group Council was held on 26 October. Dr. N. STRANG was re-elected Chairman and Dr. L. E. BURKEMAN Deputy Chairman.

Dr. E. GREY-TURNER, Deputy Secretary, said that the old Group Council had been summoned, though its constitution was about to be changed, and that it was proposed that it should be replaced by a new and smaller Group Committee. The Council of the Association had approved that proposal on 25 October, so there had been no option but to summon the old Group Council.

The CHAIRMAN said that consideration had to be given to the method of electing representatives to the new committee.

S.H.M.O.s in Declining Specialties

Dr. N. V. WILLIAMS reminded the Group Council that it had suggested at its last meeting that the following paragraph should be included in the hospital doctors' "charter": "The Government should provide facilities for the rehabilitation of S.H.M.O.s in declining specialties." Dr. Williams asked what was happening to S.H.M.O.s in that position.

Dr. GREY-TURNER said that he knew of two S.H.M.O.s who were considering taking junior appointments in other specialties in order to retrain, but he did not know whether either of them had yet come to a definite decision.

The CHAIRMAN asked if it was possible for an S.H.M.O. to take a junior appointment and retain his terms and conditions of service as an S.H.M.O. on a personal basis. Dr. GREY-TURNER said that he had consulted the Ministry of Health about paragraph 97 of the Review Body's seventh report, which had recommended that when a doctor took an appointment in a lower grade for approved training purposes he should continue to receive the salary he was getting in his last appointment in the higher grade. He had asked the Ministry whether this paragraph applied to an S.H.M.O., and the Ministry had said that it did, provided that the acceptance by a senior hospital medical officer of a more junior appointment was a move which was regarded by the hospital authority as legitimate and sensible for retraining purposes.

In reply to Dr. WILLIAMS, Dr. GREY-TURNER said that an S.H.M.O. on completing his retraining would have to apply for a post in the new specialty, but he would take with him to the new post, as a residual S.H.M.O., his existing terms and conditions of service which he held on a personal basis.

The CHAIRMAN suggested that the matter might go to the Negotiating Subcommittee of the Central Committee for Hospital Medical Services.

The Group Council agreed to put forward a recommendation that "S.H.M.O.s who wish to go into another specialty should have an opportunity for a period of rehabilitation without any personal loss to themselves."

its last meeting had been incorporated in the "charter." Dr. GREY-TURNER said that the charter, published in the Annual Report of Council in May (*Supplement*, 13 May, p. 93) had stated in general terms that S.H.M.O.s should retain their personal terms of service in all circumstances, but it had not specifically said (a) that residual S.H.M.O. posts should be designated as supplementary consultant posts; (b) that S.H.M.O.s should have the unrestricted right to undertake domiciliary consultations; and (c) that S.H.M.O.s should have the option to be whole-time or maximum part-time, like consultants, which were the points to which Dr. Meir had referred.

The CHAIRMAN said that his regional hospital board took the view that domiciliary consultations should be done by consultants, but, if there were too few, S.H.M.O.s should also be allowed to do them. His board also thought it had the right to decide whether a post should be part- or full-time.

Dr. GREY-TURNER said that domiciliary consultations were supposed to be done only by consultants. The only exception was when there were not enough consultants to meet the demand. Then it had been open to a board to allow selected S.H.M.O.s to do these consultations. Before the publication of H.M.(64)94 (a Ministry circular in 1964 entitled "Medical Staffing Structure in the Hospital Service") regional boards could say which S.H.M.O.s might do domiciliary consultations. After the issue of the circular any S.H.M.O. who had previously been allowed to do domiciliary consultations could continue to do so.

Dr. MEIR moved: "That S.H.M.O.s, being members of the senior hospital medical staff, should be allowed to do domiciliary consultations."

The motion was lost.

Mr. G. WARING ROBINSON referred again to the point that residual S.H.M.O. posts should be designated as supplementary consultant posts. He asked that unless that suggestion had been rejected by the Ministry it should be reconsidered. The CHAIRMAN said that it had been rejected, but that did not mean the matter could not be raised again. Dr. V. M. HAWTHORNE suggested that fresh evidence would be needed if there was to be any chance of success.

Dr. MEIR suggested that the question of S.H.M.O.s being given the option of whole- or part-time appointments should be further investigated.

The CHAIRMAN said it had been proposed that the difference between part- and full-time consultants should be abolished and an ordinary contract should be one of ten-tenths, with the right to do private work. So far this recommendation had not been accepted.

After further discussion it was proposed: "That when consultant sessions become available they should first be offered to part-time S.H.M.O.s in the relevant specialty in the region."

The motion was seconded and carried.

Group Committee and the question of co-option had to be considered. The new constitution provided that "the new Committee will consist of 18 members—one from each region in England and Wales, two from Scotland, and one from N. Ireland." This had been discussed, and the opinion had been that the best way of electing representatives would be on a regional basis, perhaps by postal vote.

Dr. GREY-TURNER said that either nominations from each region could be asked for—and if more than one name was received an election could be held in that region—or a regional convener could be appointed who would convene a meeting at which a representative to the Committee would be elected.

It was decided to implement the second suggestion. The Group Council then proceeded to elect representatives from each region to act as a convener.

The new constitution also allowed that the new Group Committee would have power to co-opt not more than two additional members, and it was provisionally agreed that Dr. W. Griffel and Dr. V. M. Hawthorne should be co-opted.

The Committee agreed that the election of a representative to the Central Committee for Hospital Medical Services should be deferred until the first meeting of the new committee, but if the C.C.H.M.S. met in the meantime it was agreed that Dr. Strang should attend.

Other Matters

The CHAIRMAN said that evidence to be sent to the Review Body on behalf of S.H.M.O.s had been collated, and he had been invited to attend a meeting of the Negotiating Subcommittee of the Central Committee for Hospital Medical Services in July.

Dr. WILLIAMS asked what was the composition of the Negotiating Subcommittee ("Committee of Fifteen"). Dr. GREY-TURNER explained that it consisted of nine members appointed by the C.C.H.M.S., of whom six were senior staff and three were junior staff; five members appointed by the Joint Consultants Committee; and one member appointed by the Central Dental Consultants and Specialists Committee.

Mr. WARING ROBINSON asked again if it was worth while pursuing the question of supplementary consultant posts for S.H.M.O.s, and whether it was a matter which was supported by the Council of the B.M.A.

Dr. GREY-TURNER said that it had been supported by the Council in principle, but the C.C. and S. Committee (as it then was) had turned it down.

It was suggested by Dr. HAWTHORNE that information collated from a questionnaire which had been circulated to S.H.M.O.s recently might be used to make a full questionnaire or plebiscite of all doctors, or all doctors in the hospital service, as had been done in respect of merit awards. In that way it would be possible to find out what support there was among consultants for the establishment of a new grade of supplementary consultant to take in residual S.H.M.O.s.

Domiciliary Consultations

Dr. M. MEIR asked if the other points which the Group Council had discussed at

New Constitution

The CHAIRMAN said that a more detailed method of electing representatives to the

"Mediflash"

The Chief Commissioner, Metropolitan Police, deprecates the use by doctors of Mediflash, a portable, flashing green light for fixing to the roof of a doctor's car when travelling to emergencies (*Supplement*, 14 October, p. 15).

A letter to the B.M.A. states that the Commissioner has been advised that Mediflash does not infringe the law, but he deprecates its use because "any further proliferation of flashing lights is bound to detract from the effectiveness of those that are already fitted to vehicles belonging to the fire, ambulance, and police services." Moreover, he doubts whether, without an audible warning device, the light will be of any great benefit. Metropolitan police officers have been told of the existence of Mediflash and that its use confers no special privileges in relation to the law and to traffic regulations.

The Secretary of the Association has written to honorary secretaries of B.M.A. Metropolitan Divisions informing them of the Chief Commissioner's attitude, and stating that there is no reason why doctors should not use Mediflash "provided that they adhere absolutely" to the conditions laid down.

Opportunities Overseas for Retired Practitioners

A deputation from the Association's Committee on Overseas Affairs visited the Ministry of Overseas Development on 1 November to discuss a resolution of the Annual Representative Meeting 1967 that inquiries should be made into the "desirability of setting up a system whereby retired but fit doctors might give the benefit of their services for a period in the developing countries which are short of medical manpower. . . ."

The deputation consisted of Professor D. E. C. Mekie, Professor F. E. Stock, and Dr. W. Norman-Taylor, and the outcome of what was said to have been "a useful meeting" will be reported to the Committee on Overseas Affairs.

H.M. Forces

Appointments.—Group Captain R. S. Peill (anaesthetic duties, R.A.F. Hospital, Wroughton); Wing Commander F. P. Stephens (neuro-psychiatry duties, R.A.F. Hospital, Muharraq); Wing Commander F. S. Black (officer in charge of Central Medical Trade Test Board, R.A.F. Halton); Wing Commander A. H. Cox (senior medical officer, R.A.F. Locking).

REGULAR ARMY RESERVE OF OFFICERS ROYAL ARMY MEDICAL CORPS

Major J. K. Lawton, from Reserve of Officers, to be Major.

TERRITORIAL ARMY RESERVE OF OFFICERS: ROYAL ARMY MEDICAL CORPS

Major (Honorary Lieutenant-Colonel) G. J. H. L. Hall has resigned his commission, retaining the honorary rank of Lieutenant-Colonel.

Major B. J. Harries has resigned his commission.

Captains (Honorary Majors) O. Garrod, M.B.E., and C. J. Goodall have resigned their commissions, retaining the honorary rank of Major.

Captain (Honorary Major) W. R. Gauld, T.D., has resigned his commission.

Was it a Drug?

Regulation 16 of the National Health Service (Service Committees and Tribunal) Regulations, 1956, provides that when a practitioner prescribes under the National Health Service preparations which are not drugs or medicines, and therefore outside the scope of the Act, the executive council may recover their cost from him. If he challenges the council's action the matter may be referred to the local medical committee. Either party or the Minister can appeal to a referee or referees against the local medical committee's decision.

The referees on each occasion are appointed by the Minister of Health. They must not exceed three in number and they must not be officers of the Ministry of Health. At least one must be a general medical practitioner. In practice the number of referees appointed has usually been three. The Chairman has been a layman with legal training, and his two colleagues have been general practitioners selected from a panel chosen by the General Medical Services Committee of the B.M.A.

The findings* of the referees in some recent appeals under the regulations are reported below. The decisions in these, as in all cases, are related only to the circumstances of the particular cases and are not binding on referees who may hear other cases.

Casilan

The referees considered two cases in which Casilan had been prescribed. In each case the local medical committee, on a reference from the executive council, had decided that Casilan was a drug which the executive council was bound to provide.

In the first case Casilan had been prescribed for a patient suffering from idiopathic steatorrhoea. The reason for the local medical committee's decision had been that the patient had been advised in hospital that he should have a gluten-free diet and Casilan had been recommended. As a result his health had improved.

The medical members of the panel of referees thought that in this case Casilan should be regarded as a drug, because gluten-free flour cannot be made into bread without the addition of something to make it combine, and Casilan was useful for that purpose. The referees therefore decided that the executive council was bound to provide it in this case.

The referees were unable to support the decision of the local medical committee in the second case. Casilan had been prescribed for a patient suffering from heart failure, diabetes, blindness, and uraemia. In deciding that Casilan was a drug which the executive council should provide, the local medical committee had considered that in the circumstances the patient was likely to suffer from hypoproteinaemia and that Casilan would combat the condition.

The referees' report stated that Casilan was essentially a food consisting of concentrated protein nearly free from salt, and as such would not be one of the things executive councils were bound to provide. Traditionally, if not logically, the absence of salt had been

regarded as a medicinal property in cases where a salt-free high-protein diet was required. In the case under consideration the referees said a salt-free diet was clearly indicated, but the patient suffered from uraemia, and they had been informed that that required a low protein diet unless due to nephrosis.

The report stated that it did not appear that the doctor had at any time stated that his patient suffered from hypoproteinaemia. The referees therefore decided that in this case Casilan was not a drug which the executive council was bound to provide.

Complan

The referees were also unable to support the decision of a local medical committee that Complan was a drug which the executive council was bound to provide.

In this case Complan had been prescribed for a patient who was suffering from carcinoma and was unable to take normal food. The referees in their report stated that the patient's doctor had said that he had continued the hospital treatment when he prescribed Complan, and, in his opinion, it had kept the patient from starving. The local medical committee had considered Complan appropriate as a means of nourishment.

"All this may be true," said the referees, "but we have to apply an Act which obliges hospitals to nourish their patients while the executive councils have only to provide the medicine." The referees decided that in this case Complan was not a drug which the executive council was bound to provide.

Brandy

The referees considered a case in which brandy had been prescribed for a patient suffering from severe peripheral artery disease causing intractable ischaemic ulcers. The local medical committee, on appeal from the executive council, had decided that this was not a drug which the executive council was bound to provide.

The referees, in their report to the Minister, stated that the patient's doctor had said that he had treated the patient's malady for many years. Surgery had not helped her. In September 1966 she had become much worse, with painful and intractable ulcers on her legs. Rest in bed, various vasodilators, five systemic antibiotics, and daily dressings of Cicatrin powder and Tulle Gras had "left the problem of restoring the peripheral circulation unsolved." The doctor had then recalled the advice of a consultant in a similar case in 1963 in which brandy had been prescribed. The local medical committee at that time had decided that that brandy was properly ordered as a drug. The patient had recovered.

The doctor had stated, continued the referees' report, that with this case in mind he had ordered 1 oz. (28.4 ml.) of brandy twice a day for his patient, who had also recovered. The doctor had stated that in April this year his confidence in his argument had been shaken by an article in the *British Medical Journal*, which had said, in effect, that alcohol produced a significant degree of

* These findings are normally sent only to the interested parties. They are sent by the Ministry of Health to the *B.M.J.* with all names deleted.

vasodilatation in normal, healthy subjects but that its effects on occluded or arteriosclerotic vessels had not been shown. Nevertheless, the doctor had contended that a belief among doctors that alcohol was a useful vasodilator was sufficiently widespread to justify its prescription in a case of this sort. Asked by the referees why he had not prescribed rectified alcohol, the doctor had replied that he preferred brandy. To the suggestion that the real purpose of the prescription was to produce a state of euphoria the doctor had said that 2 oz. of brandy a day would not be enough for that.

The referees' report stated that the Minister's representative had argued that alcohol was not the proper remedy because the area of occlusion might be high up, in which case alcohol would not have been effective. The medical members of the panel of referees accepted that argument. They thought the doctor should have had regard to the Report on the Definition of Drugs which held that alcoholic beverages were not to be regarded as drugs. The third referee thought that there had been too many decisions that whisky, brandy, and gin could be regarded as drugs for the advice of the Joint Committee on the Classification of Proprietary Preparations to be taken strictly.

The referees decided that in this case brandy was not a drug which the executive council was bound to provide.

Sketofax

A case in which two tubes of Sketofax had been prescribed for a patient suffering from marked irritation of the face and body probably associated with fleas was considered by the referees. The local medical committee had decided that Sketofax was a drug which the executive council was bound to provide.

The patient had been referred to a hospital where the diagnosis of flea-bites had been confirmed, and she had been given Sketofax. The

patient's doctor had thought he was justified in repeating the treatment.

The referees reported that they were not impressed by that argument. Their report continued: "The *British National Formulary* recommends that when some of a family living together are infected with scabies all should be treated with benzyl benzoate. From this the local medical committee infer that executive councils may have to provide

preventive drugs. We agree, but for such drugs to be properly charged to the executive council there must be some probability that the patient will contract a disease. Everyone is liable to a flea-bite. There is nothing to show that this patient is more likely than anyone else to suffer another flea-bite."

The referees decided that in this case Sketofax was not a drug which the executive council was bound to provide.

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

- Haggis, G. H.: *The Electron Microscope in Molecular Biology*. 1966.
Hahn, P., and Koldovsky, O.: *Utilization of Nutrients during Postnatal Development*. 1966.
Hanna, C. (Editor): *Symposium on Suppression of Graft Rejection*. 1966.
Hoyt, W. F., and Beeston, D.: *The Ocular Fundus in Neurologic Disease*. 1966.
Hutchison, J. H.: *Practical Paediatric Problems*, 2nd edition. 1967.
Jackson, Q. M.: *A Handbook of Paediatrics for Nurses in General Training*, 3rd edition. 1967.
Jones, H. K.: *Towards a Christian Understanding of the Homosexual*. 1967.
Lingjaerde, P. S.: *Biochemical Investigations in Mental Diseases*. 1966.
Low, A. A.: *Lectures to Relatives of Former Patients*. 1967.
Luffingham, R. L.: *A New Look at Industrial Medicine*. 1967.
McKusick, V. A.: *Mendelian Inheritance in Man*. 1966.

- Minney, R. J.: *The Two Pillars of Charing Cross*. 1967.
Noble, E.: *Play and the Sick Child*. 1967.
Post, F.: *Persistent Persecutory States of the Elderly*. 1966.
Rayner, C.: *Essentials of Outpatient Nursing*. 1967.
Rodahl, K., and Issekutz, B. (Editors): *Nerve as a Tissue*. 1966.
Rosier, M.: *Nursing Mathematics*. 1967.
Ross, K. F. A.: *Phase Contrast and Interference Microscopy for Cell Biologists*. 1967.
Scheier, H.: *Prognose und Behandlung der Skoliose*. 1967.
Sherif, M.: *Group Conflict and Co-operation*. 1966.
Shryock, R. H.: *Medicine in America: Historical Essays*. 1966.
Spence, T. F.: *Teaching and Display Techniques in Anatomy and Zoology*. 1967.
Taylor, S. J. L.: *First Aid in the Factory*, 3rd ed. 1967.
Thalhammer, O.: *Pränatale Erkrankungen des Menschen*. 1967.
Todd, F. J.: *Social Work with the Mentally Subnormal*. 1967.
West, N. C.: *A Handbook for Nurses*. 1967.
Whitby, H. A. M.: *Bio-Electronic Detection of Cancer and Other Diseases*. 1967.
Wiersma, C. A. G. (Editor): *Invertebrate Nervous Systems*. 1967.
Woodburne, R. T.: *A Guide to Dissection in Gross Anatomy*, 2nd edition. 1967.
Wulff, R. M.: *Village of the Outcasts*. 1967.

Association Notices

Armed Forces Committee Nomination of Members for Co-option

The constitution of the Armed Forces Committee was amended at the Annual Representative Meeting of the Association in July 1967 to allow greater representation of serving medical officers, especially younger members, by means of co-option to the Committee. The Committee may now co-opt two representatives of the rank of major or equivalent (lieutenant-commander or squadron leader) or below, one of whom should preferably be of specialist status, from the medical branch of each of the Services.

Notices appeared in the *B.M.J. (Supplement)*, 26 August and 16 September, pp. 124 and 130 respectively) inviting serving medical officers to nominate members of the Association in the armed Forces in these ranks for co-option to the Committee.

At its meeting in October the Armed Forces Committee considered the nominations received and the following have been co-opted to the Committee:

Army.—Major T. R. Austin, specialist in anaesthetics, at the Cambridge Military Hospital, Aldershot.

Navy.—Surgeon Lieutenant-Commander J. A. M. Wright, medical specialist at the Royal Naval Hospital, Plymouth; Surgeon Lieutenant-Commander D. S. Wright, G.D.O., H.M.S. *President*.
R.A.F.—Squadron Leader J. B. Crowe, Consultant Radiologist, P.M.R.A.F. Hospital, Halton, Bucks.

The Committee thought it was most important that non-specialists should be represented from each of the Services, and it decided to seek further nominations for the non-specialist vacancy in the Army and in the R.A.F. representation.

Serving medical officers in the Army and the R.A.F. are therefore invited to nominate members of the Association in the rank of major, squadron leader, or below of non-specialist status for co-option to the Committee. It is hoped that those nominated would have a reasonable expectation of being available to attend meetings in London in the foreseeable future.

Nominations should be sent to the Secretary of the Association by 23 December 1967 for subsequent consideration by the Armed Forces Committee.

DEREK STEVENSON, *Secretary*.

Diary of Central Meetings

NOVEMBER

- 14 Tues. Standing Subcommittee (Central Ethical Committee), 11 a.m.
- 14 Tues. G.M.S. Disciplinary Machinery Working Group, 2 p.m.
- 15 Wed. Committee on the Mental Health Act, 10.30 a.m.
- 15 Wed. Executive Subcommittee (Film Committee), 2 p.m.
- 15 Wed. Rural Practices Subcommittee (G.M.S. Committee), 2 p.m.
- 15 Wed. Executive Subcommittee (Film Committee), 2 p.m.
- 15 Wed. G.M.S. Dispensing Working Group, 5 p.m.
- 16 Thurs. Chairman's Subcommittee (Organization Committee), 9.30 a.m.
- 16 Thurs. General Medical Services, 10.30 a.m.
- 16 Thurs. Film Committee, 2 p.m.
- 16 Thurs. Membership and Information Subcommittee (Organization Committee), 2 p.m.
- 17 Fri. Working Party on Postgraduate Medical Centres, 2 p.m.
- 17 Fri. Welsh Committee (at the Metropole Hotel, Llandrindod Wells, Radnorshire), 2.15 p.m.
- 21 Tues. General Purposes Committee, 10.30 a.m.
- 22 Wed. Working Party on Amphetamine Preparations (Committee on Medical Science, Education, and Research), 9.30 a.m.
- 22 Wed. Journal Committee, 10.30 a.m.
- 22 Wed. Psychological Medicine Group Committee, 2 p.m.
- 23 Thurs. Executive Subcommittee (C.C.H.M.S.), 10 a.m.
- 23 Thurs. Compensation and Superannuation Committee, 2 p.m.
- 23 Thurs. Negotiating Subcommittee (C.C.H.M.S.), 2 p.m.
- 23 Thurs. Dermatologists Group Committee, 2.30 p.m.
- 23 Thurs. Representatives of Negotiating Subcommittee (C.C.H.M.S.) and Ministry of Health, 4 p.m.

DECEMBER

- 4 Mon. Scottish Committee for Hospital Medical Services (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
- 13 Wed. Journal Committee, 2 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

ALDRSHOT AND FARNHAM DIVISION.—At Queen's Hotel, Farnborough, Thursday, 16 November, 8 p.m., wine and cheese tasting. Guests are invited.●

BLACKBURN DIVISION.—At 13 Merlin Road, Sunday, 19 November, 12.15 p.m., annual general meeting.

BRIGHTON AND MID-SUSSEX DIVISION.—At Sussex Postgraduate Medical Centre, Thursday, 16 November, 8.30 p.m., jointly with B.D.A., Dr. E. M. Widdowson: "Nutrition of Children in Underdeveloped and Affluent Societies." (Preceded by dinner, 6.30 for 7 p.m.) Guests are invited.●

CITY OF DUNDEE DIVISION.—At Room 9, Queen's College Tower, Nethergate, Friday, 17 November, 8.15 p.m., B.M.A. lecture by Dr. John J. A. Reid: "Some Socio-medical Aspects of Diabetes Mellitus."

CORNWALL DIVISION.—At Headland Hotel, Newquay, Friday, 17 November, 7.30 for 8 p.m., annual dinner and dance. Guests are invited.●

CROYDON DIVISION.—At Medical Centre, Mayday Hospital, Tuesday, 14 November, 8.30 p.m., Mr. J. E. H. Pendower: "Surgical Aspects of Peptic Ulceration and Gastric Carcinoma."

DUMFRIES AND GALLOWAY DIVISION.—At Cairndale Hotel, Dumfries, Thursday, 16 November, annual dinner dance.

DURHAM DIVISION.—At Ramside Hall, Thursday, 16 November, 8 for 8.30 p.m., dance.●

ENFIELD AND POTTERS BAR DIVISION.—At Academic Centre, Chase Farm Hospital, Thursday, 16 November, 8.30 p.m., meeting to elect representative to Representative Body, and talk by Dr. J. Menon: "Eyes for Every Man—Fact and Fiction."

GLASGOW DIVISION.—Tuesday, 14 November, visit to Ravenscraig Steel Works, Motherwell. Transport will leave Glasgow Regional Office at 5.30 p.m.●

HASTINGS DIVISION.—At Outpatient Department, Royal East Sussex Hospital, Tuesday, 14 November, 8.15 p.m., clinical meeting. Followed by discussion of cases in Board Room (preceded by report on Annual Representative Meeting).

HENDON DIVISION.—At Hendon Hall Hotel, Tuesday, 14 November, 8.45 p.m., medical films: "Congenital Heart Defects in Young Children"; "Pulmonary Function."●

HEREFORD DIVISION.—At Board Room, Hereford County Hospital, Wednesday, 15 November, 8.15 p.m., meeting to receive report on Annual Representative Meeting, Bristol, and to elect representatives for 1968-9.

KETTERING DIVISION.—At Postgraduate Centre, Kettering General Hospital, Tuesday, 14 November, 8.30 p.m., film by Dr. A. N. Exton-Smith: "Accidental Hypothermia in the Elderly." (Preceded by buffet supper, 8 p.m.) Guests are invited.

KINGSTON-UPON-THAMES DIVISION.—At Kingston Medical Centre, Tuesday, 14 November, 8.30 p.m., Dr. A. J. Thomas: "Cholesterol in Atherosclerosis."

MID-GLAMORGAN DIVISION.—At Seabank Hotel, Porthcawl, Friday, 17 November, 7 for 7.30 p.m., annual dinner dance.

MONMOUTHSHIRE DIVISION.—At Friars Pavilion, Royal Gwent Hospital, Newport, Thursday, 16 November, 7.30 for 7.45 p.m., B.M.A. lecture by Mr. T. H. L. Rosser: "Investigation and Treatment of some Congenital Cardiac Abnormalities."

NORTHAMPTON DIVISION.—At Board Room, Northampton General Hospital, Friday, 17 November, 8 for 8.20 p.m., the Branch president will present the Scroll of Fellowship to Mr. E. E. T. Taylor; 8.30 p.m., B.M.A. lecture by Dr. W. W. Sargent: "Brainwashing" (illustrated).

NORTH-EAST ULSTER DIVISION.—At Nurses' Home, Route Hospital, Ballymoney, Tuesday, 14 November, 8.30 p.m., Dr. A. C. Glendinning: "X-ray Examinations in Pregnancy."

NORTH OF ENGLAND BRANCH.—At Royal Victoria Infirmary, Newcastle upon Tyne, Thursday, 16 November, 7 for 7.30 p.m., lecture by Mr. C. J. Dewhurst.

NORTH STAFFS DIVISION.—At Medical Institute, Hartshill, Wednesday, 15 November, 8.15 p.m., Mr. K. Baker: "Psychiatric Problems in Gynaecology."

PRESTON DIVISION.—At Sharoe Green Hospital, Fulwood, Tuesday, 14 November, 8.30 p.m., B.M.A. lecture by Professor T. N. A. Jeffcoate: "Frequency and Urgency of Micturition in the Female."

READING DIVISION.—At Library, Royal Berkshire Hospital, Friday, 17 November, 8.30 p.m., meeting to consider election of representatives to Annual Representative Meeting followed by Mr. N. G. Rothnie: "Management of Arterial Insufficiency of the Leg" (illustrated).

REDBRIDGE AND STRATFORD DIVISION.—At Whipps Cross Hospital Medical Centre, Wednesday, 15 November, 8 p.m., buffet, Dr. T. Gardiner will speak on "Effect on Medicine in this Country resulting from Entry into the Common Market." Ladies are invited.

REIGATE DIVISION.—At Burford Bridge Hotel, Friday, 17 November, 7.30 p.m., annual dinner dance.●

SOUTHAMPTON DIVISION.—At Postgraduate Medical Centre, Wednesday, 15 November, 8 for 8.30 p.m., B.M.A. lecture by Mr. G. Qvist: "The Acute Abdomen."

SOUTH-EAST ESSEX DIVISION.—At Board Room, Southend General Hospital, Wednesday, 15 November, 8.30 p.m., B.M.A. lecture by Dr. M. O'Donnell: "Looking Sideways at Medical Journalists." Guests are invited.

STIRLING BRANCH.—At Falkirk and District Royal Infirmary, Thursday, 16 November, 8.30 p.m., jointly with Falkirk Medical Society, Professor A. Goldberg: "Anaemia."

SUTTON COLDFIELD, LICHFIELD, AND TAMWORTH DIVISION.—At Lecture Hall, Postgraduate Medical Institute, Good Hope Hospital, Thursday, 16 November, 8.30 p.m., Professor A. G. W. Whitfield: "The Connective Tissue Disorders."

SUTTON DIVISION.—At Downs Club, Sutton General Hospital, Tuesday, 14 November, 8.30 p.m., Dr. R. A. Zeitlin: "Modern Aspects of Blood Transfusion." Guests are invited.

TUNBRIDGE WELLS DIVISION.—At Elizabethan Barn, Tuesday, 14 November, 7.30 for 8 p.m., jointly with Law Society, dinner meeting, Dr. J. Dunwoody, M.P., Mr. D. Fraser: "The Proposed New Abortion Laws."

WEST BROMWICH AND SMETHWICK DIVISION.—At Sandwell Hotel, West Bromwich, Wednesday, 15 November, 8.15 for 8.30 p.m., annual general meeting. (Preceded by supper.●)

WEST SUSSEX DIVISION.—At Burlington Hotel, Worthing, Wednesday, 15 November, 7 for 7.30 p.m., dinner meeting, Professor J. A. Stallworthy: "Abortion and the Law."

WIGTOWNSHIRE DIVISION.—At King's Arms Hotel, Glenluce, Monday, 13 November, 7.30 p.m., Dr. T. S. R. Train: "Recent Advances in Obstetrics and Gynaecology."

HOSPITAL JUNIOR STAFFS GROUP: SOUTH-WEST METROPOLITAN REGION.—At B.M.A. House, London W.C., Tuesday, 14 November, 8 p.m., general meeting to re-establish H.J.S. Group and to elect officers.

Branch and Division Officers Elected

BELFAST DIVISION.—Chairman, Dr. P. Steen. Vice-chairman, Dr. D. L. W. Chapman. Honorary Secretary, Dr. Charlotte C. Arnold. Assistant Honorary Secretary, Dr. H. W. Dunn. Honorary Treasurer, Dr. G. T. C. Hamilton.

EAST SUFFOLK DIVISION.—Chairman, Dr. R. Wilton. Vice-chairman, Dr. J. P. R. Richardson. Honorary Secretary, Dr. F. O. Wells. Honorary Treasurer, Dr. R. A. Leader.

LONDONDERRY DIVISION.—Chairman, Dr. R. Haire. Chairman-elect, Dr. F. C. Calvert. Vice-chairman, Dr. J. J. Cosgrove. Honorary Secretary, Dr. M. D. L. Eakin. Honorary Treasurer, Lieutenant-Colonel D. G. C. Whyte.

NORTH-EAST ESSEX DIVISION.—Chairman, Dr. D. A. Lamont. Vice-chairman, Dr. D. A. Logan. Honorary Secretary and Treasurer, Dr. P. Snell.

Meetings of Branches and Divisions

SOUTH WALES AND MONMOUTHSHIRE BRANCH.—The annual meeting of the Branch was held on 21 September at Ysgyborwen Country Club, Aberdare. The new President, Dr. J. L. Ryce, was installed in office, and he gave an address on the development of medicine in Wales.

Correction

Dr. W. E. Dornan is chairman of the Medical Practices Committee and not Dr. A. N. Mathias, as stated in the report of the Proceedings of Council (*Supplement*, 4 November, p. 29).

British Medical Journal · Supplement

LONDON SATURDAY 18 NOVEMBER 1967

CONTENTS

Assistants and Young Practitioners Subcommittee	53	General Practice Finance Corporation	56
Fellowship for Freedom in Medicine	55	Diary of Central Meetings	56
Computers in Medicine	55	Branch and Division Meetings	56

Assistants and Young Practitioners Subcommittee

Younger general practitioners in their representative subcommittee discussed the implications to British medical practice if Britain joined the Common Market. They also gave their views on the place of general practitioners in district general hospitals. They thought that general practitioners should have beds in these hospitals for cases they were competent to treat. A survey among young general practitioners had shown an enthusiasm for having hospital beds. Older doctors had shown little interest.

A meeting of the Assistants and Young Practitioners Subcommittee of the General Medical Services Committee was held on 3 November. Dr. M. A. WILSON was re-elected to the chair.

The Chairman and Dr. D. F. Rickards were elected to represent the Subcommittee on the General Medical Services Committee.

Further consideration was given to a draft of a model assistantship agreement. It was reported that the G.M.S. Committee had not accepted the Subcommittee's view that an assistant who was in breach of his contract should still be entitled to any holiday period or payment in lieu of holiday that was due to him. The G.M.S. Committee, however, had agreed that provision should be made in the model agreement "to entitle the assistant to two weeks' sick leave at half-pay in addition to the two weeks at full-pay."

European Economic Community

At its last meeting the Subcommittee had decided that a memorandum setting out details of medical practice in the six countries of the European Economic Community should be referred to the Subcommittee's forward planning group. Dr. G. H. Curtis Jenkins, a member of the group, had agreed to prepare a report on the changes which had taken place in medical practice in the Common Market countries since 1963, and the effects on medical practice in this country if Britain joined the Common Market. These papers were before the Subcommittee for its consideration.

Dr. JENKINS explained that the European Economic Commission was the executive body which made proposals to the Council of Ministers, and when health matters were discussed the Ministers of Health for the various countries would attend council meetings. The Council of Ministers was empowered to make and implement decisions without necessarily obtaining the assent of the national Governments and Parliaments. Ideally the Common Market was a supranational organization.

Britain, Dr. Jenkins said, was the only country in Europe which had an organization like the General Medical Council, which was independent of Government. To other countries in Europe that independence seemed irrational. The Civil Service in the Common Market Countries had a far greater responsibility for the day-to-day running of their countries than the British Civil Service had in Britain. The Ministerial decisions in Europe were less important than those of the civil servants.

Dr. Jenkins believed that few doctors would want to come from Europe to work in Britain. Those to whom he had spoken could not understand how a "free-at-the-time" service could be made

to work, or how it was possible to practise good medicine on demand with no barrier between the patient and the doctor. Some doctors might come for training in hospitals, but he did not think that any, or only a few, would come into general practice.

Hurdles to Overcome

Dr. P. R. SMITH asked to what extent Commonwealth doctors were likely to go to Europe to practise rather than to Britain. Dr. JENKINS said he believed that there were considerable hurdles of language and "approach" for Commonwealth doctors to overcome if they wished to practise in Europe. Even those Commonwealth doctors whose mother tongue was not English were taught medicine in English and were therefore more likely to come to Britain than to Europe.

In reply to a question about the General Medical Council, Dr. Jenkins said that the duties laid down for the Council could not be altered without legislation.

Dr. J. M. DUNLOP commented on the fact that decisions were made by the Council of Ministers on a supranational basis. "Was that on a majority basis?" he asked. "Would a Minister of Health who was opposed to a decision have to agree to a majority opinion?" Dr. JENKINS said that up to now every decision had been unanimous. A use of the veto could prevent decisions being taken at all.

Dr. DUNLOP said that doctors from a country where there was an excess of doctors might come to Britain despite its Health Service.

Dr. A. W. MACARA pointed out that though no other country had followed Britain completely in a free-at-the-time service most countries had advanced varying distances along the road towards subsidized medicine. The reason why they had not gone so far as Britain was an economic one rather than a functional one—they were afraid of the cost. In fact their services cost as much if not more than the British service. So long as there was adequate control over standards Britain should welcome doctors from Europe.

Dr. JUDITH ATKINSON wondered whether the National Health Service might break down as Britain came into contact with other systems, and whether the British system might eventually come into line with the European health schemes. Dr. JENKINS said it was not a matter of Britain coming into line. It was not standardization which was wanted but harmonization.

Dr. MACARA, commenting on the British public health service, said that the statutory requirement that a medical officer of health should have a diploma in public health, and the fact that he could not be dismissed without the agreement of the Minister of Health, had given the medical officer of health status and security. Was the public health service likely to risk the loss of these privileges if Britain entered the Common Market?

Dr. JENKINS replied that a subcommittee of the European Economic Community had examined the contractual rights, pensionable rights, and ethical status of public health medical officers in Europe, and those doctors, said Dr. Jenkins, would become a powerful body.

The CHAIRMAN believed that the B.M.A. should continue to send observers to the meetings of the medical profession in the European Economic Community. This was important, because if agreement was reached on the main issues, and if Britain did not enter the Community for several years, this country would have to accept the agreements as they then existed.

Charges for Services

The Subcommittee discussed the Council's recommendation that "All Association committees should be invited to consider the question of charges for services, if any, in their respective fields and to make recommendations."

The CHAIRMAN said that for some B.M.A. services, such as the Medical Practice Advisory Bureau, car-parking badges, or photocopying by the Nuffield Library, a charge was made to non-members and sometimes to members, and the difference between the two charges was not always substantial.

Dr. DUNLOP hoped that advice would be given free to potential members, particularly students. The CHAIRMAN said that the British Medical Students' Association usually catered for students. When a student asked the B.M.A. for information on careers in medicine it was sent without charge.

The Subcommittee agreed that in those cases where the Association charged a fee to non-members it should be a realistic one, so that a much reduced fee could be charged to members if it was necessary to charge one at all.

Dr. D. G. EMERY thought non-members should pay at least three times the fee that members paid.

District General Hospitals

The Subcommittee discussed a questionnaire received from the Central Health Services Council's committee on the functions of the district general hospital. The questionnaire had been sent to local medical committees and B.M.A. Divisions earlier in the year.

The questionnaire stated that the existing doctrine on accident and emergency services was based on the advice given by the Subcommittee of the Standing Medical Advisory Committee in 1962, that "all injured patients requiring hospital treatment should be taken direct to accident and emergency units staffed and equipped to deal immediately with major injuries, and other emergency cases at any hour of the day or night."

Dr. EMERY said that in rural areas all district hospitals should have general accident emergency services, but in large towns it might be advantageous to have several specialized accident departments. Dr. DUNLOP thought that in rural areas a long ambulance ride to hospital could be dangerous. He suggested that helicopters should be used for conveying emergency cases to hospitals from outlying areas.

Dr. JENKINS said that helicopters had

disadvantages. It would be far better to "take the hospital" to the patient in the case of an emergency or accident. That was done in Germany, where a doctor went out in a fast ambulance to the scene of an accident.

Dr. G. J. DAVIES said that in Birmingham a district general hospital had been built with lavish new emergency and accident departments, but it had been difficult to obtain staff. Therefore the city had been zoned into areas, and the patient had to be taken to the hospital in the zone where the accident happened.

Dr. G. T. WALKER, representing the Hospital Junior Staffs Group, agreed that in large areas of population it would be better to have a central accident department which was well staffed and well equipped, rather than three or four inadequately equipped units. Dr. D. F. RICKARDS believed that it was important to have a doctor of consultant status available 24 hours a day in accident and emergency departments.

The questionnaire asked to what extent provision should be made in district general hospitals for rehabilitation and for what types of patient. Dr. MACARA said that the answer depended on the definition of rehabilitation. He suggested that there should be provision for occupational therapy and for consultation between consultants, general practitioners, and social workers. More specialized physical rehabilitation units should be provided only in the bigger hospitals. The CHAIRMAN agreed that the simpler forms of treatment should be available in district hospitals and more sophisticated forms in specialist hospitals. Selected district general hospitals should include a special unit for young chronic sick patients.

Obstetrics

The questionnaire asked whether all potentially abnormal obstetric deliveries should take place in a district general hospital. Dr. DAVIES said that normal deliveries, either in hospital or at home, were carried out by midwives. He knew of a general-practitioner unit attached to a new district general hospital where the only occasions on which a general practitioner was called to see a patient was when a perineum needed repairing. That was disgraceful: a general practitioner should be allowed to do a forceps delivery in a general-practitioner maternity unit.

The Subcommittee gave its qualified agreement to the proposition in the questionnaire that all potentially abnormal deliveries should take place in the district general hospital, and it suggested that the words "or a suitably equipped obstetric unit" might be added.

On the question of the size of district general hospitals, the CHAIRMAN said he believed that they should be big enough to allow for two consultants in each major specialty.

The Subcommittee next considered what clinical facilities there should be for general practitioners in district general hospitals. The questionnaire stated that it was now generally accepted that general practitioners should have "open access" to pathology and radiology departments, and it asked: (1) "Do you consider that they should also have open access to electrocardiography, electroencephalography, or other diagnostic services?" and (2) "Do you consider that the district general hospital should include

beds in which general practitioners treat their own patients? If so, for what types of case? What should be the allocation of clinical responsibility as between the general practitioner and his consultant colleagues?"

The Subcommittee agreed that open access to departments of electrocardiography should be available to general practitioners, but it did not consider that open access to any other diagnostic service was necessary.

Dr. JENKINS said that the hospitals were now thinking in terms of "departments of medicine," with a hierarchical structure. Patients would be looked after by their own general practitioners or by general practitioners attached to the hospital who would take over the care of patients who came from distant parts. Many consultants were unaware of what general practitioners could do in a hospital, and when they found out they were only too willing to enlist their help. Dr. Jenkins thought that in future general practitioners might carry out all outpatient investigations before the patient saw a consultant. Having a few general-practitioner beds "tacked on to the end of the hospital," with little contact with consultants, had been shown to be disappointing in practice in most cases.

It had often been said that general practitioners were overworked, but, said Dr. Jenkins, those who had organized themselves had been freed of the burdens of trivia, and it was those doctors who wanted to participate actively in a hospital unit.

General-practitioner Beds

Dr. RICKARDS said that it was unrealistic for general practitioners to expect to have beds of their own. They should work more in hospitals but forget about having beds. General practitioners should be on the staff of a hospital on a part-time basis, the degree of their responsibility being decided between themselves and their next superior.

Dr. SMITH said that general practitioners were not part of the staffing hierarchy of a hospital, and should not accept a superior.

Dr. DAVIES said he would welcome the opportunity of access to hospital beds. In Nottingham, where relations between general practitioners and hospitals were good, he could get investigations on patients done first and then present them to the consultant for advice on treatment. Dr. RICKARDS agreed that the more open access to diagnostic departments available to general practitioners the less they would need hospital beds.

Dr. J. F. HUGHES said that a survey among young South Warwickshire general practitioners had shown some enthusiasm for general-practitioner hospital beds. A survey among general practitioners who had been in practice for a minimum of 15 years had shown little interest in the idea of hospital beds with consultant opinion available. There had been no support for beds without consultant opinion available.

The Subcommittee decided that general practitioners should have beds in district general hospitals for cases "which the general practitioner felt he was competent to deal with." It was thought that no decision could be come to about the allocation of clinical responsibility.

The Subcommittee agreed that its comments on the questionnaire should be submitted to the General Medical Services Committee.

Fellowship for Freedom in Medicine

Mr. DESMOND DONNELLY, Labour M.P. for Pembroke, gave an address, entitled "Can the Health Service Survive?", at the annual general meeting of the Fellowship for Freedom in Medicine at Caxton Hall, Westminster, on 4 November.

Dr. P. A. T. WOOD, chairman of the Fellowship, was in the chair.

Dr. E. C. WARNER paid a tribute to Dr. R. Hale-White, president of the Fellowship and its former chairman, who had died suddenly during the week.

Survival of N.H.S.

Mr. DONNELLY, who said he believed he was the first Labour M.P. to attend one of the Fellowship's annual gatherings, pointed out that the Government was trying to enter Europe, to deflate the economy, and to continue Government spending at the same rate as in preceding years. These were a series of conflicting objects. The largest single item in Government spending was the £6,500m. on the welfare service, of which £1,500m. went to the National Health Service. There was no reason why any Government should be exempt from that immutable law of intelligent economics that "if you spend more than you are producing or earning, and do not pay attention to the earning capacity of the country, you are going to find yourselves in a very serious condition indeed."

Mr. Donnelly contrasted the situation in the 1940s, when Beveridge and others were planning post-war social security, and the situation today. In terms of aspirations and hopes the situation 25 years ago was totally divorced from the situation now, when the average income in this country was somewhere in the region of £19 a week, and five million people took their holidays abroad every year. So far as the National Health Service was concerned, he sensed "very considerable frustrations." The medical services, including a number of specialties, were inadequate, and there was an overall feeling of disillusionment with a National Health Service that was to provide free medical attention regardless of income but solely based on the individual's need. That had turned out to be "a sad disillusionment" in its practical operation. Politicians who defended the N.H.S. as it stood were either ignorant of the true situation or they were clinging to antediluvian slogans because they lacked the guts to face up to the truth. The medical profession needed to take a look at itself, too. "Our British medical profession and its standards, once among the best in the world, have crumbled," Mr. Donnelly said.

The whole Health Service concept needed rethinking. The system as it stood today should be scrapped and something quite new put in its place. "We have got to spend much more money on our Health Service, whatever form it takes. If we were to give our medical services the same priority as in the U.S.A., where there is no National Health Service, we should need another £500m. a year immediately." Mr. Donnelly said that no British Government could face that kind of bill. There was too much taxation in this country, and people were lacking incentives to produce more simply because of the incidence of taxation.

Dignity of Choice

Mr. Donnelly maintained that the money needed could not be obtained by cutting out other expenditure, such as on the armed Forces. The money could be got only out of personal consumption. "People have got to be allowed to spend more of their own money on the services they want. . . ."

People must be given the dignity of choice. At present the public had virtually no choice and no voice. "We are just told what we should have, and I do not really think we are all that competent in Westminster to determine all the time what people should have. If we start to pay directly instead of through the gargantuan machine of taxes we shall be in a better position to insist on the kind of service we want, and much more likely not to overuse the services that are available. If you think you are not paying—but of course you are, through taxes—you tend to overuse." There was no practical way at all of providing the services that the poor people needed desperately until the principle of selectivity, or each according to his ability, each according to his needs, was introduced.

Mr. Donnelly said in conclusion: "We are following a number of conflicting objectives, and we have got to get this whole strategy straight. The key factor is: How are we going to order our welfare services to make them compatible with the needs of the people and compatible with the resources available? This is really what we have got to address our minds to in the coming years. What we need is a return to the questions that were asked twenty years ago . . . and to ask ourselves whether the answers were right. We know they were not."

Chairman's Address

Dr. WOOD took the theme of "Adventure in Medicine" for his chairman's address. What had happened in the twentieth century, he asked, which had given so much to doctors in the way of weapons to fight disease, and which yet had taken so much away from them in morale and self-respect? All were a little tired of the hackneyed phrase "the stress of modern living," but it was unfortunately true.

He believed that among the great causes of stress were the powerful trends which had developed all over the world towards uniformity and conformity. In Russia, China, and much of Europe, including Britain, egalitarianism had become the motivating force behind many of the changes in politics and social life. He believed that those pressures towards uniformity and conformity were a self-destructive element in their civilization, for they were directly opposed to the variety and diversity which was in nature. If he might put it in an evolutionary nutshell, "the more you conform the less you adapt." Much of the stress of modern life developed from the frustration of the individual who wanted to be different from the herd, who wanted to be true to himself, who wanted to be responsible for himself, and stand on his own feet.

In medicine the twin dangers of uniformity and conformity affected doctors to a greater extent than any other profession, for egalitarianism in the treatment of disease had

immense emotional appeal. Fair-minded people of all kinds rejected the idea that one person should be able to get better medical attention than another, although only a moment's logical thought would convince them that equality in diagnosis and treatment was quite impossible to achieve in practice. But there they were in an area where logic counted for nothing.

The main dangers to the doctor in the National Health Service were a great lack of variety and experiment, that nonconformity was discouraged, the individual received little stimulation or encouragement, and security had replaced adventure. Those were the very reasons why young doctors were forced to emigrate. The Fellowship believed in freedom not because it wished to escape discipline, not because it wished to encourage private practice to line doctors' pockets, but because it believed in experiment, in diversity, in encouraging the individual to develop along his own lines, and especially in preserving the spark of adventure in medicine.

Fellowship Business

Presenting the accounts and balance sheet, the honorary treasurer, Mr. C. A. JACKSON, said the Fellowship was continuing to run at a deficit. Were it not for the generous anonymous donor who had been able to maintain his subscription (of £1,000) over a large number of years the Fellowship would be in a sorry state.

The honorary secretary, Dr. J. M. ALSTON, gave an account of the Fellowship's activities during the past year.

Mr. R. S. MURLEY proposed the following resolution:

"Knowing that the future expansion of medical care in Great Britain will necessitate a massive injection of additional funds, convinced that bold experiment is vitally needed in devising supplementary and alternative sources of income for the health services, and recognizing that two important surveys of public opinion confirm that many people are prepared to make more direct personal payment for medical care, this meeting of the Fellowship for Freedom in Medicine calls for a radical reform of the National Health Service so as to ensure (1) increased personal payment at the time of service (with proper safeguards for pensioners and poorer people); (2) the promotion of greater independence at the periphery, including the encouragement of fund-raising by individual hospitals; and (3) stimulation of private medical practice by tax relief and other appropriate methods."

After a short debate the motion was carried unanimously.

Computers in Medicine

The B.M.A. and the Institute of Mathematics and its Applications are holding a symposium at B.M.A. House on 6 December on the application of mathematical and computer methods to problems in medicine. Papers will be read by Dr. Bryan Thwaites, President of the Institute of Mathematics and its Applications and Principal of Westfield College, London ("Mathematical Models in Medi-

General Practice Finance Corporation

cine"); Dr. H. R. A. Townsend, consultant neurophysiologist, Western General Hospital, Edinburgh ("Wave Forms of Biological Origin"); Professor John Anderson, King's College Hospital, London ("Problems in Medical Vocabulary"); Professor Paul Hall, Karolinska Hospital, Stockholm, Sweden ("Automated Diagnosis"); and Dr. J. Howlett, Director of the Science Research Council's Atlas Computer Laboratory ("Data Bank Problems").

There is an advance registration fee of 15s. for members of the Association or the Institute and of £2 for non-members. The fee includes a hamper lunch and tea. An additional charge of 17s. 6d. will be made to those staying on for a buffet supper. The number attending the symposium will be limited to 300.

Further particulars and registration forms are obtainable from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London W.C.1.

Information has now been provided by the General Practice Finance Corporation on the amount of money paid out in loans for various purposes, or for which authorizations had been made, up to 20 October. The first report of the Corporation covering the first few months of its existence, from 21 November 1966 to 31 March 1967, was published on 23 October (*Supplement*, 4 November, p. 41).

Up to 20 October the Corporation had received 462 inquiries from general practitioners and had made loans totalling approximately £950,000. Authorizations for 144 loans amounting to £696,500 had been made, but three of these, totalling £5,200, had been withdrawn. Actual payments made to doctors up to 20 October had amounted to £136,000. The Corporation had also taken over outstanding applications from general practitioners to the Group Practice Loans

Scheme. These applications had been for loans amounting to £779,000, of which £136,000 had been paid out to date.

Twenty-four loans totalling £182,750 for the erection of purpose-built premises had been made, and £175,400 had been paid out in loans to enable general practitioners to purchase existing premises. Conversion of premises had accounted for 27 loans totalling £111,050, and 26 loans totalling £107,550 had been made for repayment of loans raised from other sources for the purchase of premises, etc.

Twelve loans had been made for the repayment of bridging loans for purchasing premises and/or making conversions amounting to £67,200, and 21 loans totalling £47,350 had been made to enable general practitioners to purchase a share in practice premises.

Association Notices

Diary of Central Meetings

NOVEMBER

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|----|--------|--|
| 21 | Tues. | General Purposes Committee, 10.30 a.m. |
| 22 | Wed. | Fees for Part-time Services Subcommittee (Private Practice Committee), 9.30 a.m. |
| 22 | Wed. | Working Party on Amphetamine Preparations (Committee on Medical Science, Education, and Research), 9.30 a.m. |
| 22 | Wed. | Private Practice Committee, 10.30 a.m. |
| 22 | Wed. | Journal Committee, 10.30 a.m. |
| 22 | Wed. | Psychological Medicine Group Committee, 2 p.m. |
| 23 | Thurs. | Executive Subcommittee (C.C.H.M.S.), 10 a.m. |
| 23 | Thurs. | Compensation and Superannuation Committee, 2 p.m. |
| 23 | Thurs. | Negotiating Subcommittee (C.C.H.M.S.), 2 p.m. |
| 23 | Thurs. | Interim Negotiating Subcommittee (C.C.H.M.S.), 2 p.m. |
| 23 | Thurs. | Dermatologists Group Committee, 2.30 p.m. |
| 23 | Thurs. | Finance Committee, 2.30 p.m. |
| 23 | Thurs. | Representatives of Negotiating Subcommittee (C.C.H.M.S.) and Ministry of Health, 4 p.m. |
| 27 | Mon. | Alcohol and Road Accidents Committee, 2 p.m. |
| 29 | Wed. | Council, 9 a.m. |

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

ARMAGH AND WEST DOWN DIVISION.—At Ardmore Hotel, Newry, Thursday, 23 November, 8.30 for 9 p.m., dinner dance. Guests are invited.●

AYRSHIRE DIVISION.—At Ballochmyle Hospital, Cairne, Sunday, 26 November, 7.30 p.m., B.M.A. lecture by Dr. J. J. R. Duthie: "Rheumatoid Arthritis."

BLACKBURN DIVISION.—At De Tabley Hotel, Ribchester, Thursday, 23 November, 8.30 p.m., annual dinner dance.●

CARDIFF DIVISION.—At Park Hotel, Thursday, 23 November, 7.30 for 8 p.m., autumn supper meeting. Mr. Gwynfor Evans, M.P.: "This Wales."●

CLEVELAND AND MIDDLESBROUGH DIVISION.—At Corporation Hotel, Middlesbrough, Thursday, 23 November, 8.30 p.m., B.M.A. lecture by Dr. I. G. W. Pickering: "Crime and the Treatment of the Offender."

COVENTRY DIVISION.—At Lecture Theatre, Walsgrave Maternity Hospital, Tuesday, 21 November, 8.15 p.m., discussion: "A Reappraisal of Pelvic Examination." Speakers: Mr. J. L. Marcus, Mr. M. E. E. White.

DORSET DIVISION.—At Postgraduate Medical Centre, Dorset County Hospital, Dorchester, Wednesday, 22 November, 8.30 p.m., Dr. P. Robinson: "Recent Trends in Neurology."

DUDLEY DIVISION.—At Nurses' Lecture Room, Guest Hospital, Friday, 24 November, 8.30 p.m., annual general meeting.

EAST HERTS DIVISION.—At Herts and Essex General Hospital, Bishops Cleeve, Tuesday, 21 November, 8.15 p.m., clinical meeting.

EAST KENT DIVISION.—At "Chez Laurie," Thanet Way, Herne Bay, Thursday, 23 November, 7.30 for 8 p.m., annual medico-legal dinner. Speaker, Dr. J. D. K. Burton.●

EAST SUFFOLK DIVISION.—At Ipswich Postgraduate Medical Centre, Wednesday, 22 November, 8.15 p.m., Dr. O. Morton: "Recent Advances in Oral Contraception."

EXETER DIVISION.—At Library, Royal Devon and Exeter Hospital, Thursday, 23 November, 8.30 p.m., meeting and election of representatives to Annual Representative Meeting, followed by Dr. John Lloyd: "Why I Came Back."

GLASGOW DIVISION.—At Maurice Bloch Lecture Theatre, Royal College of Physicians and Surgeons of Glasgow, Monday, 20 November, 8.30 p.m., Mr. A. Gibson (Director of the Scottish Opera and Conductor of the Scottish National Orchestra): "Music in Scotland." (One guest not member.)

HUDDERSFIELD DIVISION.—At George Hotel, Friday, 24 November, 8 for 8.30 p.m., annual dinner and dance.

LEEDS DIVISION.—At Guildford Hotel, Wednesday, 22 November, 8.45 p.m., meeting and discussion: "Drugs and Young People." Speakers, the Bishop of Pontefract, the Rt. Rev. E. Treacy, Dr. W. A. Weston. (Preceded by dinner, 7.45 p.m.) Ladies are invited.●

LEWISHAM DIVISION.—At Mermaid Theatre Restaurant, Thursday, 23 November, 7 p.m., dinner-theatre party, "Climb the Greased Pole."●

MAIDSTONE DIVISION.—At Preston Hall Hospital, British Legion Village, Friday, 24 November, 8 p.m., wine and cheese party, one-hour film show, followed by annual general meeting.

MANCHESTER DIVISION.—At Boyd House, Tuesday, 21 November, 8.30 p.m., Mr. F. G. Wood: "Alcoholics Anonymous." Guests are invited.

MIDLAND BRANCH.—At Postgraduate Centre, Selly Oak Hospital, Thursday, 23 November, 8.15 p.m., Clinicopathological Section meeting.

NORTH BEDFORDSHIRE DIVISION.—At Medical Institute, Bedford General Hospital, South Wing, Thursday, 23 November, 8.30 p.m., special general meeting to elect representative to Annual Representative Meeting.

NORTH DEVON DIVISION.—Friday, 24 November, clinical evening.

NORTH MIDDLESEX DIVISION.—At Outpatients' Department, North Middlesex Hospital, Tuesday, 21 November, 2 p.m., clinical meeting.

PLYMOUTH DIVISION.—At North Friary House, Greenbank, Thursday, 23 November, 8.30 p.m., jointly with Pharmaceutical Society, Professor F. E. Camps: "Poisoning, Accident, Suicide, or Murder?" (Preceded by dinner at Duke of Cornwall Hotel, 7 for 7.15 p.m.)●

RENFREWSHIRE DIVISION.—At Lecture Hall, Administrative Block, Bridge of Weir Hospital, Sunday, 26 November, 3.30 p.m., annual general meeting.

ST. MARYLEBONE DIVISION.—At Royal Society of Medicine, Tuesday, 21 November, 7 p.m., meeting: "Medical Aspects of Adult and Teenage Crime." Speakers will include Dr. W. Lindesay Neustatter, Judge G. Rogers, Mr. A. McLean. Guests are invited.

SCARBOROUGH DIVISION.—At Board Room, Scarborough General Hospital, Thursday, 23 November, 8.30 p.m., B.M.A. lecture by Mr. W. Mills: "Modern Methods of Contraception."

SOMERSET DIVISION.—At County Hotel, Taunton, Thursday, 23 November, 7.30 for 8 p.m., annual dinner and dance. Guests are invited.●

SOUTHAMPTON DIVISION.—At Hampshire Suite, Skyway Hotel, Friday, 24 November, 7.30 for 8 p.m., annual ball.●

SOUTH-WEST WALES DIVISION.—At Hotel Mariners, Haverfordwest, Saturday, 25 November, 7 for 7.30 p.m., dinner meeting; 8.30 p.m. (approx.), Professor H. Scarborough: "Management of Chronic Renal Failure."●

SUNDERLAND DIVISION.—At Medical Society Lecture Room, Sunderland General Hospital, Thursday, 23 November, 3 p.m., annual address by Professor S. Shuster, followed by annual dinner at Seaburn Hotel, 7.30 for 8 p.m.

SWINDON DIVISION.—At Princess Margaret Hospital, Friday, 24 November, 8 for 8.30 p.m., annual dinner dance.●

TYNESIDE DIVISION.—At Grand Hotel, Tynemouth, Thursday, 23 November, 8.30 p.m., B.M.A. lecture by Dr. Alan L. Bass: "Sponging Around the World."

WAKEFIELD, PONTEFRAC, AND CASTLEFORD DIVISION.—At gymnasium of Pontefract General Infirmary, Wednesday, 22 November, 8 p.m., clinical meeting.

WINCHESTER DIVISION.—At Board Room, Royal Hampshire County Hospital, Winchester, Saturday, 18 November, 7 p.m., annual general meeting, followed by reception at Postgraduate Medical Centre.

WEST SUFFOLK DIVISION.—At Drummond Hall, West Suffolk General Hospital, Bury St. Edmunds, Tuesday, 21 November, 8.30 p.m., B.M.A. lecture by Dr. J. D. J. Havard (Under-Secretary, B.M.A.): "Recent Legislation Affecting the Medical Profession."

EAST ANGLIAN REGIONAL CONSULTANTS AND SPECIALISTS COMMITTEE.—At Bell Hotel, Thetford, Monday, 20 November, 8.30 p.m., meeting.

British Medical Journal Supplement

LONDON SATURDAY 25 NOVEMBER 1967

CONTENTS

Ophthalmic Group Committee - - - - -	57	Travelling Expenses - - - - -	58
Hospital Medical Staffs' Negotiators - - - - -	58	Memorial to Dr. Kate Harrower - - - - -	58
Public Health Medical Officers' Salary Claim - - - - -	58	Association Notices - - - - -	58

Ophthalmic Group Committee

At a meeting of the Ophthalmic Group Committee held on 3 November, Mr. A. G. CROSS was re-elected chairman and Dr. D. STENHOUSE STEWART deputy chairman.

Central Professional List

The CHAIRMAN reported on a meeting between representatives of the General Medical Services Committee and representatives of the Ophthalmic Group Committee, the Ophthalmic Qualifications Committee, and the Faculty of Ophthalmologists on 13 October to discuss criteria for admission to the central professional list of ophthalmic medical practitioners.

The Chairman said that he had reminded the representatives of the G.M.S. Committee that the fundamental requirements for acceptance of any doctor on the central professional list were that he should have the Diploma of Ophthalmology and two years' full-time (or its equivalent of six sessions a week) experience in ophthalmology. The G.M.S. Committee had asked for some modification in these requirements.

The Group Committee agreed that the Diploma of Ophthalmology and two years' experience should remain the criteria for admission to the central professional list.

The next matter to be discussed by the joint meeting, said the CHAIRMAN, had been the constitution of the Ophthalmic Qualifications Committee. The G.M.S. Committee's representatives had thought that a period of membership of the committee of six years was too long, and they wanted a shorter period—say three years. They had welcomed the suggested addition to the Ophthalmic Qualifications Committee of a general practitioner whose name was on the central professional list, but had thought there might be difficulty in finding a nominee. They had also asked for provision for the appointment of a deputy.

Mr. N. CRIDLAND referred to the period of service on the Ophthalmic Qualifications Committee, and said that in his view it did not matter much whether election to the committee was for six or three years. Appointment for six years was perhaps wiser. It ensured continuity in a committee which had a difficult task to perform and much of whose work depended on its own precedents.

Mr. T. KEITH LYLE suggested that if it were common practice for members to be re-elected, which apparently it was, it would be simple to reduce the period. Mr. M. J. GILKES agreed. One of the underlying factors was a feeling that there was a touch of the "old boy network" about it.

The Group Committee agreed that members of the Ophthalmic Qualifications Committee should retire every three years, retiring members being eligible for re-election.

The CHAIRMAN reported that the G.M.S. Committee's representatives had said that it might be difficult to nominate a general practitioner to the Ophthalmic Qualifications Committee whose name was on the central qualifications list and who was also a member of the G.M.S. Committee. Mr. CRIDLAND said that the G.M.S. Committee could co-opt such a member. The CHAIRMAN thought that if a doctor was a member of the Ophthalmic Qualifications Committee he ought also to be on the central professional list. The G.M.S. Committee had also asked that there should be a

deputy for the general-practitioner member, the Chairman said, and there seemed to be no objection to that provided the deputy's name was also on the central professional list.

Mr. GILKES proposed, and the Committee agreed, that the general-practitioner member of the Ophthalmic Qualifications Committee should be on the central professional list and that provision for a deputy would be welcomed, provided the deputy was also on the central list.

Membership of Appeals Committee

The CHAIRMAN said that the G.M.S. Committee's representatives had thought that it was undesirable for a member of the Ophthalmic Qualifications Committee to serve on the appeals committee that considered appeals from doctors who had unsuccessfully applied to the Ophthalmic Qualifications Committee to have their names placed on the central professional list of ophthalmic medical practitioners. An appeals body, they thought, should not include members who had already taken a decision on the case. They had envisaged that a representative of the Ophthalmic Qualifications Committee would present the Committee's case but would not join in the discussion. The G.M.S. Committee's representatives had also hoped that there would be some general-practitioner representation on the appeals committee, and that the possibility of increasing the Ministry of Health's representation might be considered.

Mr. GILKES said that he strongly agreed with the view, expressed by the G.M.S. Committee's representatives, that the appeals committee must not consist of people who made the original judgement. The CHAIRMAN said that the ophthalmic representatives had thought it essential for a member of the Ophthalmic Qualifications Committee to be present at an appeal to put the case. Mr. CRIDLAND said that any appeals committee could either be completely free to make any decision it desired, irrespective of the regulations, or it could feel bound by the regulations even if it chose to interpret them liberally at times. Mr. V. PURVIS agreed that those who judged a case should not also be judges at an appeal.

Mr. P. D. TREVOR-ROPER suggested that any appeals committee should have large representation from the Ophthalmic Qualifications Committee, because the problem was always that of precedent. Mr. GILKES pointed out that it had been made clear that in any independent appeals committee the precedents set would be precedents only for a particular case. Mr. KEITH LYLE said that an appeals committee must be properly constituted, and it would be wrong to have on it members of the Ophthalmic Qualifications Committee with voting powers. It should be completely independent.

Mr. CRIDLAND said that if an appeals committee was to be bound strictly by regulations and was to differ from the Ophthalmic Qualifications Committee only in the way it interpreted the regulations it did not matter what its composition might be.

The Group Committee agreed that the membership of an appeals committee should consist of a member of the Group Committee, a member of the Faculty of Ophthalmologists, a member of the National Ophthalmic Treatment Board Association, a general practitioner on the central professional list, a representative from

the Ministry of Health, and a member of the Ophthalmic Qualifications Committee in attendance but not voting.

The Group Committee also agreed that exceptional cases which were clearly outside the regulations would be referred to the Group Committee by the Ophthalmic Qualifications Committee.

Residential Appointment Necessary

The CHAIRMAN said that another point discussed with the G.M.S. Committee's representatives had been the requirement of a general practitioner applying to go on the central professional list that he should have had at least six months in a resident hospital appointment in ophthalmology. Only if the practitioner had been qualified for over seven years would the Ophthalmic Qualifications Committee waive this requirement. The G.M.S. Committee's representatives had thought that that period should be reduced to five years. They accepted the need for adequate ophthalmic experience, but wished a general practitioner to be able to obtain that in the shortest possible time. It was suggested that there might be a scheme for trainee ophthalmic medical practitioners and that their experience could count towards approval for the central professional list.

The Group Committee decided that the period of experience should not be reduced any further. The Group Committee also thought that there was no substance in the suggested scheme for trainee ophthalmic medical practitioners.

Solar Retinopathy

Mr. GILKES drew the attention of the Group Committee to a paper by Dr. A. E. A. Ridgway on solar retinopathy (*B.M.J.*, 22 July, p. 212). The author had advocated more effective methods of prevention, and had urged that the public should be warned of the dangers. Mr. Gilkes recalled that it was a point he and his colleagues had made when they took the matter up before a major eclipse in 1961. He said that representations should be made to the Ministry suggesting that it should issue a national warning before every solar eclipse about the dangers of looking directly at the sun and of using inadequate filters. The Ministry should be told that representatives of the Group Committee would be prepared to discuss the matter with the Ministry.

The Committee agreed to Mr. Gilkes's suggestion.

Mr. PURVIS emphasized that polaroid sunglasses offered no protection against the sun's rays, and the importance of making that known to the public.

Hospital Medical Staff's Negotiators

The Joint Consultants Committee (J.C.C.) has appointed the following as its representatives on the Negotiating Subcommittee of the Central Committee for Hospital Medical Services (C.C.H.M.S.): Sir John Richardson, Bt. (chairman of the J.C.C.); Mr. T. L. T. Lewis (in place of the vice-chairman of the J.C.C., Mr. Walpole S. Lewin, who is one of the C.C.H.M.S. representatives on the Subcommittee); Dr. C. W. Clayson, P.R.C.P.Ed. (representing Scotland); and Dr. K. Robson and Dr. D. P. Stevenson (Joint Secretaries of the J.C.C.).

The Central Committee for Hospital Medical Services at its meeting on 20 October (*Supplement*, 4 November, p. 36) deferred until its meeting on 14 December the appointment of the Negotiating Subcommittee for 1967-8, and it reappointed the existing Interim Negotiating Subcommittee to complete the preparation of evidence for the Review Body.

Public Health Medical Officers' Salary Claim

At a meeting on 16 November the B.M.A.'s Public Health Committee considered an amendment to the offer of the Management Side of Whitley Committee C in response to the public health medical officers' salary claim (*Supplement*, 28 October, p. 27). After some debate the Committee resolved:

"That the Council be informed that a firm offer has now been received from the Management Side of Committee C to the claim on behalf of public health medical officers. This offer, though not entirely satisfactory, does in the opinion of the Committee represent an acceptable basis for the conclusion of negotiations, and the Staff Side has been asked to negotiate a number of drafting amendments to the offer. The Committee therefore recommends that the

ban on advertisements for local authority medical appointments in the *B.M.J.* be removed."

Dr. C. METCALFE BROWN was in the chair. The Committee's recommendation will be before the Council at its meeting on 29 November.

Travelling Expenses

Dr. David Owen, of Fishguard, failed to persuade the Court of Appeal that travelling expenses from his home to hospital for emergency cases ought to be deductible for income tax purposes under Schedule E (*The Times*, 6 November).

Dr. Owen carried on general practice in Fishguard and held part-time appointments as obstetrician and anaesthetist at the Pembroke County War Memorial Hospital in Haverfordwest, 15 miles from Fishguard. He had to do stand-by duty and "flying squad" duty. All his work at the hospital was to do with emergency cases.

The Court of Appeal found by a majority (Lord Denning dissenting) that Dr. Owen was not performing the duties of his office while travelling. It was not a necessary part of his duties that he should live 15 miles from his place of work, and the expenses were not "wholly exclusively and necessarily" incurred in the performance of the duties of his office. Accordingly the appeal was dismissed. Leave was granted to appeal to the House of Lords.

Memorial to Dr. Kate Harrower

On 7 November the General Medical Services Committee (Scotland) remembered one of its most distinguished former members, the late Dr. Kate Harrower. During a short ceremony the chairman, Dr. A. A. CLARK, recalled Dr. Harrower's outstanding contribution to general practice in Scotland (see *B.M.J.*, 10 December 1966, p. 1459). As a memorial to her a watercolour, "A West Coast Bay," has been hung on a wall of the committee room in the B.M.A.'s Glasgow Regional Office, with which Dr. Harrower had close associations. It was presented by past and present members of the G.M.S. Committee (Scotland), together with members of the Scottish Council of the British Medical Association.

Association Notices

Fellowship and Awards for Medical Research

The Council of the British Medical Association invites applications for the following fellowship and research awards.

Fellowship

A new whole-time research fellowship to the value of £1,500 is offered to assist research into any subject relating to the causation, prevention, or treatment of disease. It will be tenable for one year, and normally renewable for a second year subject to a satisfactory progress report.

Research Awards

The Council will also consider applications for the Ernest Hart and Walter Dixon Research Awards, each up to the value of £300, and other research awards. The awards are granted to assist

specific research work in any subject relating to the causation, prevention, or treatment of disease.

Applications for the fellowship or research awards should be submitted not later than 27 January 1968. The appropriate form and information on the conditions of the awards are obtainable from the Secretary, British Medical Association, Tavistock Square, London W.C.1.

DEREK STEVENSON, Secretary.

Diary of Central Meetings

NOVEMBER

27. Mon. Alcohol and Road Accidents Committee, 2 p.m.
29. Wed. Council, 9 a.m.

DECEMBER

1. Fri. Planning Subcommittee (Occupational Health Committee), 10.30 a.m.
1. Fri. Working Party on Medical Assistants (C.C.H.M.S.), 2.15 p.m.

British Medical Journal Supplement

LONDON SATURDAY 2 DECEMBER 1967

CONTENTS

General Medical Services Committee	59	Hospitality	63
Advanced Specialty Training Courses	62	Was it a Drug?	63
Educating the Public	62	B.M.A. Nuffield Library	63
Medical Charities	62	H.M. Forces	64
Medical Assistants	63	Association Notices	64

General Medical Services Committee

The G.M.S. Committee was reluctant to agree that the B.M.A.'s independent Planning Unit should examine the provision of primary medical care in Britain to see what modifications were needed in the light of changes in medicine. Many speakers feared that the Planning Unit's opinions would be taken to be those of the B.M.A., and some thought that some publicly stated views of the Unit's director, Professor Henry Miller, might seem to have prejudged the issues. One member thought it was the Committee which was doing the prejudging. Other speakers were insistent that the G.M.S. Committee should get a preview of the Unit's report in order to comment on it early. Mrs. M. Jefferys, the lay chairman of the Planning Unit's working party on primary medical care, and Dr. D. H. Irvine, one of its members, are to be asked to meet the G.M.S. Committee's Planning Subcommittee, and later Professor Miller is to be asked to meet the G.M.S. Committee itself. General practitioners are to be encouraged to upgrade the ancillary staff they employ, so that general practice should compete more equally with hospitals as employers of medical secretaries. There were many criticisms of the Government's proposed legislation on drugs and medicines, and it was decided to recommend that a B.M.A. deputation should put the points raised to the Minister of Health.

A meeting of the General Medical Services Committee of the B.M.A. was held on 16 November. Dr. J. C. CAMERON was in the chair.

Recruitment to General Practice

The Committee discussed the latest figures on recruitment to general practice, which had been provided by the Medical Practices Committee.

Dr. A. ELLIOTT said he thought that the Committee should express its apprehension. Though the Ministry had said that the number of doctors was increasing, more were needed to keep pace with the increase in population.

Dr. T. J. CARTER wanted to know what offers the Ministry had made to British doctors in Canada and the United States to coax them back. Had any promises been made to them, and were their return travelling expenses paid?

The Committee agreed to record its continuing anxiety about the number of general practitioners.

Ancillary Staff

Dr. A. A. CLARK, Chairman of the G.M.S. Committee (Scotland), commented on a letter from the Scottish Home and Health Department on the subject of direct payments to general practitioners for the cost of ancillary help. The letter stated that every second Scottish practice (which meant much more than every second doctor) employed ancillary staff, with on average two ancillaries working hours equivalent to about 1.2 full-time workers. In Scotland a full-time ancillary (commonly described as a secretary/receptionist or simply as a receptionist) could expect to be paid rather less than £100 a quarter or £400 a year. That, the letter continued, was of "particular interest in view of the suggestions that have been made from time to time that there should be 70% reimbursement of salaries up to a higher level than the existing £500 per annum."

Dr. Clark said that unfortunately the majority of receptionists trained at a college in Glasgow obtained work in hospitals at the end of their 12 months' training, because they were paid better in hospitals than in general practice.

Dr. W. W. FULTON said that the better girls from the college who went into hospitals were successful in being graded as personal secretaries at £668 a year, and if they had higher typing or shorthand speeds they could earn up to £776 a year at the age of 18. General practitioners could not pay that. Dr. B. ALEXANDER said that in many parts of England ancillary staff could not be obtained at £400 a year. Dr. D. R. COOK also agreed that that salary did not apply

in England. Girls who had the Diploma for Medical Secretaries were recommended by the college that trained them for salaries of between £800 and £1,000 a year. That indicated the kind of salary doctors in the London area had to pay for a reasonably trained ancillary worker.

Dr. A. ELLIOTT pointed out that the girls who took the training course for general-practice receptionists were usually young, and there was a good case for encouraging more mature students to take the course. If doctors would pay a more realistic figure they could expect a more realistic reimbursement from the Ministry. Mature students were not interested only in the financial side if the work was interesting.

The Committee decided that doctors should be encouraged to upgrade the ancillary staff they employed.

Expenditure on N.H.S.

The Committee considered a reference from the Council of the following resolution of the Annual Representative Meeting 1967: "That this meeting has grave doubts whether the wishes of the public are being carried out in regard to the proportion of the national income spent on the N.H.S. That it be a recommendation to the Council of the Association to consider employing the modern techniques of sampling public opinion to obtain evidence of this question."

Dr. I. M. JONES said that few people had any accurate knowledge of how the N.H.S. was paid for or how the social services in general were financed. The B.M.A.'s planning unit was to conduct a survey which could provide some information on the matter in question.

Dr. R. B. L. RIDGE said that a survey of the type suggested in the A.R.M. resolution would be a fairly expensive undertaking. Even if an expression of public opinion was obtained of what use would it be? The strength of the Association lay in its knowledge of professional matters, not in making a case on behalf of the public. He hoped that the Committee would advise the Council that it could see no useful purpose being served by the B.M.A. undertaking an inquiry of this nature.

Dr. B. D. MORGAN WILLIAMS disagreed with Dr. Ridge. Once upon a time the B.M.A. had been one of the strongest pressure groups in the country. If it did a survey and the results were published people would take notice of it. Dr. R. A. KEABLE-ELLIOTT said that he thought the wishes of the public were not being carried out, but he could conceive of no greater waste of money than to carry out a survey of public opinion. It was nonsense to think that the Government would "rush off and spend more money on the N.H.S."

Part of a Whole

Dr. H. N. ROSE pointed out that the whole of the country's budget would have to be considered—how much was spent on defence, how much on education, how much on welfare, and so on. The doctors thought that not enough money was spent on health, but it was not for them to say where the money should come from. It was Parliament's job to determine what proportion of the national income was going to be spent on the Health Service.

Dr. G. CORMACK said that implicit in the motion was a belief that the amount of money spent on the N.H.S. could be increased. The amount of money expended on any particular activity could be only a percentage of the total national expenditure, and in the last resort only the Government could decide how much was spent on each activity. All doctors could do was to compare what was spent on health in this country with what was spent in other countries with a comparable standard of living. A comparison could be made with the United States, where people could spend their money largely as they wished, and they chose to spend a greater proportion on health—about 2% more.

Dr. J. E. MILLER said that if such an expensive undertaking (the Committee was advised that a worth-while survey would cost £50,000) was to be paid for by, among others, the general practitioners' defence trusts the

Committee would have to be sure that it was going to yield some benefit not only to the profession and to the N.H.S. but also to doctors in the other branches of the Service.

Dr. I. M. JONES said that it had been shown that the health of a nation could be related to the proportion of its income that it spent on health services. In the world league table Britain came no higher than eighth. Where the money came from was another issue, and it was an issue on which the attitude of the British public was not known. The extra money needed to bring the standard of the British health services up to the best in Europe was about £500m. to £600m. a year. To get that out of taxation would mean the equivalent of 2s. more on the standard rate of income tax. The money would have to come either from indirect taxation or from what people spent themselves on consumer goods and services. Such surveys as had been carried out indicated that many people would be willing voluntarily to spend their money on their health. In the last resort money spent on the community came from the community. The debate was whether it should come almost exclusively from taxation or whether usefully and with advantage to the whole community it could come from other sources.

The Committee decided to defer further consideration of the matter until a future meeting.

Association's Planning Unit

The CHAIRMAN outlined to the Committee the steps that had been taken to set up the B.M.A.'s Planning Unit under the direction of Professor Henry Miller, of Newcastle upon Tyne. It had set up various groups to study particular subjects in detail—one on intensive medical care, another on aids to the disabled, another on the use of computers in medicine, and so on (*Supplement*, 14 October, p. 14).

One of the subjects which the Planning Unit was going to study was the provision of primary medical care. A working party had been appointed with Mrs. Margot Jefferys, director of the social research unit, of the department of sociology, Bedford College, London, as its chairman. The CHAIRMAN (Dr. CAMERON) said that he had met Professor Miller and had proposed, bearing in mind the interest and responsibility which the G.M.S. Committee had in the matter of primary medical care, that there should be a joint working party of the G.M.S. Committee and the Planning Unit. Professor Miller had thought that the G.M.S. Committee's activities were more in the medico-political field. He did not think that a joint working party was a good idea, because it was essential that the Planning Unit should maintain its independence. Any report it produced should not be influenced by any other body.

The Chairman said that he had then suggested to Professor Miller that two or three members of the G.M.S. Committee might join the Planning Unit's primary medical care working party, because the Committee was anxious that no publication should throw any doubt on to the future of general practice. He had then invited Professor Miller at some date to meet the G.M.S. Committee to discuss the matter.

Letter from Professor Miller

The Committee had before it a letter to Dr. Cameron from Professor Miller, which, after referring to their discussion, continued as follows:

"The Planning Unit recognizes that, however it is furnished, the provision of primary medical care is the bedrock of the Health Service. It also appreciates that if this provision is to keep pace with the rapid changes that are occurring throughout medicine it is bound to need progressive modification. As you know, there are many views on how new needs can best be met, ranging from the provision of specialist polyclinics on the Central European pattern to a thorough upgrading of general practice as a career in the matter of more extended postgraduate training, improved physical facilities, grouping of practitioners, possibly some degree of specialization within group practice, and the possibility of frequent hospital attachment. My personal guess would be that the second alternative is the more likely ultimately to prevail under British conditions, and indeed it seems that the Ministry is steadily moving in this direction. At any rate the advantages and disadvantages of these two approaches and of many immediate possibilities will be examined carefully and objectively, and as far as possible an attempt will be made to cost the various possible arrangements. . . .

"The nucleus of the Working Party has been carefully selected to try to achieve a combination of intimate personal experience with present general practice with the freshness of approach that can be brought to it by expert opinion from outside the profession. It must be emphasized, however, that it is a collection of individuals and in no sense whatever of representatives of any special interests. . . . I am certain that if its report is to be useful it will take a considerable time to prepare. We don't wish to produce merely another discussion of generalizations.

"There is, I am sure, no need for me to point

out that the purpose of the Planning Unit and its working parties is to take a fresh look at a series of problems of contemporary medicine and in no sense to formulate policy. We aim to discuss alternative solutions and to try to weigh their respective advantages and disadvantages. No source of relevant evidence or opinion will be overlooked.

"At some stage I would be pleased to talk to the G.M.S. Committee either about the work of the Planning Unit in general, or, if this were considered too diffuse, about the particular approach of the Working Party on Primary Medical Care. However, I really feel there is nothing I can say now in this last connexion that would amount to more than the facile generalizations with which we are all too familiar. When we have got our teeth into the problem I think it would be worth while talking to your committee and to sound its opinion about the various aspects of the problem we are investigating."

Brick by Brick

Dr. RONALD GIBSON, Chairman of Council, pointed out that the Planning Unit was not a committee of the Association. It had been thought that the Association's committees were so overburdened with current work that they might not have the time to look to the future. They had been caught out on this in the past and had been criticized for it. It was hoped that any committee of the Association, or the Council, or the Representative Body would commission the Planning Unit to examine subjects which were of importance or to deal with a section of that subject. The Planning Unit would give the committee its views resulting from its detailed study. In the case of primary medical care the working party and the Planning Unit would go through their project brick by brick and build up the structure of the Health Service. The G.M.S. Committee would be free to comment in any way it wished on the Planning Unit's report when it was published.

When Professor Miller had used the word "independent," he meant that he wished to be independent of any committee of the Association, said Dr. Gibson. If the G.M.S. Committee asked for representation on the Planning Unit then the Central Committee for Hospital Medical Services and the Public Health Committee would want representatives, and the unit would become another B.M.A. committee. If the Association was not seen to be doing this kind of future planning the Ministry or another association or college outside the B.M.A.'s control would do it.

Dr. CORMACK said that the Planning Unit, with Professor Miller as its director, had been appointed and the B.M.A. had to accept the consequences. One consequence was that it had "a tiger by the tail," with all the difficulties which ensued when it might want to let go. Professor Miller was a radical thinker. For him to direct a planning operation for what was perhaps a rather conservatively minded profession was bound to cause misgivings to some people. Dr. Cormack said there was a good case for setting up a planning unit—the old Amending Acts Committee had been a good example of how ineffective a committee of the Association could be in planning work. He thought it would be a mistake for the G.M.S. Committee to appoint anyone to the working party. It was better that the Committee's point of view should be heard, and then they should leave it to the working party to get on with their

planning. He was sure that Professor Miller would give good reasons for any recommendations he made. Though the Planning Unit's report should be published, the B.M.A. committees concerned should be allowed to publish their own commentary at the same time.

Prejudging Issues

Dr. J. E. MILLER said he did not cavil at the appointment of a radical thinker as director of the Planning Unit. However, it should not be forgotten that the unit had been established by the British Medical Association and its activities would be seen as representing the views of the B.M.A. Some of Professor Miller's pronouncements, particularly about general practice, had already been taken to represent the views of the Association. Dr. Miller said that he knew the Planning Unit had been set up as an independent body, and as such ought to be allowed to do its work and to publish its results, but when pronouncements made by its chairman seemed to prejudice issues before the unit had done its work and seemed to represent a contrary view from that held by the vast majority of members of the B.M.A. "we should reconsider our position." He thought it was "highly improper" that at such an early stage in the activities of the Planning Unit statements should appear which in effect were an attack on general practice as it was today and the possibility of general practice in the future. "We must call a halt, because the periphery will ask 'Is this the view of the Association?' . . . Professor Miller and the members of his unit should hold their tongue on the views which they hold until such time as they have analysed the situation and provided a report which can be balanced by the views of the various committees which they are asking for information from."

Spawn a Monster

Dr. H. S. HOWIE WOOD said that the Chairman of Council had told the Committee about bricks being used to build up a new structure. He (Dr. Howie Wood) would like an assurance that that would not be brought about by pulling down the brickwork of "our old established structures. One can be destructive or constructive. I am sure that the Chairman of Council knows his man, but it is possible to spawn monsters. There is just the possibility that the B.M.A. will get more than it bargained for if we do not have an assurance that any report will come to us before it ever reaches the outside world."

Dr. ALEXANDER said he was "disappointed and disheartened." This was a Planning Unit of the B.M.A. and was financed by it. It would have the imprint of the Association, and such reports as were printed would be quoted as Association policy. "We are the primary physicians; we are the people responsible for and entrusted with primary medical care in this country; we are the people who should be represented on this working party. I do not think we should have anything to do with the Planning Unit until we are represented on the working party. We have been speaking in metaphors—it is possible to put tigers in cages."

Dr. COOK said that he was unhappy about the working party. The chairman was a woman of experience. The doctors on it were

in the early years of their professional life. There ought to be a general practitioner on the working party who had spent many years in general practice. It was not entirely correct to say that if the G.M.S. Committee was represented other committees should also be represented, because primary medical care specifically concerned general practitioners.

Dr. RIDGE said that to make projections based on ascertained facts and to devise a plan to deal with an expected situation was a scientific process, and it was proper to employ a scientific method of planning. In that context a planning unit of the type set up was appropriate to the British Medical Association. However, primary medical care was not a subject which was wholly scientific. There was still a not inconsiderable element in it which was art, and the development of an art could not be planned. The Fraser Working Party had come to the conclusion that the doctor-patient relationship could not be evaluated. It was a question of art and not of science. General practice developed in response to the demands of its clients.

Preconceived Views

Dr. SPEAKMAN was confident about the future for general practice, but he was afraid that any preconceived views of the director of the Planning Unit, of whatever good intent, would filter through as the views of the B.M.A. Public opinion was formulated in a subconscious way. Something said often enough began to be believed. Professor Miller should not make any public statements before the official report of the Planning Unit had been published.

Dr. A. ELLIOTT said that primary medical care was exercising the minds of doctors all over the world. He looked forward to the publications of the Planning Unit, so long as the G.M.S. Committee was not committed to the unit's views. The Committee must reserve the right to examine any of the unit's reports.

Dr. E. TOWNSEND said: "I have listened to the debate with some dismay. We have in our wisdom in the Association decided to have a planning unit. We have appointed a very well-known, perhaps controversial, figure, and given him a job . . . let him get on with it and let him see what he can do. We have been accusing him of prejudging the situation, yet we have proceeded to prejudice him here. If you read his letter carefully he says that he is already persuaded that there is a future for general practice and that he thinks that general practice is going to alter along the lines that it is beginning to alter now. . . . Surely none of us thinks that general practice is going to go on in its present form. Our younger colleagues do not think so, and many of our older ones don't. They find it an unattractive branch of the profession. . . . General practice has not caught up with the other services. Here is a man with new ideas, a man with great intelligence, perhaps with advanced views which may not meet with our approval. We should give him our blessing. Let us hear what he has to say and then criticize."

Dr. GIBSON, replying to the debate, said it was unfair to say that Professor Miller was against general practice. He had mentioned polyclinics, and it had been suggested that that was prejudging the issue, but it would be foolish to discuss the future of general practice without discussing the possibility of polyclinics—if only to get rid of them. He agreed that the G.M.S. Committee must not be asked to commit itself to the views of the working party. The Planning Unit was not a policy-making body: it investigated, and it produced its views.

The Committee agreed that Mrs. Jefferys and Dr. D. H. Irvine, a member of the working party, should be asked to meet the G.M.S. Committee's Planning Subcommittee in the first instance, and that later Professor Miller should be invited to meet the G.M.S. Committee.

Drugs Legislation

The Committee considered the Government's White Paper on the forthcoming legislation on the safety, quality, and description of drugs and medicines (*B.M.J.*, 16 September, p. 734).

Dr. RIDGE explained that the two particular issues which concerned the Committee were the procedure to be adopted before a drug was licensed for sale or supply and the procedure for issuing licences. The Sainsbury Committee had recommended the setting up of a medicines commission, and this was in line with the B.M.A.'s evidence. The Sainsbury Committee recommended that the examination of a preparation for efficacy, toxicity, and safety should be the function of the medicines commission, with advice from expert bodies. The White Paper reserved to the Ministers both the power for making regulations relating to the preliminary stages and the power to issue, withhold, or withdraw licences for preparations to be sold or supplied.

Dr. Ridge said that this raised the question of interference with the freedom of general practitioners to prescribe any preparation which they thought necessary for the treatment of a patient, because the Ministers

would have powers which could conceivably prevent the introduction of a new preparation, prevent its availability for supply, and, even more seriously, they could do a retrospective examination at a later date of any preparations currently in use.

Much would depend, said Dr. Ridge, on the membership of the medicines commission and the expert committees. It was suggested that some 20 organizations should be consulted about the membership of the medicines commission. The B.M.A. would be lucky if it got two members and might get only one, who might or might not be a general practitioner. He would have to battle against some high-powered members in the pharmaceutical field on whether a drug should be available for use by general practitioners.

The most important aspect was who had the statutory power. The Minister of Health was a principal consumer of the drug industry's products. On many occasions in the past Ministers had wanted to exercise control over prescribing. The Minister could, under new legislation, use his powers under licensing or in the preliminary stage, to influence the drug bill in the National Health Service. It might be proper for him to do

this provided his actions were dictated solely by scientific evidence.

Dr. Ridge hoped the Committee would express to the Council its disquiet that the Minister of Health should be the Minister responsible for licensing in relation to new preparations, and at a later date for licensing in relation to all preparations currently in use.

Bureaucratic Machine

Dr. S. WAND said that the White Paper envisaged an enormous bureaucratic machine. Paragraph 16 of it stated: "If the Commission wished, as it well might, to recommend the appointment of separate expert committees for human drugs, for veterinary aspects, and for devices it would be able to do so. It would be open to it to recommend to Ministers the names of persons knowledgeable in the relevant field, whether members of the Commission itself or not, who would in the opinion of the Commission be suitable for appointment to particular expert committees. After considering the Commission's advice and consulting appropriate organizations the Ministers will set up expert committees undertaking function or groups of functions." It was the work of those committees that might affect general practitioners, and it was there that they should have adequate representation. The Commission was likely to accept the advice of its committees.

Dr. MORGAN WILLIAMS said that the Sainsbury Committee had recommended that the medicines commission should be independent. He did not see how a body appointed by the Minister could be considered to be independent. The National Formulary Committee was independent, and he hoped the G.M.S. Committee would suggest that the National Formulary Committee should remain. Dr. Morgan Williams also deplored the haste with which legislation was being rushed.

Adamant Against Advice

Dr. ROSE said it had been urged upon the Minister that he should not be the licensing authority, but he had been absolutely adamant and would not accept that the medicines commission should do the licensing. There were safeguards in regard to licensing. The Minister would not refuse a licence unless he had referred it to the expert committee for its guidance, but it was possible that in an emergency he might be able to refuse to grant a licence.

Paragraph 53 of the White Paper stated that the Minister of Health would have statutory power to prohibit the sale or supply of a drug. That could apply to a drug like heroin. The profession ought to oppose this; reference should be made to the Royal College of Physicians and the B.M.A. when any prohibition of any drug was suggested. Paragraph 72 stated that enforcement in relation to hospitals and similar institutions and in relation to general practitioners would not be delegated. Did that mean that inspection would be done by doctors from the Ministry? Paragraph 74 stated: "Provisions requisite for the purposes of enforcing the legislation will be included—for instance, right of entry and inspection, the procuring, by purchase or on reasonable payment, of samples, the production of appropriate books and documents, the seizure and holding of articles liable to forfeit under the Bill and documents relating to them which may be required in proceedings." The G.M.S. Committee should see to it that the general practitioner's interests were safeguarded.

Authorization

Dr. D. L. WILLIAMS said that the proposals were authoritarian in the extreme. It was said that there would need to be a large increase in Civil Service staff. The proposals gave the impression that the Minister would be able to determine the rate of growth of the

pharmaceutical industry. That was alarming, because the progress of medicine in this country had been restricted by lack of money, yet now the Ministry was being given the responsibility for the growth of the pharmaceutical industry.

Dr. WILLIAMS said his second worry was that the medicines commission would be the principal source of information about drugs. That was control of scientific information, and it was a terrible thing. If its pronouncements were cautious they were valueless: if they were controversial they would give to the opinions of the commission the appearance of being "instant truth."

Dr. FULTON quoted from a letter from the Ministry of Health of 20 October: "The White Paper proposed that the commission should be a professionally independent body exercising mainly advisory functions." That was rather less than the truth. The White Paper actually said that the commission would be appointed by the Ministers after consultation with the appropriate organizations, and later that the Ministers would set up expert committees after considering the commission's advice and consulting appropriate organizations. The bodies were actually being set up by the Ministers. It was important that this statement in the Ministry's letter should be challenged, because it was untrue.

The Committee decided to recommend that the Chairman of Council should be asked to lead a deputation to the Minister without delay to put all the points which had arisen. The Minister should also be asked to restate the assurances which had been given by his predecessors on the general practitioners' freedom to prescribe, subject to the safeguards which had already been agreed.

Remainder of Business

It was decided to postpone considerations of other items on the Committee's agenda until a special meeting on 7 December.

Advanced Specialty Training Courses

A scheme has been agreed by the Ministry of Health and the British Postgraduate Medical Federation to provide selected courses of advanced specialty training for up to 50 hospital doctors at a time. Some of the places will be allocated to doctors from Scotland. The Central Committee on Postgraduate Medical Education (the Aitken Committee) has commended the scheme.

The courses will be at "post-membership or fellowship level," but will not be directed at the fellowship or membership examinations. They will usually last about ten weeks and are intended to assist doctors who have qualified in the United Kingdom and who are undergoing specialist training. The Ministry of Health, in a letter to senior administrative medical officers and secretaries of hospital boards and committees, has stated that attendance at the courses should be regarded as study leave, and hospital boards will be repaid the cost. This will include payment of the trainee's expenses, including the fee for the course, and the cost of a locum tenens when necessary.

Hospital boards will be notified in the autumn of each year of the courses being organized for the year beginning the following April, and they will be expected to tell the appropriate staff.

In making its selection from applicants for the courses the Federation is to give preference to: (1) doctors who have their membership or fellowship; (2) senior registrars approaching consultant posts whose training has omitted important clinical experience or who wish to develop a line of interest; (3) senior registrars in hospitals with restricted range of educational opportunities; (4) consultants who have not had the opportunity for systematic revision of the theoretical basis of their practice, or wish to expand their knowledge in some branch; (5) doctors in understaffed specialties; and (6) doctors returning from overseas or tropical service secondments.

The Ministry hopes that after a time courses may be arranged in centres and institutes other than those comprising the British Postgraduate Medical Federation.

Educating the Public

The Minister of Health is to continue this winter the campaign to educate the public in the use of doctors' services. A Ministry circular states that the Minister "considers it important" that the appeal to the public and the information in the campaign literature should be "pressed home." The continued co-operation of television authorities has been asked for, and leaflets, posters, and stand-up cards for surgeries have been reprinted.

Medical Charities

The Association's Charities Committee is to launch a "medical charities year" as soon as is practicable in aid of the Sir Charles Hastings Fund, the Dain Fund, the Royal Medical Benevolent Fund, and the Royal Medical Foundation of Epsom College. The appeal to begin with will be only to members of the medical profession. An appeals sub-committee will have the help of a paid whole-time organizer in managing the appeal.

It was also decided to rename the Contingency Fund, one of the B.M.A.'s charitable funds, the "Kate Harrower Contingency Fund." Dr. Kate Harrower, who died in 1966, bequeathed £200 to the Charities Trust Fund.

Dr. R. Cove-Smith is the chairman of the Charities Committee.

Medical Assistants

Medical assistants in Northern Ireland have formed a "Northern Ireland Medical Assistants Group," with Dr. Daniel C. S. M. McAlister, Belfast, as its chairman, to consider the problems of the grade which are causing concern, including the term "assistant."

When the grade was first introduced in the United Kingdom many doctors objected to the title "medical assistant," and the Ministry of Health and the Joint Consultants Committee agreed that posts should be advertised as "Assistant in (specialty)." The Central Committee for Hospital Medical Services has since supported a proposal that the new title for the grade should be "Assistant Grade," and that individual doctors should be known as "assistant surgeon," "assistant physician," etc. (*Supplement*, 15 July, p. 67). The C.C.H.M.S. has also set up a working party, with Dr. G. E. Owen Williams as chairman, to consider the particular problems of medical assistants and how they should be represented (*Supplement*, 4 November, p. 30). Mr. J. P. Capel (Bristol) has been appointed to the C.C.H.M.S. to represent medical assistants.

Hospitality

An Italian doctor living in Naples would like his son aged 19 to stay with a British medical family on an exchange basis from 20 December to 15 January 1968. The doctor has seven sons aged from 22 to 6 years.

A French doctor living in Octeville (Manche) would like his 14-year-old daughter to stay with a British medical family living in or near Southampton from 20 December for six weeks as a paying guest. If a paying guest arrangement is unsuitable the doctor will receive in exchange a British girl of similar age during the Easter holidays.

A French doctor living in Brunoy (Seine-et-Oise) would be pleased to receive a British doctor's daughter aged about 14 during the Christmas holidays. In exchange he would like his own daughter aged 14 to stay with the British medical family during the summer holidays.

A French doctor living in Pontivy (Morbihan) would like his 21-year-old daughter to stay *au pair* with a British medical family living in London from January 1968 for 12 months.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

Was it a Drug?

Regulation 16 of the National Health Service (Service Committees and Tribunal) Regulations, 1956, provides that when a practitioner prescribes under the National Health Service preparations which are not drugs or medicines, and therefore outside the scope of the Act, the executive council may recover their cost from him. If he challenges the council's action the matter may be referred to the local medical committee. Either party or, the Minister can appeal to a referee or referees against the local medical committee's decision.

The referees on each occasion are appointed by the Minister of Health. They must not exceed three in number, and they must not be officers of the Ministry of Health. At least one must be a general medical practitioner. In practice the number of referees appointed has usually been three. The chairman has been a layman with legal training, and his two colleagues have been general practitioners selected from a panel chosen by the General Medical Services Committee of the B.M.A.

The findings* of the referees in some recent appeals under the regulations are reported below. The decisions in these, as in all cases, are related only to the circumstances of the particular cases, and are not binding on referees who may hear other cases.

Chiron Deodorizing Cleanser

The referees considered a case in which Chiron Deodorizing Cleanser had been prescribed for a patient who had had a colectomy for severe ulcerative colitis. On a reference from the executive council the local medical committee had decided that this was a drug which the council was bound to provide.

In their report the referees stated that the cleanser was a cleansing and deodorizing

preparation for use with ileo-colostomy bags. In their opinion it was not a substance which had any pharmacological effect, and they had therefore decided that in this case it was not a drug which the executive council was bound to provide.

ProDermide Solid

The referees also disagreed with the decision of a local medical committee in a case where six tablets of ProDermide Solid had been prescribed for a boy suffering from severe eczema. The executive council had appealed to the local medical committee, which had decided that these tablets were a drug which the council was bound to provide.

The referees were of the opinion that the "soap," while being non-irritating to an eczematous patient, was basically a cleansing agent and had no pharmacological action or effect, and they decided that it was not a drug which the executive council was bound to provide in this case.

Totmosol Soap

The referees considered a case in which six tablets of Totmosol soap had been prescribed for a patient suffering from a chronic skin condition. The local medical committee had decided that this was a drug which the executive council was bound to provide.

In their decision on this case the referees stated that "beyond the fact that the patient suffered from what is described as a chronic skin condition, we have no information as to the nature or degree of the complaint save that it resisted all conventional forms of treatment. In the absence of much fuller information as to the circumstances in which the use of Totmosol soap was prescribed in this case, we are bound to decide that this soap was not a drug which the executive council was bound to provide."

* These findings are normally sent only to the interested parties. They are sent by the Ministry of Health to the B.M.J. with all names deleted.

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

- Allen, A. C.: *The Skin*, 2nd edition. 1967.
- Ashton, W. L.: *Human Atheroma*. 1967.
- Berrill, N. J.: *Biology in Action*. 1967.
- Bion, W. R.: *Second Thoughts*. 1967.
- Brown, W. M. C.: *Human Population Cytogenetics*. 1967.
- Cartwright, F. F.: *The Development of Modern Surgery*. 1967.
- Chusid, J. G., and McDonald, J. J.: *Correlative Neuroanatomy and Functional Neurology*, 13th edition. 1967.
- Comfort, A.: *The Anxiety Makers*. 1967.
- Cooper, P.: *Ward Procedures and Techniques*. 1967.
- Copel, S. L.: *Psychodiagnostic Study of Children and Adolescents*. 1967.

- Davis, P. E., and Hershelman, N. V.: *Medical Shorthand*. 1967.
- Davison, M. H. A.: *The Evolution of Anaesthesia*. 1965.
- Dawes, E. A.: *Quantitative Problems in Biochemistry*, 4th edition. 1967.
- Drummond-Jackson, S. L. (Editor): *Intravenous Anaesthesia*, 3rd edition. 1967.
- Fiddle, S.: *Portraits from a Shooting Gallery*. 1967.
- Filley, G. F.: *Pulmonary Insufficiency and Respiratory Failure*. 1967.
- Fish, F.: *Clinical Psychopathology*. 1967.
- Fomon, S. J.: *Infant Nutrition*. 1967.
- Ford, E. B.: *Genetic Polymorphism*. 1965.
- Gardiner-Hill, H. (Editor): *Modern Trends in Endocrinology—3*. 1967.
- Giannestras, N. J.: *Foot Disorders*. 1967.
- Gray's Anatomy, 34th edition. Edited by D. V. Davies. 1967.
- Hartland, J.: *Medical and Dental Hypnosis*. 1966.
- Jeffcoate, T. N. A.: *Principles of Gynaecology*, 3rd edition. 1967.
- Kalmus, H. (Editor): *Regulation and Control in Living Systems*. 1966.

H.M. Forces

A Supplement to the *London Gazette* has announced the following awards:

Territorial Efficiency Decoration.—Lieutenant-Colonel I. W. Pinkerton (now R.A.R.O.), Majors J. L. Butler (now R.A.R.O.), S. M. Frazer, retired, and D. L. Golightly, R.A.M.C.

Surgeon Lieutenant-Commanders J. S. Hales and J. K. Ross, R.N.R., have been awarded the Royal Naval and Royal Marine Forces Reserve Decoration.

Appointments.—Group Captain D. S. Light (radiological duties, Princess Mary's Royal Air Force Hospital, Akortiri); Wing Commander R. C. Robb (to command (with acting rank of Group Captain), R.A.F. Hospital, Changi); Wing Commander J. J. Henry (senior medical officer, Episkopi).

ROYAL NAVY

Surgeon Lieutenant-Commander A. M. MacGillivray has been placed on the Emergency List.

ROYAL NAVAL RESERVE

Surgeon Lieutenant-Commander D. E. R. Richardson has been placed on the Retired List.

The notification concerning Surgeon Lieutenant-Commander R. A. J. Baily, R.D., published in the *London Gazette* dated 4 July 1967, and in the Supplement to the *B.M.J.* dated 5 August, p. 110, has been cancelled.

Surgeon Lieutenant D. M. Jenkins to be Surgeon Lieutenant-Commander.

ARMY

Colonel D. D. Maitland, O.B.E., late R.A.M.C., has retired on retired pay.

ROYAL ARMY MEDICAL CORPS

Majors H. C. Ferguson, W. G. Thomson, R. J. Belas, T.D., and B. P. V. O'Duffy, M.B.E., to be Lieutenant-Colonels.

Major P. A. North has retired, having received a gratuity.

Major J. R. Bannister has resigned his commission.

Short Service Commission.—Captain R. Wilson to be Major.

ROYAL AIR FORCE

Air Commodore A. Muir, C.B., has retired. Squadron Leader J. M. Clifford to be Wing Commander.

Squadron Leaders R. Baird and M. Leahy have been transferred to the Reserve.

Flight Lieutenants I. F. Elliott and N. G. Flanagan to be Squadron Leaders.

Association Notices

Diary of Central Meetings

DECEMBER

- 4 Mon. Scottish Committee for Hospital Medical Services (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
- 7 Thurs. Junior Members Forum Advisory Committee, 9 a.m.
- 7 Thurs. Organization Committee, 10 a.m.
- 7 Thurs. General Medical Services Committee, 10.30 a.m.
- 7 Thurs. Committee on Therapeutic Abortion, 2 p.m.
- 8 Fri. Planning Unit Committee, 5 p.m.
- 12 Tues. Medical Science Committee, 10.30 a.m.
- 13 Wed. Committee on a Cervical Cytology Service, 2 p.m.
- 13 Wed. Journal Committee, 2 p.m.
- 14 Thurs. General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 10.30 a.m.
- 28 Thurs. Central Ethical Committee, 10 a.m.
- 28 Thurs. General Purposes Committee, 10.30 a.m.

JANUARY

- 17 Wed. Annual Meetings Committee, 10.30 a.m.
- 26 Fri. Venereologists Group Committee, 2 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

BIRKENHEAD AND WIRRAL DIVISION.—At Larch House, Clatterbridge Hospital, Thursday, 7 December, 8 for 8.30 p.m., discussion on "The Effects of Drugs on Driving." Speakers: Professor A. Wilson, Mr. Rex Taylor, Major S. J. Harvey, Dr. F. J. Zacharias.

BOURNEMOUTH DIVISION.—At Postgraduate Medical Centre, Friday, 8 December, 8 p.m., meeting to elect representatives.

BRENT DIVISION.—At Commonwealth Institute of the Royal Postgraduate Medical School, London W.1, Tuesday, 5 December, 8.30 p.m., meeting: "Computers in Medicine."

BRISTOL DIVISION.—At University Senate House, Tyndall Avenue, Friday, 8 December, 8 for 8.30 p.m., banquet and ball.●

CAMDEN AND ST. MARLYBONE DIVISIONS.—At Berners Hotel, Thursday, 7 December, 8 for 8.30 p.m., informal Christmas dinner meeting. Speaker, Mr. Lionel Hale. (Followed by election of Camden representatives to Annual Representative Meeting.) Guests are invited.●

CROYDON DIVISION.—At Selsdon Park Hotel, Thursday, 7 December, annual dinner and dance.●

DARTFORD DIVISION.—At Livingstone Hospital, Thursday, 7 December, 8.15 for 8.30 p.m., meeting to elect representative to Representative Body.

DUNBARTONSHIRE DIVISION.—At Canniesburn Hospital, Thursday, 7 December, annual general meeting.

DURHAM DIVISION.—At Lecture Theatre, Postgraduate Medical Centre, Dryburn Hospital, Monday, 4 December, 8.15 for 8.30 p.m., Dr. Christine Cooper: "Developing Child Health Services in Sierra Leone."

EALING DIVISION.—At Mylett Arms Hotel, Greenford, Thursday, 7 December, 8.30 p.m., annual general meeting. Ladies are invited.

EAST HERTS DIVISION.—At Homestead Court Hotel, Welwyn Garden City, Thursday, 7 December, 9 p.m. (approximately), panel discussion: "Drug Addiction." (Preceded by dinner, 7.30 for 7.45 p.m.) Ladies are invited.●

EAST SUFFOLK DIVISION.—At Ipswich Postgraduate Medical Centre, Friday, 8 December, 8.15 p.m., film meeting: "Chronic Bronchitis"; "The Smallest Enemy."

EAST YORKSHIRE BRANCH.—At Royal Station Hotel, Thursday, 7 December, 8 for 8.30 p.m., annual dinner dance.

ENFIELD AND POTTERS BAR DIVISION.—At Academic Centre, Chase Farm Hospital, Wednesday, 6 December, 8.30 p.m., Brigadier R. V. Phillipson: "Drug Addiction." Medical guests are invited.

FERNANAGH DIVISION.—At Imperial Hotel, Enniskillen, Tuesday, 5 December, 8.30 p.m., meeting, (1) election of representatives to Representative Body; (2) film strip: "The 50,000 Years War."●

FURNESS DIVISION.—At Old England Hotel, Bowness-on-Windermere, Friday, 8 December, 8 for 8.30 p.m., annual dinner dance.●

HARROW AND HILLINGDON DIVISION.—At Whittington Hotel, Cannon Lane, Pinner, Tuesday, 5 December, 8.45 p.m., Lord Moran: "The Life of Sir Winston Churchill."

HAVERING DIVISION.—At Harold Wood Hospital, Sunday, 3 December, 10.30 a.m., annual clinical meeting.

LANCASTER DIVISION.—At Midland Hotel, Morecambe, Friday, 8 December 8 for 8.30 p.m., dinner dance.●

MAIDSTONE DIVISION.—At Great Danes Hotel, Hollingbourne, Saturday, 9 December, 7.30 for 8 p.m., dinner and dance.●

MEDWAY AND GRAVESEND DIVISION.—At Bull Hotel, Rochester, Tuesday, 5 December, 8.30 p.m., medical films and discussion.

MIDLAND BRANCH.—At University Staff House, Edgbaston, Wednesday, 6 December, 7 for 7.30 p.m., annual dinner, and B.M.A. lecture by Mr. G. B. Spenceley: "South Georgia" (exploration of an antarctic island, with coloured slides).●

NORTH DEVON DIVISION.—Thursday, 7 December, Mr. W. E. Strachan: "Intercranial Haemorrhage."

NORTHERN IRELAND BRANCH.—At Park Avenue Hotel, Holywood Road, Belfast, Thursday, 7 December, 8 for 8.30 p.m., annual dinner dance. Guests are invited.●

NORTH MIDDLESEX DIVISION.—At Committee Room, North Middlesex Hospital, Tuesday, 5 December, 8.30 p.m., wine tasting.●

NORTH NORTHUMBERLAND DIVISION.—At Berwick Infirmary, Tuesday, 5 December, 8.30 p.m., address by Mr. E. L. Farquharson.

READING DIVISION.—At Library, Royal Berkshire Hospital, Wednesday, 6 December, 8.30 p.m., Professor R. B. Duthie: "Musculo-Skeletal Pain" (illustrated).

REDBRIDGE AND STRATFORD DIVISION.—At King George's Hospital, Ilford, Tuesday, 5 December, 8.45 p.m., meeting with Ilford Medical Society. Sir Ronald Tunbridge: "Fashion, Fact or Fiction."

ROCHDALE DIVISION.—At New Outpatient Hall, Rochdale Infirmary, Saturday, 9 December, 7 for 7.45 p.m., annual dinner.●

SALISBURY DIVISION.—At Medical Centre, Salisbury Infirmary, Tuesday, 5 December, 8 p.m., symposium: "Wives' Eye View." (Preceded by buffet supper.)

SCARBOROUGH DIVISION.—At Grand Hotel, Saturday, 9 December, 7.45 for 8.15 p.m., annual dinner.

SCUNTHORPE DIVISION.—At Wortley Hotel, Thursday, 7 December, 7.30 for 8 p.m., annual dinner dance.●

SOUTH BEDFORDSHIRE DIVISION.—At Biscot Mill Hotel, Wednesday, 6 December, 8 p.m., annual general meeting (followed by supper).●

SOUTH STAFFS DIVISION.—At Mount Hotel, Tattenhall Wood, Wolverhampton, Wednesday, 6 December, 7.30 for 8 p.m., supper meeting. Mr. C. Jones (editor of *Express and Star*): "The Press Council."●

STIRLING BRANCH.—At Allan Water Hotel, Bridge of Allan, Wednesday, 6 December, annual dinner and dance.

TORQUAY DIVISION.—At Sun Lounge, Victoria Hotel, Thursday, 7 December, 8.30 p.m., meeting to elect representatives to Annual Representative Meeting followed by B.M.A. lecture by Mr. G. Gorer: "Death, Grief and Mourning—an anthropologist's approach." Preceded by informal dinner, 6.45 for 7 p.m.●

WAKEFIELD, PONTEFRAC T AND CASTLEFORD DIVISION.—At Holmfild House, Wakefield, Wednesday, 6 December, 8 p.m., B.M.A. dinner-lecture by Mr. A. Dickson Wright.

WALTHAM FOREST DIVISION.—At Medical Education Centre, Whipps Cross Hospital, Wednesday, 6 December, 8.30 p.m., Dr. R. S. Francis: "Mycobacteria versus Mankind." (Preceded, 8 p.m., by meeting to elect representatives to Representative Body). Guests are invited.

● Branch and Division Officers Elected

BARNET DIVISION.—Chairman, Dr. R. Clark. Joint Honorary Secretaries, Dr. J. H. Muende, Dr. P. Clark. Honorary Treasurer, Dr. J. H. Muende.

BRISTOL DIVISION.—Chairman, Dr. T. G. F. Hudson. Vice-chairman, Mr. J. Angell James. Chairman-elect, Dr. K. C. P. Smith. Honorary Secretary, Dr. A. J. G. Dickens. Assistant Honorary Secretary, Dr. D. C. Jeffery. Honorary Treasurer, Dr. W. Woolley.

DERBY DIVISION.—Chairman, Dr. K. Gurling. Chairman-elect and Vice-chairman, Dr. D. H. Rhind. Honorary Secretary and Treasurer, Dr. R. A. A. Lawrence. Assistant Honorary Secretary, Dr. J. B. S. Morgan.

British Medical Journal Supplement

LONDON SATURDAY 9 DECEMBER 1967

CONTENTS

Proceedings of Council - - - - -	65	General Medical Council - - - - -	73
Private Practice Committee - - - - -	71	Association Notices - - - - -	74

British Medical Association Proceedings of Council

The Association is likely to have a deficit of £20,000 on its budget for 1968. The inevitable rise in costs increased expenditure at a rate of about £20,000 a year, said the Treasurer, and the deficit in 1969 might well be £42,000. The Finance Committee proposed that the Representative Body should be recommended to increase the subscription in 1970. The Council would not agree on a date for raising the subscription until the Organization and Journal Committees had been consulted. Meanwhile B.M.A. Divisions are to be told what decisions of the Representative Body could not be implemented without heavy cost.

The Minister of Health is to be asked to discuss his proposals for studying the administrative structure of the medical services. A B.M.A. working party is to correlate the views of the standing committees on how to bring the Porritt Committee's report "up to date," and the Welsh Committee's report on a scheme for area health boards in Wales is to be published in January. Professor Henry Miller, chairman of the B.M.A.'s Planning Unit, outlined to the Council how the Unit intended to proceed. A resolution of the Representative Meeting in 1967 instructing the Council to "use whatever method it chooses to prepare an alternative Health Service" was referred to a panel under the chairmanship of Dr. I. M. Jones. It is to have £2,250 to analyse the economics of different ways of organizing medical care. It will give an interim report in 1968 and a full report in 1969.

Public health medical officers have received a firm offer in reply to their salary claims and the Public Health Committee considers it acceptable, but its recommendation that doctors should no longer be asked not to apply for local health authority appointments was amended by adding the words: "provided the Management Side of Committee C agrees that the revised salary scales are operated from 1 October 1966 and that note 3 of paragraph 2 of the appendix to the draft circular be deleted." The Council decided that public health service appointments should continue to appear in the "Important Notice" in the B.M.J.

A meeting of the Council of the Association was held on 29 November. Dr. RONALD GIBSON was in the chair.

The Council received with acclamation a report that LORD ADRIAN, a Gold Medallist of the B.M.A., had been elected Chancellor of the University of Cambridge.

The CHAIRMAN referred with regret to the death of Dr. R. HALE-WHITE, a member of Council from 1948 to 1957. A tribute to Dr. Hale-White was paid by Dr. C. M. SCOTT.

Administrative Structure of N.H.S.

The CHAIRMAN drew the Council's attention to a statement in Parliament by the Minister of Health on 6 November that he was reviewing the administrative structure of the medical and related services (*B.M.J.*, 11 November, p. 367). The Chairman suggested that the Minister's statement might be considered in conjunction with the report on area health boards from the Association's Welsh Committee.

The Minister had announced, said the Chairman, that he had begun a full examination of the administrative structure of the medical services that was needed not only for today but for ten to twenty years ahead. His studies would relate entirely to the administrative pattern. He would not consider the possibility of what would amount to an alternative health service, as had sometimes been suggested, involving, for instance, "a switch in financing from the public to the private sector." The Minister said he would aim in due course, but not for some months, to set out his views as a basis for public discussion and wide consultation. Only after that would the Government introduce legislation, if it were necessary.

The Minister had said that he had told the Royal Commission on Local Government in England and the Seebohm Committee, which was considering the local authority and allied personal social services in England and Wales, that he aimed to have proposals about the administration of medical and related services ready to be looked at alongside their own recommendations. He had also informed the Royal Commission on Medical Education, and he would be keeping in touch with the forthcoming reorganization of local government in Wales.

In reply to Dr. J. S. NOBLE, Dr. D. P. STEVENSON, the Secretary, said that on 21 December 1966 he had informed the Minister of Health of the following resolution of the Council of the B.M.A.: "Council believes that the present method of financing and organizing medical care in Great Britain requires re-examination and reassessment in the best interests of the community, and that it is of the opinion that the Government should be requested to set up immediately an independent inquiry into the finance, administration, and staffing of the National Health Service." The Minister had replied that he had noted the Council's views, which would receive consideration.

Welsh Committee's Views

Dr. A. WESLEY HILL said that the Welsh Committee had received with dismay the Council's decision to refer to the standing committees yet again the Welsh Committee's report on area health boards before allowing it to be published. Those committees had already commented, and their comments had been incorporated in the report. "We cannot go on sending it back in a never-ending process of this kind," said Dr. Wesley Hill. Now that the Minister of Health was about to stimulate discussion on future reforms of the N.H.S., there was a danger that the Welsh report on area health boards would be published too late for the B.M.A. to receive any credit for having itself provoked discussions on those matters.

Dr. Wesley Hill emphasized that the report was on only a pilot scheme applicable to Wales. The Welsh Committee, he said, thought it important that there should be no delay in the publication of its report beyond the meeting of the Council on 10 January, and it therefore recommended that the standing committees should be asked to forward their further views on the report to the Welsh Committee not later than 20 December.

Dr. A. SKENE said there was not much time, and it was probably true that the B.M.A. had no firm policy on the administration and organization of the National Health Service. As a matter of urgency, he suggested that the autonomous committees must grapple with the problem at the earliest opportunity, and that in the light of their views the Council might be able to make some informed representations to the Minister on this matter—a matter which

might concern legislation affecting the practice of medicine in this country for many years.

Dr. R. B. L. RIDGE suggested that before taking any decision the Council should consider why the Minister had made his statement now, when he could have made it any time in the past 20 years. The answer might well be because the Royal Commission and the Seeborn Committee were at work. "If the Minister uses the opportunity to play off the report of one of these bodies against the other, and the Welsh Committee is relying on Ministerial action to forward its particular case, then we may in fact be bogged down worse than ever."

Dr. A. V. RUSSELL said it was difficult to see why the Welsh Committee's report on area health boards should not be published forthwith. Dr. C. C. LUTTON thought that surely it was right that the B.M.A. should attempt to influence the Minister's thinking. The report on area health boards should be published now.

Need for Further Study

Mr. H. H. LANGSTON, Chairman of the Central Committee for Hospital Medical Services, said it would be a mistake to publish the Welsh Committee's report now. It contained matters which his Committee was unhappy about and would wish to study further. The concept of hospital management committees as they were at present constituted was in question, and there were other aspects of the hospital service which were under active consideration. If the report were published as a B.M.A. document the feeling in certain circles would be that the Association was a long way behind in its thinking.

Dr. JOAN CHAPPELL thought that doctors would be encouraged to put forward ideas now that there was a possibility of Parliamentary time being available to consider reforms in the N.H.S. Dr. C. P. WALLACE expressed the view that the Welsh Committee's recommendation that standing committees be asked to give their views on the area health board report not later than three weeks before the date of the January Council meeting was reasonable.

Dr. S. WAND, Treasurer, said that the Association should welcome the Minister's inquiry as a sequel to the Porritt Committee's report. The proposals on administration in the Porritt report could be brought up to date, and that could be done while the Minister was doing his review. When the Minister's paper was published the Council could debate it with up-to-date knowledge. Dr. J. L. MCCALLUM pointed out that for the first time the Association had been first in the field and ahead of the Ministry by some five to six years.

Dr. SKENE suggested that the Welsh Committee's report on area health boards might prove, after full discussion by the autonomous committees, not to be the sort of lead that the B.M.A. on mature reflection would wish to give. The fact that the Minister had said he would produce a paper was not an indication for the Association to panic and to take precipitate action.

The CHAIRMAN suggested that the Council might consider the following courses of action. Firstly, the Minister should be asked for immediate consultation on his statement, and that the Association might be brought in

on any policy which he proposed to set out in his paper. Secondly, that a working party should be set up to bring the report of the Porritt Committee up to date and to correlate the views of the standing committees. Thirdly, that the Association's views on area health boards, as submitted by the Welsh Committee and commented on by the standing committees, be published for discussion in January.

Dr. J. E. MILLER said he thought it would be better for the Welsh Committee's report on area health boards to be published before discussions were held with the Minister. Dr. I. M. JONES agreed with Dr. Miller. He also suggested that the Council should support the Minister in asking for an inquiry, but, at the same time, should insist that it was not the usual type of interdepartmental inquiry. It should be an inquiry conducted by a completely independent and authoritative body.

Dr. J. S. ROSS said it was important that the medical profession should consult the Minister forthwith to find out what was really in his mind, and, at the same time, feed into him certain ideas which it was hoped he would accept. Once the Minister had published his paper it would be more difficult to shift him away from his proposals, even though they might be only for discussion.

Demand for Inquiry

Dr. NOBLE moved and Dr. Jones seconded: "That the Council welcomes the decision of the Minister to study the administration of the National Health Service. It is, however, concerned at the mode of approach outlined by the Minister and repeats its demand for an inquiry to cover the whole field of finance and administration of the National Health Service, and that

it be considered by an independent body."

Dr. Noble said that after twenty years the N.H.S. was ripe for a full inquiry. The profession, in the last year or two, had come near to having more clear ideas on what the Health Service might look like in the future. He believed that the financing of the N.H.S. could not be separated from its administration. Dr. A. N. MATTHIAS, Chairman of the Representative Body, supported the motion. He said that the Minister's reference only to administration was a clear negation of the resolution which was passed by the Council in 1966.

Dr. STEVENSON pointed out that there was a risk that an independent inquiry would not be by a body of doctors. It would be an inquiry in which the point of view of doctors would play a minor part, because it was an administrative rather than a clinical matter. Also an independent inquiry would probably take two years. In Dr. Stevenson's view it would be preferable to see the Minister first and to ask for a discussion on all the relevant matters.

Dr. R. COVE-SMITH and Mr. LANGSTON supported Dr. Stevenson.

The motion was lost.

The Council finally agreed that the Minister should be asked for an opportunity for representatives of the profession to discuss his proposals with him. It was also agreed that a working party should be appointed to bring the report of the Porritt Committee up to date and to correlate the views of the standing committees. The members of the working party would be appointed by the Chairman of Council in consultation with the three standing committees. It was agreed, thirdly, that in January the considered views on area health boards submitted by the Welsh Committee and commented on by the standing committees should be published for discussion.

Association's Finances

Dr. S. WAND presented the report of the Finance Committee and drew the Council's attention to the financial situation of the Association. The recent devaluation of the currency had greatly affected the B.M.A.'s budget for 1968. It was expected that devaluation would increase the deficit on the Secretariat's budget by £8,000, making a total deficit of £20,000 for 1968.

Each year, said Dr. Wand, because of the inevitable rise in cost of essential services, the Association's expenditure increased. Based on experience in the past it was estimated that the deficit of £20,000 in 1968 might well become £42,000 in 1969. The Finance Committee felt strongly that much greater regard must be paid by the Representative Body to the costs of carrying out some of its resolutions.

Proposals for Subscription Increases

The Finance Committee had considered the view of the General Purposes Committee that an increase in subscription rates had become inevitable, and that a recommendation should be made to the Representative Body in 1968. The Finance Committee concurred that an increase was inevitable, but had serious reservations on its timing. The full effects of devaluation would not be known until the latter part of 1968. It was

desirable that members should know of the Association's worsening financial position and be given ample warning of Council's intentions. It was also right that the Council should have an opportunity of re-examining current expenditure before going forward with specific proposals for an increase in subscription rates. For those reasons the Finance Committee was unanimously of the opinion that 1969 would be the right time to make firm proposals to the Representative Body for an increase in the subscription.

The Finance Committee proposed that a recommendation should be submitted to the Representative Body in 1969 for an increase in the membership subscription rates to take effect on 1 January 1970, and that in drawing up the new scale of subscriptions particular consideration be given to those members paying the concessionary rates. It further proposed (1) that Divisions should be informed of the decisions of the Representative Body that could not be implemented without incurring heavy costs; and (2) that steps should be taken to inform members of the financial position and of the likelihood that the membership subscription might have to be increased.

Mr. LANGSTON asked why the Treasurer did not recommend an increase in subscriptions for 1969. Dr. RIDGE said he was concerned at the proposal to budget for a deficit. It

was apparent that there must inevitably be an economic blizzard. If the Association carried forward a growing deficit members would be faced not with a moderate increase in subscription in 1969 or 1970 but with a massive increase. To defer the increase for a year seemed to be a policy of despair.

Dr. WAND, in reply to Mr. Langston, said that the Finance Committee did not know yet how much more money the Association would want. To ask for an increase in subscription that would allow for the possible effects of devaluation and would avoid the need to ask for a further increase in another year or two would mean asking for a big increase. By 1970 a big increase might still be needed, but it would at least be done in one go.

Pay for Work Done

Dr. LUTTON maintained that the Association would have to spend more money in some sectors and less in others. It should spend more on information. It would have to decide what was essential activity. Members would pay according to what they saw was being done. The expansion of the Association's work had to go on, and it was up to each member of Council to ensure that the members in his area knew of the work being done in B.M.A. House. Dr. Lutton suggested that the subscription should be raised in 1969.

Dr. JONES supported the comment of the General Purposes Committee and opposed the recommendation of the Finance Committee to defer an increase in subscriptions till 1970. He recalled that on each of the last two occasions when the subscription was raised the Council had followed the policy being advocated by Dr. Wand. The Council had allowed the Association to go into the red before action was taken. By the time the new subscription rates came into effect there would be a substantial backlog to make up. No one could foresee the reaction of the Representative Body to any recommendation, but that did not excuse a failure to recommend what was clearly right. If the Representative Body were informed of all the facts and was assured that priority would be given to those Association activities which were concerned with direct service to its members it was doubtful, said Dr. Jones, whether its reaction would be very different in 1968 from what it would be in 1969.

Dr. R. P. HENDRY recalled that when the subscription had been increased from 4 to 6 guineas it had taken a long time before the United Kingdom membership recovered to what it had been before the increase. With a drop in membership there was also a loss of prestige. Full reasons must be given for any increase in subscriptions.

Dr. ROSS said that the Association was still not in a position in which the profession was as keenly behind it as it should be, and it was necessary to improve the information services. Furthermore, it had to be remembered that it was what the Association did that mattered. The individual doctor took the view that far too much money was spent on things that did not really matter. The Association's activities should be gone through with a fine toothcomb to see which things could be dispensed with in order to save money. The effects of devaluation could not be judged, and Dr. ROSS advised the Council to wait for a few months before

deciding to make a firm recommendation to the Representative Body next year to increase the subscription.

Dr. WALLACE supported the Treasurer's view. Dr. Wand was well aware of the repercussions that an increase in subscription might have, and there was much to be said for choosing the right moment.

Many members of the Association were ill-informed. But that was not the Council's fault. In Dr. Wallace's view it should call a halt to any increase in information services. "Many of us are suffering from having more information than we can digest," he added. "The B.M.A. is not a business organization. It is a scientific body with a medico-political side to it." In Dr. Wallace's opinion it was a mistake at the present juncture for Council to tie itself to a decision on what it would do the year after next.

Cut Costs

Dr. G. E. CRAWFORD asked whether the Finance Committee had considered sending a questionnaire to each member of the Association setting out the plain facts, and asking whether the member would prefer an increase in subscription now or a larger one later. Mr. G. E. MOLONEY said there was nothing wrong in expanding the B.M.A.'s activities, but now everybody had to cut their costs, including the B.M.A. Serious consideration had to be given to the question of raising subscriptions at a time when the periphery would expect it.

Dr. H. FIDLER suggested that the B.M.A. subscription was ridiculously low. Members were getting all the benefits of membership on the cheap. If the members were not aware of those hard facts they ought to be told. But if it were thought that no rise in subscription could be suggested in the near future Dr. Fidler suggested that consideration should be given to asking members whether they would be willing to pay a voluntary levy, because of the great change in the financial circumstances.

Dr. NOBLE stated that the membership drive was beginning to show results. Members would pay for service, and the Organization Committee had always held the view that the membership depended on the Association having positive policies and "propagating them with force." The Organization Committee thought that it would be disastrous to increase subscriptions unless greater efforts were made than at present to let the profession see that not only was the B.M.A. acting for it but was actively doing something for it. Dr. Noble pointed out that his Committee had not been informed of the recommendations of the Finance Committee, and he moved the reference back of those recommendations.

Dr. A. C. HOUGHTON said that, in his view, members at the periphery really had very little out of the B.M.A. It was necessary to keep a very careful watch on expenditure. Dr. CATHERINE GRAY said it was essential for members to know why the subscription was being increased. There was a belief that money was rather wasted at Headquarters. Members did not understand what the money was used for, and it would be impressive if they knew that Headquarters was trying to effect some economies. For instance, though the amount involved would be small, Dr. Gray suggested that members

of the Council, of the Representative Body, and of committees might perhaps be refunded only second-class railway fares.

Economies First

Dr. A. M. RANKIN suggested that it would be bordering on madness to increase the subscription. Every member he had spoken to on the subject considered that 12 guineas was about the limit to which they would go. It was clear that the subscription would need to go up at least to 20 guineas, and members would not be willing to pay that. The Association had not been able to get for general practitioners all that had been hoped for. Hospital junior staff were in a state of revolt, and provincial consultants would be the next. In Dr. Rankin's view any increase in subscription now would lead to a great loss of members. The Association would be weakened, and, since it was the only body which negotiated with the Government, the whole profession would suffer. He was opposed to any increase in the subscription until such time as economies which had been suggested from time to time had been effected.

Dr. J. M. DUNLOP suggested that subscriptions to the Defence Trusts should be compulsory and be part of the Association's annual subscription. Shortly there was likely to be an increase in the retaining fee of the General Medical Council, and it might be possible to add that fee to the annual subscription to the B.M.A., and the B.M.A. could then take over the G.M.C. That would then mean 100% membership of the B.M.A.

Dr. R. E. W. OLIVER said that the subscription should be increased, because psychologically it was the right time and members expected it to be increased, and because the Council should have enough confidence to decide what the Association's policy should be, to go out and sell it, and to make sure doctors realized that they were getting value for money.

Dr. WAND said that the Association had certain reserves which provided it with a substantial part of its income. Nevertheless, these were exceptional times and reserves were for use in exceptional times. It was important to let members know that events had overtaken the Association financially and that they must be prepared for some increase in subscription. Dr. Noble had made a valid point when he had said that the Organization Committee had not been consulted. Indeed, said Dr. Wand, the Journal Committee might have views on the subject. Therefore he suggested the following revised form of words for the Finance Committee's first recommendation: "That the Council supports that a recommendation be submitted to the Representative Body in 1969 for an increase in the membership subscription rates to take effect on 1 January 1970, and that in drawing up the new scale of subscriptions particular consideration be given to those members paying the concessionary rates, and that this be referred to the Organization Committee and to the Journal Committee for their consideration."

Dr. NOBLE accepted the revised wording of the recommendation, but Dr. RIDGE moved the reference back of Dr. Wand's revised recommendation. Mr. MOLONEY seconded the reference back.

Dr. RIDGE explained that he moved the

reference back on the ground that the Council was not satisfied that 1 January 1970 was the optimum date for the increase in the subscription.

The reference back was carried.

It was agreed that the recommendation should be sent to the Organization Committee and the Journal Committee for their expert opinion.

The second recommendation of the Finance

Committee, (1) That Divisions should be informed of the decisions of the Representative Body which could not be implemented without incurring heavy costs, and (2) that steps be taken to inform members of the financial position and of the likelihood that the membership subscription might well have to be increased, was adopted.

The report of the Finance Committee, duly amended, was adopted.

Planning Unit

The Council proceeded to consider a report prepared for the Planning Unit by its Working Party on Intensive Care, and a report on the activities of the Planning Unit.

The CHAIRMAN informed the Council that Professor Henry Miller, the Chairman of the Planning Unit, would be attending the meeting later in the day. The Unit was not prepared to come to any conclusions after a hurried and superficial investigation into the Health Service. The Unit's idea was, as he had explained to the G.M.S. Committee (*Supplement*, 2 December, p. 60), to go through its project brick by brick to build up the structure of a health service. The Unit had begun to study the question of primary medical care. The £10,000 set aside by the Association for planning included the cost of staffing the Unit.

The Chairman drew the Council's attention to the report of the General Purposes Committee, in which the particular position of the Advisory Panel under the chairmanship of Dr. I. M. Jones was pointed out. The Planning Unit had felt unable to accept Dr. Jones's Advisory Panel as an integral part of the Unit. It seemed to the General Purposes Committee that the Council might well consider it appropriate to refer the following resolution of the A.R.M., 1967, to Dr. Jones's Panel, but, in view of the present financial position, the Committee did not consider it would be justified in authorizing the additional sum of £2,250 asked for by Dr. Jones's Panel to carry out the task:

"That the results of the recent negotiation with the Ministry of Health have done little to alter the deficiencies of the National Health Service, the majority of which stem from the inadequate finance which is available at present, or will be available in the future from direct taxation. The Annual Representative Meeting instructs Council to use whatever method it chooses to prepare an alternative Health Service. That this alternative shall be presented with adequate time for discussion by the profession before the Annual Representative Meeting as soon as possible."

The General Purposes Committee recommended that the resolution be referred to Dr. Jones's Advisory Panel, but that he be asked to prepare an interim report for consideration by the Council and the Representative Body within the limits of the existing resources of the Association and without embarking on the economic research which was proposed.

Alternative Service

Dr. A. V. RUSSELL said that the Planning Unit had developed into something completely different from what had been envisaged by the Representative Body when it asked for something to take the place of the former Amending Acts Committee. The Unit seemed to be working in an extremely rarefied atmosphere, and many of its activities appeared

to be of an academic nature. There was no sense of urgency that could be detected. Furthermore, the Unit did not seem to be keen on the idea that Dr. Jones's Panel should get to work on what the Representative Body asked for as a matter of some urgency—namely, the framing of a desirable alternative medical service.

Dr. J. BENYON said he disagreed with the General Purposes Committee's recommendation. In his view every effort should be made to find the £2,250 required for Dr. Jones's Panel to get on with the job that most members of the Association imagined was being done. Dr. RIDGE suggested that it was extraordinary that the argument used by the Chairman of the Planning Unit, Professor Henry Miller, was that he could not take Dr. Jones's Panel under the Unit's umbrella because he (Professor Miller) did not have the opportunity of selecting the members of the Panel. The Council had been responsible for setting up the Unit, but it had not had an opportunity of expressing an opinion on Professor Miller's appointment nor on the members of the Unit which he had selected.

Dr. MARY ESSLEMONT pointed out that though there was one woman doctor on the Unit there did not appear to be any women doctors on the working parties it had set up. According to the report on the activities of the Unit, B.M.A. Divisions and Branches had been invited to nominate one of their younger doctors who had a special interest in "looking ahead" to act as liaison officer with the Planning Unit. Dr. Esslemont said she had no knowledge of any such invitation being received in her area. Referring to the Unit's report on intensive care, Dr. Esslemont suggested it was lamentable that such a report should be produced when there were other more important basic problems to be dealt with.

Dr. W. H. N. ANGUS asked what was meant by an "alternative service." Did it mean the eclipse of the N.H.S. and its replacement by a private service, or did it mean an alternative National Health Service? If it meant the former then Dr. Jones's Panel was probably the right body to look into it. If it meant an alternative National Health Service, differently financed and differently administered, then he could understand Professor Miller's objection to Dr. Jones's Panel going beyond a certain limit.

Fogging the Issue

Dr. NOBLE referred to the report on Intensive Care, and said it did the Association great credit. At the same time the Planning Unit was proceeding with other matters. The Council would fog the issue if it criticized either Dr. Jones or Professor Miller. The Association could gain something from Dr. Jones's Panel and from Professor Miller's

Unit. "If this Association instead of looking at this narrowly looks at it in a big way, we can do a great deal of good for British medicine," Dr. Noble said. "I hope Council will ensure that both units continue to carry out the wish of the Representative Body."

Dr. C. M. SCOTT suggested that the type of thing coming from the Planning Unit was not the real bread-and-butter stuff that the Association hoped to see. The Unit, though undoubtedly first-class, would not produce the type of report that the general practitioners wanted.

Dr. G. R. OUTWIN supported Dr. Noble and refuted the comments made by Dr. Mary Esslemont about the report on intensive care. It was important that some authoritative document should be published at a time when so few hospitals were being built.

Dr. WALLACE said that he had no doubt that the Guildford Division, from whom the resolution emanated, meant an "altered" National Health Service. The Guildford Division was aware that the National Health Service brought into being in 1948 was based on a set of circumstances that existed in 1930, and that since then the affluent society had arrived. In his view the matter would be best answered by having a report from Dr. Jones's Panel. Dr. Wallace said he supported the recommendation of the General Purposes Committee.

Dr. OLIVER said it would seem that two planning units were required, one to deal with the scientific and the other the political work. Professor Miller's Unit could look after the scientific aspect and Dr. Jones's Panel could look after the medico-political.

Dr. J. C. CAMERON, Chairman of the General Medical Services Committee, said that Dr. Jones had set up his panel in good faith, and the Council should not hamstring him in the work he had set out to do. The G.M.S. Committee had considered the Planning Unit's intention to study the future of primary medical care. Dr. Cameron pointed out that the reports of the Planning Unit would gain currency throughout the profession as being Association policy. That, in his view, was a danger.

When it came to medico-politics the Council should consider carefully whether it was right that reports from a source within the B.M.A. should be published independently. Professor Miller had insisted on the Planning Unit's right to publish its own reports.

Dr. W. T. COOKE said that the report on intensive care was in his view a first-class document. It could be used throughout the hospital service as a far-seeing report. The problem over the next 10 years would be a shortage of doctors, and it was necessary to get the facts. He did not believe that by assessing the existing position it was possible to project into the future, but it was absolutely necessary to have the facts.

Dr. SKENE drew the Council's attention to the following paragraph contained in Appendix IV of the report on the activities of the Planning Unit:

W. S. Lewin said that the Planning Unit, if it was to have any impact, must come to terms with itself. In his view, in the last analysis the really powerful voice to which the Minister would listen would be a powerful independent body, especially if it was seen to have the support of the standing committees. He suggested that if the various working parties of the Planning Unit were to go to the appropriate standing

committees for help and advice then the confidence of these bodies in the Planning Unit would be established.

Dr. CRAWFORD said that if the Planning Unit was to be of any use it must be completely independent, and it was up to Council to point out where it went wrong if it did go wrong.

Professor Henry Miller

At this point the CHAIRMAN introduced Professor Henry Miller to the Council, and invited him to present the Planning Unit's report on intensive care and to speak on the work of his Unit.

Professor HENRY MILLER said that the Council would probably be surprised that the first report of the Unit was on intensive care. The reason why the first two or three reports would be on particular aspects of medical services rather than on major issues was that to offer any worth-while observations on major problems would require the collection of information, the sounding of opinion, and much organization and deliberation. The Unit therefore thought it wise to sharpen its operational teeth on a number of matters which, though not major issues, were of urgency to the Health Service. Intensive care was a good example. Almost all hospital management committees and boards were under pressure to establish intensive-care units, and they could do that on their existing budgets only by depriving their hospitals of some other service. The report was designed to deal with a pressing and urgent situation in furnishing what the Unit believed to be expert advice.

Professor Miller said he did not wish the Council to think that the Unit's efforts would be limited to purely technical matters. A working party was being established to examine the use of computers in medicine. Most people concerned with the employment of computers in medicine were keen that the B.M.A. should undertake a study. It was a topical problem which gave the Unit an opportunity to present something useful while its wheels ground more slowly over issues in which it was more interested—namely, what would happen to general practice, how the hospitals would be organized, and how the kind of hospital that was needed would be provided.

Professor Miller said that the problems of general practice were not specifically problems of the National Health Service. It would be a mistake to call the Unit's working party a working party on general practice. What the Unit was really concerned with was how the need for doctors was to be met. It had to look at various possible ways in which the need could be met and examine their advantages and disadvantages. Professor Miller hoped that it would be possible to collect evidence and to arrange for the conduct of experiments on primary medical care on a modest basis before producing a report.

Association Policy

Dr. SKENE said there was an overlap between the scientific and medico-political fields, and he asked Professor Miller how the Planning Unit, when it entered the medico-political field, would acquaint itself with Association policy in order to avoid publishing a report which might be at variance with established policy.

Professor MILLER replied that the medical members of the Planning Unit were fairly well acquainted with B.M.A. policy. But there were many instances when the Unit would wish to consult the appropriate B.M.A. committee or to submit drafts of the Unit's reports for amendment and comment.

Dr. WALLACE asked whether it would be possible to devise a way for the Council to see the Unit's reports and for commenting on them before publication. The report on intensive care, for instance, was issued as a B.M.A. publication, which meant that the Council must inevitably take some responsibility for it.

Professor MILLER said he was sure that the Unit would be delighted if the Council or committees of the Association debated draft reports of the Unit and made suggestions.

Mr. MOLONEY congratulated the Planning Unit on its report on intensive care. He asked Professor Miller how far he thought the Unit's activities should spread.

Professor MILLER replied that the Planning Unit regularly discussed possible projects. A number of things which the Unit would like to investigate were really beyond the scope of a predominantly professional working party. The Planning Unit itself held a series of meetings on a subject, interviewed people in the field concerned, and tried to get a picture of the type of brief it wished to give to a working party. It then selected the chairman of the working party. The technology of the exercise was carried out by the working party, and it furnished draft reports which were discussed by the Planning Unit. As to the range of subjects covered, it was obviously impossible to cover them all, and only the major subjects could be dealt with. Of those, the first was to be the provision of primary medical care and the second hospital staffing.

In answer to Dr. WESLEY HILL, who asked how the Unit defined the problems in general practice, Professor MILLER said that, as the Dean of a Medical School, one problem he thought arose was the ever-decreasing inclination on the part of medical students to choose general practice. Most of the vocal discontent within the profession came from general practitioners. There were many countries where that situation had progressed to the point where general practice, as it was known in this country, had virtually closed down.

Dr. JOAN CHAPPELL said that the Council was under pressure to provide plans for an alternative N.H.S. It would be useful if Professor Miller could give some idea of the Unit's programme in that connexion.

Professor MILLER said that either the Unit should look at the whole situation and make a general statement or it should divide the problem up. A study of primary medical care was almost bound to bring up questions concerning the organization of the Health Service as a whole, and it was doubtful whether anything worth producing would be produced before another year at the earliest.

Critical Approach

Dr. J. H. LANKESTER suggested that any analysis of general practice should be based on how it was possible to stop existing general practice from degenerating. Professor MILLER said that the Planning Unit did not regard itself as setting out to find evidence to

support either the existing organization of general practice or any potential organization. It set out to look at it critically to see where it could be improved or where it could be maintained. It would be foolish to think there was no alternative to the existing arrangement.

Dr. C. J. BOLT asked Professor Miller whether he felt that young doctors should be represented on all the working parties, and, if so, what steps had he taken to ensure that. Professor MILLER agreed with emphasis that at least half the members should be under 35, and he would try to achieve that.

Dr. RIDGE said he noted that the Planning Unit did not consider that what was called for in the A.R.M. resolution (producing plans for an alternative Health Service) was properly within its terms of reference. It had become apparent in the Council's debate that the significance of the term "alternative" was related to an alternative within the National Health Service itself. In the light of that, Dr. Ridge wondered whether Professor Miller thought there was any possibility of his Unit modifying its attitude.

Professor MILLER said he did not think that the Unit was in a position to produce plans for an alternative health service, because there were obviously many alternatives which ought to be considered. It would be a formidable task. They seemed to be rather political considerations.

Dr. OUTWIN asked Professor Miller what his reaction would be if a working party voicing the views of the Association produced a report in advance of and in conflict with a corresponding report from the Planning Unit. Would the Unit produce its report, would it withdraw it, or modify it, or what?

Professor MILLER replied that there was room for a considerable difference of opinion, and if it assisted in reaching the truth it was to be welcomed. It seemed to him that if there were a conflict between the two planning units it would reflect a conflict which existed in the profession.

Dr. NOBLE said that the Planning Unit was supported by the profession, which was very interested in what it was doing. He asked whether the Unit had considered any means by which it could improve its public relations within the profession.

Professor MILLER agreed that the Unit should do more to publicize its activities.

A vote of thanks to Professor Miller for attending the meeting and for replying to questions was carried by acclamation, and Professor Miller then withdrew.

Money for Job

Dr. RIDGE reminded the Council that the remit to Dr. Jones's panel was primarily medico-political. It was essential that it should be done properly, and Dr. Ridge wanted to know whether that was possible without additional expenditure.

Dr. JONES said it was not impossible to provide an interim report, for which the General Purposes Committee asked, but his Panel was unanimous that it could not do its job properly without, as set out in the report, analysing (1) the economic basis of the National Health Service and the reasons for its failure to raise sufficient finance to provide medical care at the standards required to satisfy rising expectations; (2) public and consumer expenditure and the possibilities of

providing more money from taxation and/or consumer expenditure; (3) the merits and defects of private medical care and insurance in North America and their lessons for Great Britain; and (4) private medical care and health insurance and the merits and defects of systems of organizing and financing medical care in Europe and Australasia, and their significance for Great Britain.

It was proposed to remit each of these tasks, each one costing approximately £500, to an expert who, with the help of others, would produce a report to be considered by the panel. The A.R.M. resolution could not be properly carried out unless those exercises were carried out. If the Council granted the money it could expect that the final analysis would be available to the Panel in the autumn of 1968, and that the Panel would complete its report for the Council before the Annual Representative Meeting of 1969.

Dr. OUTWIN moved: "That such is the urgency of the implementation of the A.R.M. resolution submitted by the Guildford Division that the Council authorizes the provision of £2,250 requested by Dr. Jones in order that his Panel may undertake this work, and produce an interim report in 1968 and a complete report in 1969."

Dr. WAND pointed out that in the budget for 1967 some £4,000 was provided for the Planning Unit. For 1968 £9,000 was provided, and it was expected to cover all that was to be done in the way of planning. The Finance and the General Purposes Committee had decided that Dr. Jones and his Panel should try, within the limits of the budget and with the resources available in B.M.A. House, to provide an answer to the A.R.M. resolution. At the moment the Association had not the extra money. "If I am to be asked continually for money in this fashion I cannot see how it is possible for me to continue to try to manage the affairs of the Association," Dr. Wand concluded.

The CHAIRMAN asked Dr. Jones whether it was absolutely necessary to have four experts at work. Dr. WALLACE asked whether it was seriously being suggested that the Representative Body should be informed that its project was to be postponed or carried out in a second rate manner for the sake of some £2,000. Dr. JONES said he would do whatever Council instructed him to do to the best of his ability. But he could not withdraw his request that the money should be made available to his panel. He pointed out that the Treasurer had not taken exception to the motion at the Representative Meeting, and the Representative Body had every reason to believe that the money would be forthcoming.

A motion that the question be now put was carried, and Dr. Outwin's motion was put to the meeting and carried.

Public Health Service Appointments

Dr. J. M. DUNLOP moved: "That the Chairman of the Central Ethical Committee be invited to look into the advisability of ensuring that immediately the present ban is lifted all authorities which have defied the ban of the British Medical Guild (Surrey, Tees-side, etc.) be permanently named in the 'Important Notice' which appears each week in the *British Medical Journal*."

Dr. WALLACE said he had the gravest doubts about the motion. There had been a settlement, and he wondered whether it was

wise, in the light of a settlement, to carry on as if the Association was still half at war.

Dr. H. L. LEAMING said the motion would militate against Tees-side recruiting staff of good quality in the future. Dr. Ross urged Council to reject the motion.

Dr. DUNLOP pointed out that if the invitation were not so given to the Chairman of the Central Ethical Committee there would be no point in having a ban in the future.

The motion was carried by 18 votes to 16 votes.

At this point Dr. Gibson left the meeting and Dr. Wand took the chair.

Public Health Committee

Dr. C. METCALFE BROWN presented the report of the Public Health Committee.

He said that a firm offer had been received from the Management Side of Committee C in reply to the Staff Side's claim for an increase in the salaries of public health medical officers submitted to the Management Side in June 1966. While the offer was not entirely satisfactory, the Committee believed that in the existing economic climate it was extremely unlikely that any further concessions would be gained. In the circumstances the Committee thought the offer represented an acceptable basis for the conclusion of negotiations.

The Public Health Committee therefore recommended that (1) the British Medical Guild be asked to withdraw its recommendation to doctors not to apply for local authority public health appointments; (2) the public health service be withdrawn from the "Important Notice" in the *British Medical Journal*; and (3) the *British Medical Journal* be empowered to accept advertisements for local authority public health appointments forthwith.

Dr. Metcalfe Brown expressed gratitude to the Council for its strong and prolonged support for the public health medical officers, and to the *British Medical Journal* for its co-operation. The CHAIRMAN congratulated the Public Health Committee on what it had achieved.

Dr. DUNLOP moved by way of amendment to add to recommendation (1) the words "provided the Management Side of Committee C agrees that the revised salary scales are operated from 1 October 1966 and that note 3 of paragraph 2 of the appendix to the draft circular be deleted."* Dr. G. N. MARSH seconded the amendment.

Dr. DUNLOP said that before the ban was lifted it was necessary to get a quid pro quo from the Management Side. The ban had been very effective, and though he agreed that the time had come to remove it it should not be removed without gaining some concession from the Management Side. He reminded the Council that the claim had been submitted to the Management Side on 16 June 1966, a month before the Government's pay freeze.

Dr. METCALFE BROWN assured the Council that the Committee had fought to achieve the date 1 October instead of 1 February in the

*Note 3 of the draft agreement on revised salaries for public health medical officers, which was before the Council, stated that, "Save in exceptional circumstances the maximum salary of any post in the range [the proposed new upper salary range and assimilation points for senior medical officers] must be below the maximum salary prescribed by Committee C for the deputy medical officer of health of the same employing authority. This provision shall be subject to review in the light of experience."

offer. However, the Management Side had not agreed and there had been no support from the Ministry of Health. The Public Health Committee by a clear majority considered that 1 February would have to be accepted as the date.

The amendment was carried.

The Public Health Committee's second recommendation, that the Public Health Service be withdrawn from the "Important Notice" in the *British Medical Journal*, was not accepted.

The CHAIRMAN ruled that the Committee's third recommendation fell to the ground.

The report of the Committee, as amended, was adopted.

Medicines Legislation

Dr. SKENE presented the report of the *Ad Hoc* Committee on Medicines Legislation. He recommended that the memorandum prepared by the Committee be approved and forwarded to the Ministry of Health, and that a deputation be appointed to visit the Ministry for discussions on 5 December.

Dr. Skene drew particular attention to the following paragraph in the memorandum: "The Association is not in accord with the statement in the White Paper (para. 25) that 'licensing will rest with the Health and Agriculture Ministers' and would go further than the Sainsbury Report (para. 337) 'on the licensing function it is probable that the Commission will be advisory only.' The Association is of the view that for authority for licensing to be vested in an independent Medicines Commission with executive powers would be the most desirable mechanism for licensing. Whatever the arrangements for licensing may ultimately be, we regard it as imperative that an adequate appeals machinery, independent of the licensing authority, should be established."

Dr. CAMERON said that the G.M.S. Committee had considered the White Paper on forthcoming legislation on the safety, quality, and description of drugs and medicines in conjunction with the Sainsbury Report and the letter on the subject from the Ministry of Health, dated 20 October, which was reported to the last meeting of the Council. The Committee was seriously concerned that the White Paper envisaged very wide powers being given to Ministers in both the licensing of drugs and medicines and the vetting of preparations for efficacy, toxicity, and safety.

The G.M.S. Committee had noted that the Sainsbury Report proposed that the vetting of new preparations should be the responsibility of an independent Medicines Commission, and it would support that view provided that the Commission was truly independent with executive powers and not constituted on the lines proposed in the White Paper for a Commission to advise Ministers.

The White Paper intended that the Commission should be kept "to a reasonable size," but in the appointment of its members the Ministers would consult 20 or more professional organizations. Only one nominee of the B.M.A., or two at the most, could be expected to be appointed to the Commission, and the G.M.S. Committee was alarmed at the prospect of an inadequate representation of general practitioners to protect their vital interest in prescribing for their patients.

Dr. Cameron registered a protest that the G.M.S. Committee had been hurried in the

matter. More opportunity should have been given to make its views known.

Dr. SKENE said that a protest concerning the shortness of time had already been made to the Ministry with some effect. The *Ad Hoc* Committee had also made the point concerning the independence of the Medicines Commission. The matter of representation of the Association on the Commission was a valid point and should be raised with the Ministry.

Dr. CAMERON said his Committee would wish to seek from the Minister a renewed assurance that there was no intention in any way to limit the freedom of general practitioners to prescribe under the N.H.S.

Dr. J. S. HAPPEL said it was fundamental to the whole practice of medicine that the Medicines Commission should be independent.

Dr. CAMERON moved that the word "desirable" in the paragraph referred to by Dr. Skene should be deleted, and that the word "essential" be substituted for it.

Dr. RIDGE seconded the amendment, which was carried.

The recommendations of the *Ad Hoc* Committee were adopted, and the Council agreed that the deputation to see the Minister should consist of the Chairman of Council, Dr. Skene, Dr. Ridge, Dr. G. Owen Williams, and Sir John Richardson, Chairman of the Joint Consultants Committee.

Junior Hospital Doctors' Association

The Council had before it a memorandum on the representation of hospital junior staff submitted by the national executive council of the Junior Hospital Doctors' Association.

Dr. BOLT suggested that the memorandum might be referred to a small committee set

up by the Council. Dr. SKENE said it would be wrong for Council to set up a working party in anticipation of the views of the Central Committee for Hospital Medical Services and of the Hospital Junior Staffs Group Council.

Dr. NOBLE suggested, and it was agreed, that the memorandum should be sent to the Central Committee for Hospital Medical Services, to the Hospital Junior Staffs Group Council, and to the Organization Committee.

Hospital Medical Services

Dr. SKENE presented the report of the Central Committee for Hospital Medical Services in the absence of its Chairman, Mr. H. H. LANGSTON.

Ballot on Distinction Awards

Dr. RANKIN asked why it had taken 12 months to organize the ballot on distinction awards, and, secondly, why some ballot papers did not reach all consultants who were members of the Association.

Dr. SKENE replied that Headquarters did not have lists of members of the Association by category or professional activity, and it was dependent on regional hospital boards to give the names of consultants in the N.H.S. There were many consultants who were serving as honorary consultants on the staffs of universities.

Referring to the composition and terms of reference of the Negotiating Subcommittee, a matter which the Committee had under consideration, Dr. LEAMING moved that the Council should request that when considering the composition of the Negotiating Subcom-

mittee the Central Committee for Hospital Medical Services should take note of the desirability of ensuring that it contained adequate representation not only of hospital junior staff but also of consultants working exclusively in regional board hospitals.

The motion was carried.

Private Practice

Dr. I. M. JONES presented the report of the Private Practice Committee.

He referred to the Health Services and Public Health Bill (*B.M.J.*, 2 December, p. 562) and said it was clear that it was the intention of the Minister of Health to abolish completely all private beds in N.H.S. hospitals. That had the gravest implications for the freedom of the citizen as well as for the freedom of the medical profession, and in his view it was a direct breach of the undertakings given by the Government of the day to the presidents of the Royal Colleges before the National Health Service Act was passed. Dr. Jones asked for a search to be made to find out the exact nature of the undertakings given, and urged that the strongest possible protest be made on behalf of the Association to the Minister of Health.

The Council agreed with Dr. Jones's proposals.

Other Committees

The Council also considered the reports of the following: Alcohol and Road Accidents Committee, Annual Meetings Committee, Central Ethical Committee, Charities Committee, Committee on the Common Market, Film Committee, and General Medical Services Committee.

The meeting terminated at 8.40 p.m.

Private Practice Committee

The Committee agreed on the contents of a memorandum to the Council recommending what action the Association could take to extend private practice and to increase support for Independent Medical Services Ltd. Doubt was expressed about the soundness of the Central Ethical Committee's ruling that I.M.S. must not provide lists of names of I.M.S. doctors in answer to requests from the public. Draft schemes for the partial reimbursement to patients of specialists' and general practitioners' private fees were approved in general, but the Private Patients Plan, sponsored by the B.M.A., is to be consulted before the schemes are finally approved and recommended to the Council.

A meeting of the Private Practice Committee was held on 22 November. Dr. I. M. JONES was in the chair.

The Committee received with regret a report of the death of Dr. R. Hale-White (*B.M.J.*, 11 November, p. 362). He had been a member of the Private Practice Committee from 1959 to 1966, and he had been elected a Fellow of the Association in 1964.

"Mediflash"

Dr. P. R. WILSON, Assistant Secretary, informed the Committee that a letter had been sent to all chief constables about Mediflash, the portable flashing green light for fixing to the roof of a doctor's car when travelling to an emergency (*Supplement*, 11 November, p. 50). So far 19 replies had been received. Ten chief constables sup-

ported the introduction of the lamp; five had been guarded in their support, though they had not said they would ban its use; and four had merely made acknowledgement.

Post-mortem Reports

Dr. G. R. SMITH drew attention to a resolution of the Committee's forensic medicine subcommittee about charges made to general practitioners for post-mortem reports. The subcommittee had considered a complaint from a general practitioner that when he was unable to attend a necropsy on one of his patients and wanted a report on the examination he had to apply in writing and send 6s. 8d. The subcommittee recommended that the Coroners Society should be asked to take steps to "improve the position."

The CHAIRMAN said that coroners had a

right to charge a fee. However, the Coroners Society had given an assurance that this was not usually insisted upon.

Fees for Part-time Services

The CHAIRMAN gave an oral report of a meeting of the Subcommittee on Fees for Part-time Services.

The Treasury was to be asked to increase the mileage fee for part-time work for Government departments. The subcommittee had also decided to make a claim in Whitley Committee C for an increase in the payment for part-time work for local authorities. The subcommittee would be requesting television companies to arrange a fee with a doctor when they invited him to appear on a programme rather than after he had done so.

The Chairman said that fees for services for the National Society for the Prevention of Cruelty to Children had been discussed. The society had suggested that the fees relating to inquests should be taken out of the schedule, since they no longer applied. The subcommittee had considered that the remaining fees should be increased by one-third. The subcommittee had considered that fees for attendance at quarter sessions or assizes should be £7 for each case.

The Chairman said that the subcommittee had received an offer from the Ministry of Health to increase the fees paid for first-aid examinations. The existing fee was £2 per session, plus 5s. per candidate over the first six. The new offer was for a fee of £3 13s. 6d. a session including up to six candidates, with a further fee of 12s. 6d. for each person examined above the first six.

Concluding his report on the work of the subcommittee, the Chairman said that it had considered documents from the Monopolies Commission, and it proposed to inform the Commission that fees payable by patients to their doctors were a matter for agreement between the doctor and the patient. Notes of advice from the Association were in no circumstances binding upon the doctor. It would also be pointed out to the Commission that a doctor's ethical code did not allow him to withhold treatment from a patient because the patient could not pay a fee.

Transmission of Information

The Committee considered the case of a patient who had consulted a general practitioner privately on a matter of urgency. She had not wanted her N.H.S. doctor to deal with this particular ailment. The general practitioner consulted had referred the patient privately to a consultant, who had arranged for her immediate admission to an N.H.S. hospital as an N.H.S. patient. On admission a "hospital attendant" had insisted on recording the name of the patient's N.H.S. doctor and had refused to take a note of the referring private doctor's name, despite the patient's request that the private doctor should be kept informed and her express wish that she did not want her N.H.S. doctor to be informed.

On the patient's discharge from hospital progress reports and discharge notes were sent to her N.H.S. doctor, but at no time did the private doctor who referred the case receive any communication from the hospital.

Dr. P. G. JONES said that because a patient was registered with a doctor as an N.H.S. patient it did not mean that that doctor had a monopoly of that patient. The patient could go to some other doctor for private treatment. A hospital report should be sent to the general practitioner who sent the patient to the hospital. The doctor in the case in question had made "forceful protests to the secretary and chairman of the board of governors of the hospital." He had been told that it was usual when a patient was referred by a doctor other than his National Health Service doctor to send a report to the referring doctor and to the patient's N.H.S. doctor. The correct course, said Dr. Jones, would have been for the general practitioner to protest to the consultant in charge of the case.

Dr. H. FIDLER said that it was usual for a hospital to enter the name of the referring

doctor on the patient's notes. Dr. P. A. T. WOOD said that it appeared great pressure had been put on the patient in this case to give the name of her N.H.S. doctor, though she had expressly asked that he should know nothing about it.

The Committee agreed that any doctor who referred a patient, either privately or through the N.H.S., should receive a report from the consultant, and that no report should be sent to anyone else if it was contrary to the patient's wishes.

Medical Standards for Drivers

The Committee considered a motion from the Newcastle upon Tyne Division which had been among the items on the Annual Representative Meeting's agenda which, owing to lack of time, had not been considered and which had been referred *en bloc* to the Council. The motion stated that the existing method of issuing driving licences to "private drivers" was "grossly inadequate" in that no real effort was made to confirm that the minimum medical standards, as stated on the application form, existed.

Dr. FIDLER wondered whether it should be Association policy that all drivers should be medically examined, and whether the Association should draw up a set of standards for such an examination. Dr. J. T. A. GEORGE noted the words "private drivers." Presumably, he said, that was to make a distinction from public service vehicle drivers. He asked whether the B.M.A. had any policy on medical standards for driving. Drivers

now had only to pass a test to show that they could see a certain distance.

The CHAIRMAN replied that the Occupational Health Committee had drawn up standards for public service vehicle drivers. Other organizations, such as the World Health Organization, were currently considering the matter and it seemed to him better not to duplicate work but to wait for their report.

The Committee resolved to ask the Newcastle upon Tyne Division to "elaborate" its motion, and that at its next meeting the Committee would consider a report of the Occupational Health Committee, issued in 1954, on medical standards in road, rail, and air transport.

Emergency Treatment Service

The CHAIRMAN reported on a meeting of the Central Advisory Committee of the Emergency Treatment Service. He said that the position in London was "fluid." A letter had been sent to every London doctor saying that the B.M.A. service would start in London when there was enough demand for it. There had been no great increase in the number of applicants, said the Chairman, though Telephone Answering Services had several hundred subscribers. Some of the subscribers were clearly acting on behalf of other doctors who were not subscribers, and the switchboard was sometimes flooded with their work. A letter had been sent to subscribers to the Telephone Answering Service reminding them that their subscription covered only their own practices.

Independent Medical Services

The CHAIRMAN, speaking also as Chairman of the Committee of Management of Independent Medical Services Ltd., reported that the Council at its meeting on 25 October (*Supplement*, 4 November, p. 29) had accepted the Private Practice Committee's recommendation "That the Council, recognizing that the policy of extending private practice and of giving all practicable support to Independent Medical Services Ltd. has been approved by the Representative Body, urges resolute and continuous action in this respect by all concerned." The Chairman of Council had asked that the Private Practice Committee should submit a memorandum to the Council setting out specifically the action the Committee wanted the Council to take.

The Chairman said support was needed from the Association to achieve two main objectives: firstly, to acquire for I.M.S. a working capital of £200,000, which had been the original target; secondly, to get more doctors to join the scheme. "The I.M.S. office is flooded every day," said the Chairman, "with applications from patients who wish to use the scheme but who have been unable to find a doctor willing to make the scheme available to them."

The Chairman referred to some of the ways in which the scheme could be advertised more widely. The Representative Body had instructed the Council to introduce an item-of-service insurance scheme for private practice. Draft schemes for paying specialists'

and general practitioners' private fees had been prepared. It would not be impossible to start a hospital scheme without increased capital, the Chairman said, but it would be desirable to have increased capital before launching such a scheme. This applied even more to the scheme for the partial reimbursement of general-practitioner fees. That scheme presented greater difficulties because of the greater risk.

In answer to a question by Dr. SMITH, the CHAIRMAN said that the Central Ethical Committee had ruled that I.M.S. must not provide lists of names of doctors participating in I.M.S. schemes to patients who applied to the office for this information. Dr. SMITH suggested that the Central Ethical Committee should reconsider its decision. If a list of all available doctors were given the patients would have a choice, and, in his opinion, that would not be unethical.

The CHAIRMAN said that at present patients who inquired about doctors operating the I.M.S. scheme were advised by letter to ask their existing doctor whether he would look after them under the scheme. The letter stated that any doctor who wished could participate in the scheme. It then gave the names of doctors in the patient's area who, so far as was known, were operating the scheme. The I.M.S. office would continue to do that, said the Chairman.

Dr. SMITH suggested that honorary secretaries of Branches and Divisions should follow the same policy. Dr. G. CORMACK

pointed out that in some areas the list provided by the I.M.S. office might contain the name of only one doctor. He hoped that the Central Ethical Committee would consider whether its attitude was soundly based in the context of the present circumstances.

The Committee agreed to ask the Central Ethical Committee to receive a deputation to discuss the matter.

Wrong Premise

Dr. WOOD said that it was important to maintain private practice, but in his opinion Independent Medical Services provided a bad scheme, and that was why it was failing. He thought the scheme was misconceived, and that the whole scheme was wrong. The method of payment was wrong. Reimbursement to the patient of part of the doctor's fees was the best method, said Dr. WOOD. A doctor inevitably had many patients under the scheme who needed much attention. Those patients could consume more drugs than the allowance would cover.

In straightforward private practice the heavy-risk patient had to pay a heavier bill and bore the responsibility. The doctor did not have to worry about the number of those patients. Under the I.M.S. scheme the doctor stood to lose. The scheme was failing because it had to compete with straight private practice. He himself had been in private practice for 17 years, and Independent Medical Services and other insurance schemes had been running for varying lengths of time. They had all been based on the idea that private practice was not viable without a scheme. He believed that that premise was wrong. Private practice could survive without any scheme, but too few people realized that.

The CHAIRMAN said that the I.M.S. scheme had been debated twice by the Representative Body. It should be compared with the other schemes in existence. He would not accept that it was a bad scheme, and it was not unattractive to patients. The difficulty was to persuade doctors to operate it.

Dr. P. G. JONES agreed that private practice could survive, but it would be more successful if patients could be offered a scheme. They should have some choice, he said. Dr. J. E. MILLER said that the cost of drugs was often a drawback in private practice. An integral part of the I.M.S. scheme was a scheme for paying the cost of drugs. Dr. WOOD maintained that a reimbursement scheme was the only one that was reasonable. The patient should have to bear some of the ultimate risk. Under the I.M.S. scheme it was the doctor who bore it. If there was the demand from the public for this service that the Chairman had suggested why were doctors not coming forward to join the scheme? The CHAIRMAN replied that doctors appeared to be unwilling to go into private practice.

Dr. CORMACK pointed out that there were many general practitioners who ran well-organized practices from good premises with full ancillary help, and all under the National Health Service. He had been asked by those doctors what could they give their patients privately that they were not giving under the N.H.S., and he had been unable to answer.

Memorandum to Council

The Committee then proceeded to draw up a memorandum for the Council. It was agreed that the following points should be made: private practice should be encouraged; further capital for Independent Medical Services should not be asked for at this stage; efforts should be made to publicize the existing I.M.S. scheme; it should have official backing from the Association, and Division meetings should be held; Division secretaries should be provided with literature, and it was to be hoped they would use the facilities available to them to publicize the scheme.

On a question raised by Dr. MILLER, that the support of the Association for Independent Medical Services had been lukewarm, and on a point that the existence of Independent Medical Services might have created difficulty in the course of negotiations with the Review Body or with the Ministry

of Health, the CHAIRMAN said he "saw no difficulty." The Association had stated that, because of the overall situation in medicine in this country, there was an urgent need to expand the private sector. That had become the policy of the Association. It was useless for it to announce a policy and not to follow it up by all the means in its power.

The Committee agreed to forward a memorandum to the Council based on the discussion which had taken place.

Two New Schemes

The Committee considered proposals for an Independent Medical Services Scheme for specialists. Mr. J. DODD, technical adviser to Independent Medical Services Ltd., attended the meeting by invitation when this item was discussed.

He said that an attempt had been made to incorporate in the specialist scheme the best of the existing insurance schemes and at the same time to produce some original ideas. The proposed scheme was not aimed at the most wealthy sector of the community. It had been thought best to put something on the market for the "emerging middle-class," who would want to insure themselves at a reasonable subscription for the best possible benefits. Therefore there was not a large range of differential subscriptions and benefits; it was a simple, moderate scale, for both subscriptions and benefits. The benefits compared favourably with those of competitors.

After a discussion, in which some aspects of the scheme were commented on, the Committee decided to give general approval to it. It was agreed, however, that before recommending the scheme to the Council the Committee should have consultations with the organizers of the Private Patients Plan—an organization which had been sponsored by the B.M.A.

The Committee also gave general approval to a draft scheme for general-practitioner treatment, in which the benefits would include a partial reimbursement of the doctor's fee and payment for the cost of medicines.

General Medical Council

The General Medical Council met at 44 Hallam Street, London W.1, on 28 November. The President, LORD COHEN OF BIRKENHEAD was in the chair.

Appointment of Members

The appointment of the following as members of the Council was announced: (1) Sir John Richardson, Bt., as representative of the Royal College of Physicians of London, for five years from July 1967. (2) Professor P. J. Randle, as representative of the University of Bristol, for three years from August 1967.

Notice of the reappointment of the following members of the Council was received:

(1) Dr. A. T. Jones, as representative of the University of Wales, for three years from September 1967. (2) Professor R. B. Hunter, as representative of the University of Dundee, for one year from October 1967. (3) Mr. A. B. Clery, as representative of the Royal College of Surgeons in Ireland, for one year from October 1967. (4) Dr. E. T. Freeman, as representative of the Royal College of Physicians of Ireland, for the period of one year from October 1967. (5) Professor A. L. Banks, as representative of the University of Cambridge, for five years from October 1967. (6) Dr. F. J. O'Donnell, as representative of the Apothecaries' Hall of Dublin, for five years from January 1968. (7) Professor W. J. E. Jessop, as representative of the University of Dublin, for three years from November 1967.

President's Address

In the course of his address the PRESIDENT said it was gratifying to record the warm reception given to the new recommendations on basic medical education adopted by the Council at its special meeting in April. It had been widely noted and approved that, unlike earlier recommendations, which were restricted to the undergraduate curriculum, the new recommendations presented in some detail the desiderata of the preregistration period and commented briefly on the subsequent period in which doctors received, or should receive, vocational training for a particular career in medicine.

The Council, the President said, fully concurred with the view expressed in an editorial in the *British Journal of Medical Education*

that "the absence of properly organized postgraduate training (the present control of which bears striking resemblances to the state of undergraduate affairs before 1858) holds up the reform of medical education." It was suggested elsewhere in the same article that "it is in the present absence of vocational training for general practice that the impediment to reform of medical education mainly lies," and that for that and other reasons it was unfortunate that the Council was still inhibited because it had no powers in relation to postgraduate vocational training for the various branches of medicine.

The previous recommendations broke new ground in many respects, said the President, particularly perhaps in the stress which they had laid on the duty (not merely the right) of medical schools "to experiment with different courses and methods of teaching," but they had had less to say about a revision of the examination system than about experimentation in the field of instruction. The new recommendations made suggestions with a view to reducing "the load on the student of a comprehensive examination taken at the conclusion of his undergraduate career." So far as could be judged, licensing bodies were welcoming these suggestions.

There had been no serious criticism of the Council's view that, for the time being, the duration of the undergraduate curriculum should not be reduced. There had been a

wide, probably universal, agreement with the Council's view that the preregistration period stood in need of radical improvement.

Diploma of Public Health

The President referred to a further report of the Council's Special Committee on Public Health on the revision of the rules for diplomas in public health. The diploma in public health was not now regarded only as a diploma which qualified its holder for the tenure of the post of medical officer of health. It was no longer educationally realistic to regard the possession of such a diploma as in itself qualifying a doctor to hold such an appointment. Moreover, the new recommendations envisaged the diploma as fulfilling a wider function by constituting the common academic core of several schemes of training for doctors who might afterwards seek employment in any branch of community health practice. Supplemental vocational training should be arranged and related to the branch of community medicine in which the doctor planned to make his career.

The President said the likelihood that in the not too distant future considerable changes might occur in the structure of the community health services was recognized, and that such changes might affect the vocational training required to equip doctors for this field of practice. The Council was therefore

appointing a standing committee to advise when a further revision of the recommendations should be undertaken.

Pharmacopoeia Committee

The PRESIDENT, in presenting the Report of the Pharmacopoeia Committee, said that certain proposals in the Government's White Paper on forthcoming legislation on the safety, quality, and description of drugs and medicines had been carefully considered by the Pharmacopoeia Commission and by the Pharmacopoeia Committee, and it was suggested that certain further representations might be made to the Ministry of Health. A matter of importance was that the present British Pharmacopoeia Commission demitted when the new *Pharmacopoeia* was published, and the question had arisen whether, in view of the forthcoming medicines legislation, a new Commission should be appointed. The Pharmacopoeia Committee had resolved that a selection committee should be appointed and had nominated the following members of the G.M.C. as members of the selection committee: Professor R. B. Hunter, Professor D. V. Hubble, Professor W. J. E. Jessop, and the President of the General Medical Council; and that the President be appointed as chairman of the selection committee.

(A report of the proceedings of the Disciplinary Committee will be printed next week.)

Association Notices

Diary of Central Meetings

DECEMBER

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|----|--------|---|
| 12 | Tues. | Committee on Medical Science, Education, and Research, 10.30 a.m. |
| 12 | Tues. | Film Committee, 12 noon. |
| 13 | Wed. | Joint Formulary Committee, 10.30 a.m. |
| 13 | Wed. | Committee on a Cervical Cytology Service, 2 p.m. |
| 13 | Wed. | Journal Committee, 2 p.m. |
| 14 | Thurs. | Central Committee for Hospital Medical Services, 10.30 a.m. |
| 14 | Thurs. | General Medical Services Committee (Scotland) (at 7 Drumshugh Gardens, Edinburgh), 10.30 a.m. |
| 14 | Thurs. | Practice Premises Working Group (G.M.C. Committee), 2 p.m. |
| 15 | Fri. | Chairman's Subcommittee (Full-time Medical Teachers and Research Workers Committee), 10 a.m. |
| 15 | Fri. | Radiologists Group Committee, 10.30 a.m. |
| 15 | Fri. | Disciplinary Machinery Working Group (G.M.S. Committee), 11 a.m. |
| 19 | Tues. | Liaison Group of Professions on the Monopolies Commission, 2.30 p.m. |
| 20 | Wed. | Film Committee, 10 a.m. |
| 20 | Wed. | Staff Side Committee C, Medical Whitley Council (at 41 Belgrave Square, London S.W.1), 10.30 a.m. |
| 28 | Thurs. | Central Ethical Committee, 10 a.m. |
| 28 | Thurs. | General Purposes Committee, 10.30 a.m. |
| 29 | Fri. | Full-time Medical Teachers and Research Workers Committee, 2 p.m. |

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

ABERYSTWYTH DIVISION.—At Machynlleth Chest Hospital, Saturday, 9 December, 8 p.m., Dr. A. Jacobs: "Diagnosis and Treatment of Anaemia."

ALDERSHOT AND FARNHAM DIVISION.—At Queen's Hotel, Lynchford Road, Farnborough, Wednesday, 13 December, 8.30 p.m., discussion with representatives of the Regional Hospital Board and the Ministry of Health: "The New District Hospital."

BARNET DIVISION.—At Outpatients' Department, Barnet General Hospital, Tuesday, 12 December, 8 p.m., symposium on "Perinatal Care."

BATH, BRISTOL, AND SOMERSET BRANCH.—At Large Lecture Theatre, Bristol University Medical School, Thursday, 14 December, 8.30 p.m., Sir Norman Skelhorn: "The Medical Profession and the Law." Guests are invited.

BLACKPOOL AND FYLDE DIVISION.—At Savoy Hotel, Blackpool, Wed-

nesday, 13 December, 8.45 p.m., Dr. P. S. Byrne: "Here and There—General Practice at Home and Abroad." Preceded by short meeting to elect representatives to Annual Representative Meeting. (Dinner, 7.30 p.m.)●

EAST KENT DIVISION.—At Kent Postgraduate Medical Centre at Canterbury, Thursday, 14 December, Dr. K. Spittelhouse: "Recent Advances in the Laboratory as they Affect Practitioners."

EAST YORKSHIRE BRANCH.—At Postgraduate Centre, Hull Royal Infirmary, Wednesday, 13 December, 8.30 p.m., presidential address.

GLASGOW DIVISION.—At Marlborough House, Langside Avenue, Tuesday, 12 December, 7.30 for 8 p.m., annual dinner and dance.●

HASTINGS DIVISION.—At Royal East Sussex Hospital, Tuesday, 12 December, 8.15 p.m., Dr. J. A. P. Trafford: "Renal Disease and Dialysis."

HENDON DIVISION.—At Hendon Hall Hotel, Tuesday, 12 December, 8.45 p.m., Dr. J. C. Houston: "Some Unusual Disorders of the Oesophagus."●

KINGSTON-UPON-THAMES DIVISION.—At Kingston Medical Centre, Tuesday, 12 December, 8.30 p.m., Dr. E. H. Rayner: "Methods of Psychological Testing."

LANARKSHIRE DIVISION.—At Alexander Hospital, Tuesday, 12 December, 8 for 8.30 p.m., Professor Ferguson Anderson: "Recent Advances in Geriatrics."

LEEDS DIVISION.—At School of Medicine, General Lecture Theatre, Wednesday, 13 December, 8 p.m., election of representatives.

LONDONDERRY DIVISION.—At City Hotel, Thursday, 14 December, 9 p.m., annual dinner dance.●

MORPETH DIVISION.—At Queen's Head Hotel, Wednesday, 13 December, 7.30 for 8 p.m., jointly with Blythe Division, annual dinner dance.

NORTHAMPTON DIVISION.—At Board Room, General Hospital, Friday, 15 December, 8 for 8.15 p.m., buffer supper; 8.45 p.m., annual general meeting; 9.15 p.m., film: "The Cry of the Bronchi."●

NORTH STAFFS DIVISION.—At Medical Institute, Hartshill, Wednesday, 13 December, 8.15 p.m., Mr. H. Roberts: "Physiology of Menstruation and Pubertal Bleeding."

SOUTH MIDDLESEX DIVISION.—At Ashford Hospital Medical Centre, Thursday, 14 December, 8.30 p.m., annual general meeting.

SOUTH SHIELDS DIVISION.—At Ingham Infirmary, Wednesday, 13 December, 8.30 p.m., Mr. S. J. Rogers: "Economic Change in Agriculture and the Provision of Social Services."

SUNDERLAND DIVISION.—At Medical Society Lecture Room, Sunderland General Hospital, Tuesday, 12 December, 8.15 p.m., symposium by Dr. J. B. Heycock, Dr. J. W. Baird, Dr. P. B. Crone: "Upper Respiratory Infection in Childhood."

SUTTON COLDFIELD, LICHTFIELD, AND TAMWORTH DIVISION.—At Postgraduate Institute, Good Hope Hospital, Thursday, 14 December, 8.30 p.m., Dr. J. Owens: "Some Aspects of Drug Addiction." Guests are invited.

THAMES VALLEY DIVISION.—At Windsor and District Postgraduate Medical Centre, King Edward VII Hospital, Friday, 15 December, 8.30 p.m., meeting to elect representatives to Annual Representative Meeting.

WALSALL DIVISION.—At Three Crowns Inn, Tuesday, 12 December, 7.30 for 7.45 p.m., joint supper meeting with Law Association, Mr. D. D. Lindsay: "Future of Public Schools."●

British Medical Journal Supplement

LONDON SATURDAY 16 DECEMBER 1967

CONTENTS

Annual Representative Meeting: Provisional Programme -	75	Hospitality -	79
General Medical Council -	77	H.M. Forces -	80
General Practitioners in Hospital -	79	B.M.A. Nuffield Library -	80
Expulsion from Membership -	79	Diary of Central Meetings -	80
Hospital Building -	79	Branch and Division Meetings -	80

British Medical Association

Annual Representative Meeting, Eastbourne, 24-28 June 1968

President: ROBERT V. COOKE, M.D., CH.M., F.R.C.S.

Chairman, Local Organizing Committee: I. M. BROWN, M.B., CH.B.

Local General Secretary: C. M. DUNLOP, M.B., CH.B.

Executive Officer: Miss B. E. MIDDLEMISS, B.M.A. House, Tavistock Square, London W.C.1.

Provisional Programme

The Annual Representative Meeting will be held in the Congress Theatre, Eastbourne, from Monday afternoon, 24 June, to Friday, 28 June 1968, inclusive. The Annual Meeting of the Association was last held in Eastbourne in 1931.

The A.R.M. Inquiry Office will be open from 9 a.m. on Monday, 24 June, in the foyer of the Congress Theatre.

There will be a reception to welcome representatives and their ladies in the Winter Garden (adjoining the Congress Theatre) on the Monday evening.

The Representatives' Dinner and Dance will be held in the Winter Garden on the Tuesday evening.

The graduates' dinners will take place on the Thursday evening, and the Service luncheons on the Tuesday and the Wednesday.

The annual breakfast of the Christian Medical Fellowship will be on the Tuesday morning. A meeting of doctors and clergy will be held on the Friday evening.

The Ladies' Club and local information bureau will be in the Grand Hotel, three minutes' walk from the Congress Theatre. It will open on Sunday afternoon, 23 June, and will remain open throughout the Meeting. Many excursions and visits have been arranged for ladies accompanying representatives, and details will be published later.

Pharmaceutical Exhibition

There will be a small pharmaceutical exhibition during the Annual Representative Meeting on the first floor of the Congress Theatre (adjacent to the coffee bar). Further details about the exhibition will be given in due course.

Hotel Accommodation

There is a large choice of hotels with varying tariffs, the majority being situated within walking distance of the Congress Theatre. A selected list is given in the Table, but a full list can be obtained from the Information Bureau, 3 Cornfield Terrace, Eastbourne (Tel. Eastbourne 30183). The local accommodation secretary, Dr. M. J. Mynott, 26 Milnthorpe Road, Eastbourne (Tel. 20945), will be pleased to advise if difficulties arise.

Many of the smaller hotels require a weekly booking from Saturday to Saturday. Since the Meeting coincides with the start of the

holiday season, representatives are recommended to make early reservations by writing direct to the hotel *stating that they are attending the B.M.A. Meeting*. The Association cannot accept responsibility for any of the prices stated in the Table. They are the current tariffs and are subject to alteration without notice.

Selected List of Eastbourne Hotels

Name and Address	Tel. No.	Distance from Congress Theatre	Daily Tariff, Full Board	Number of Bed-rooms		Number of Bath-rooms	
				Double	Single	Total	Private
Burlington Hotel, Grand Parade	22724	½ mile	£3 12s. 6d. to £5 5s.	85	64	87	60
Cavendish Hotel, Grand Parade	27401	½ "	£4 to £8	88	32	105	94
Cumberland Hotel, Grand Parade	30342	½ "	£3 10s. to £4 18s.	44	22	63	43
Hydro Hotel, Mount Road	20643	½ "	£2 11s. to £4 1s.	60	40	62	46
Imperial Hotel, Devonshire Place	20525	½ "	£2 12s. 6d. to £3 10s.	61	69	33	17
Kenilworth and Mostyn, Willmington Square	25387	½ "	£2 9s. 6d. to £4 4s.	50	50	24	3
Lansdowne Hotel, King Edward's Parade	25174	½ "	£3 to £4	56	24	22	9
*Lawns Hotel, King Edward's Parade	25177	½ "	£3 to £4 2s. 6d.	46	14	24	12
Mansion Hotel, Grand Parade	30557	½ "	£2 17s. 6d. to £4 5s.	84	47	68	49
Queens Hotel, Marine Parade	22822	½ "	£3 17s. 6d. to £5 7s. 6d.	95	25	86	66
Sandhurst Hotel, Grand Parade	27868	½ "	£2 14s. to £3 10s.	52	18	34	22
Wish Tower Hotel, King Edward's Parade	22676	½ "	£3 to £4 7s. 6d.	47	33	54	42

Note: All hotels are licensed and have 10% service charge.

* Only Saturday to Saturday booking.

Caravan Accommodation

Representatives who wish to take a caravan to Eastbourne are advised to write to Dr. E. V. Claydon, 30 Eastbourne Road, Willing-

don (Tel. Eastbourne 53250). A block booking has been made at the Castle View Caravan Site, Pevensey Bay, three miles from the Congress Theatre.

Luncheon Arrangements

There is limited lunch accommodation available for Representatives at the restaurant adjacent to the Congress Theatre. It is expected that most representatives will return to their hotels for lunch.

Car Parking and Transport

Daily transport will not be provided from hotels to the Congress Theatre, but it will be provided to and from some of the evening functions.

Travel Facilities

There are air services from Edinburgh and Glasgow to Gatwick, which is 40 miles from Eastbourne.

A motor-rail service from Stirling to Newhaven (13 miles from Eastbourne) operates four nights a week.

Details of these services can be obtained from the M.I.A. Travel Service, B.M.A. House, Tavistock Square, London W.C.1 (Tel. 01-387 8486).

Glyndebourne

It is hoped to obtain a limited number of seats for the Glyndebourne Opera performance on Wednesday, 26 June, and information on how to apply for tickets will be sent to representatives in due course. *In the meantime it is requested that no advance application be made.*

Social Functions and Excursions

Representatives and their ladies will be sent application forms for tickets for social functions and excursions in the spring, when details of prices become available.

Ladies' Club

The Ladies' Club will be in the Sun Lounge on the ground floor of the Grand Hotel (on the sea front, three minutes' walk from the Congress Theatre). A lounge, writing-room, and powder-room will be available together with changing-rooms. There will be a licensed bar and light refreshments. The hotel amenities include a heated, open-air, salt-water swimming-pool.

Ladies' Programme

The Ladies' programme will include all-day tours to Chartwell, Arundel, Rye, Battle, and Penshurst Place; and possibly a visit to Wimbledon for the all-England Lawn Tennis Championships. Among the shorter tours will be visits to Batemans, Burwash; to Hastings, to see the embroidery; to the Brighton Pavilion; to Glynde Place; to the Pestalozzi Children's Village; and to the University of Sussex. It is hoped to arrange a fashion show, a beauty demonstration, and a display of floral art at the Grand Hotel. For the more energetic there will be a walk on the Sussex Downs.

Dinners, Luncheons, and Breakfast

The following graduates' dinners have been arranged for Thursday, 27 June: Aberdeen Dinner, Cavendish Hotel; Bristol Dinner,

Imperial Hotel; Cambridge Dinner, Beachy Head Hotel; Edinburgh Dinner, Norfolk Hotel; Glasgow Dinner, Grand Hotel; Guy's Hospital Dinner, Mansion Hotel; Irish Dinner, Congress Theatre Restaurant; Leeds Dinner, Le Chantecler Restaurant; St. Bartholomew's Hospital Dinner, Royal Eastbourne Golf Club; Welsh Dinner, Cumberland Hotel.

The following Service luncheons have been arranged: Royal Navy, Tuesday, 25 June, Le Chantecler Restaurant; Royal Air Force, Tuesday, 25 June, Mansion Hotel; Royal Army Medical Corps, Wednesday, 26 June, Cavendish Hotel.

The C.M.F. Annual Breakfast on Tuesday, 25 June, will be held at the Grand Hotel.

Further information about these functions, and on where to apply for tickets, will be given later.

Golf Competitions

All golf competitions will take place at the Seaford Golf Club, East Blatchington, Sussex, nine miles from Eastbourne:

Tuesday, 25 June, 9.30 a.m.—Golf Competition for the Nathaniel Bishop Harman Cup (formerly the Treasurer's Cup), divisional winners only.

Wednesday, 26 June, 9.30 a.m.—Ladies' Golf Competition for the Notts Ladies' Challenge Cup (open to women members of the Association and to wives and daughters of members).

Thursday, 27 June, 9.30 a.m.—Golf Competition for the Leinster and Childe Cups (open to all members, maximum handicap 18).

Further particulars available from the Golf Secretary, Dr. D. A. Craib, Westfield, Darley Road, Eastbourne (Tel. 22738).

Provisional Time-table of Meeting

Monday, 24 June

- 9.00 a.m.—A.R.M. Inquiry Office open for registration, Congress Theatre.
- 9.00 a.m.—Local Information Bureau and Ladies' Club open for registration, Grand Hotel.
- 2.00 p.m. to 6.00 p.m.—*Annual Representative Meeting* starts, Congress Theatre.
- 3.00 p.m.—Welcome by the Mayor of Eastbourne, Congress Theatre.
- 8.30 p.m.—Welcome reception, Winter Garden, given by the Eastbourne Division of the Association and the Eastbourne Corporation (Afternoon Dress).

Tuesday, 25 June

- 8.00 a.m.—Annual Breakfast of the Christian Medical Fellowship.
- 9.30 a.m.—*Annual Representative Meeting*, Congress Theatre.
- 12.30 p.m.—R.N. and R.A.F. Luncheons.
- 7.30 p.m.—Representatives' Dinner and Dance, Winter Garden, open also to the local Division (Dinner jacket).

Wednesday, 26 June

- 9.30 a.m. to 1 p.m.—*Annual Representative Meeting*, Congress Theatre.
- 1.00 p.m.—R.A.M.C. Luncheon.
- p.m.—Afternoon programme to be arranged.
- 4.00 p.m.—Glyndebourne Opera (limited number of tickets).
- 7.30 p.m.—Devonshire Park Theatre (play to be announced).

Thursday, 27 June

- 9.30 a.m.—*Annual Representative Meeting*, Congress Theatre.
- 7.30 p.m.—Graduates' Dinners.

Friday, 28 June

- 9.30 a.m.—*Annual Representative Meeting*, Congress Theatre.
- 12.30 p.m. (provisional).—Annual General Meeting, Congress Theatre.
- p.m.—Council Meeting (at conclusion of A.R.M.).
- 8.15 p.m.—Meeting for doctors and clergy, Congress Theatre Restaurant.

General Medical Council: Disciplinary Committee

The Disciplinary Committee of the General Medical Council met at 44 Hallam Street, London W.1, on 29 and 30 November and on 1 and 2 December. The President, LORD COHEN OF BIRKENHEAD, was in the chair.

Indecent Exposure

The Committee dealt first with the case of WILLIAM IRVINE HARDY, registered as of 7 Bedford Street, Belfast, M.B., B.Ch. 1930, which had been adjourned from November 1965 and from July 1967, the charge being that on 17 March 1965 he was convicted of indecent exposure and committed to hospital under section 60 of the Mental Health Act, 1959.

Dr. Hardy was not present but was represented by Mr. N. Leigh Taylor, of Messrs. Hempsons, Solicitors to the Medical Defence Union. The conviction had been admitted on behalf of the practitioner and had been found by the Committee to be proved.

Mr. A. P. P. HONIGMANN, of Waterhouse & Co., Solicitors, presenting the facts to the Committee, said that since 1965 Dr. Hardy had been in hospital and had never been able to be present for a hearing of his case.

After a consideration *in camera*, the PRESIDENT announced that, in view of the circumstances and of psychiatric evidence, the Committee had determined to postpone judgement in the case for a period of two years.

Postponed Judgement

The Committee next dealt with five cases of conviction in which judgement had been postponed.

In the case of PATRICK LAURENCE LYONS, in which judgement had been postponed in November 1965 on account of convictions for being under the influence of drink, the Committee decided, after a consideration *in camera*, to postpone judgement for a further period of one year.

The Committee, in the light of information received, determined that the name of FAROOQUE HAYDER SIDDIQUE should not be erased from the Register, and his case was concluded.

Judgement on Dr. Siddique had been postponed in November 1965 on the charge that he had in May 1964 been convicted (after pleading guilty) of indecent assault.

The case of BARRY ANTHONY ENOCH, on whom judgement had been postponed in November 1966 on a charge that he had been convicted of indecent assault on a male person, was also concluded by the Committee deciding that in view of the satisfactory reports his name should not be erased from the Register.

Name Erased

The Committee decided to erase from the Register the name of CHARLES FREDERICK

ROSS. Judgement had been postponed on Dr. Ross in November 1966 on charges that in April 1964 he had been convicted of being in charge of a motor vehicle when under the influence of drink or drugs, of assaulting a police sergeant, and causing wilful damage to property; that in August 1964 he had been convicted of driving a motor vehicle when under the influence of drink or drugs; and that in March 1966 he had been convicted of being in charge of a motor vehicle when under the influence of drink or drugs.

In announcing the Committee's decision, the PRESIDENT said that if evidence should become available at a later date that Dr. Ross had succeeded in overcoming his addictions to drugs and drink an application for the restoration of his name to the Register would then be sympathetically considered.

Dr. Ross had 28 days within which to appeal.

Further Postponement

The Committee further considered the charge against NOEL PATRICK BURNS, on whom judgement had been postponed in July 1967, that in December 1966 he was convicted of failing to keep a register of dangerous drugs. When judgement had been postponed in July for two years Dr. Burns had been told that he would be expected to make an interim appearance in November.

Mr. HONIGMANN said that the conviction had arisen out of a routine inspection by the police of chemists' registers. Dr. Burns had been purchasing unusually large quantities of morphine and pethidine by presenting prescriptions at chemists marked "Stock Emergency." When the police interviewed him he was unable to account for the way in which the supplies had been used. He had admitted that for the previous 12 months he had been injecting himself with pethidine at the rate of approximately 300 milligrams per day. At the last hearing Dr. Burns had been specifically told that he must "furnish the names of professional colleagues including a consultant psychiatrist."

Dr. BURNS, who was not represented, said that he had not really thought there was any treatment for his particular condition. The doctor advising him had wanted him to have inpatient treatment, but it had not been possible at the time for him to do this.

The PRESIDENT explained that it was not a question of treatment but that the Committee wished to have a report on Dr. Burns's condition.

After a consideration *in camera*, the PRESIDENT announced that the Committee was particularly concerned that Dr. Burns had declined to comply with its specific request, expressed in the clearest possible terms, that he should furnish the name of a consultant psychiatrist in order that the Council might communicate with him as to Dr. Burns's habits and conduct, with special reference to any addiction to drugs. Judgement would stand postponed until May 1969, but Dr. Burns would be expected to appear again in February 1968, and before then to furnish

without fail the name of a consultant psychiatrist who would be able to provide information on his condition, and to supply the names of professional colleagues and other persons of standing to whom the Council could apply for confidential information.

Use of Firearms

The Committee inquired into the charge against QAMAR UZ ZAMAN, M.B., B.S. 1958, U. Punjab (India), that he was on 13 March 1967 convicted (in the name of Abdullah) of (1) wounding with intent to cause grievous bodily harm; (2) carrying a firearm with intent to commit an indictable offence; (3) shooting with intent to murder; (4) carrying a firearm with intent to commit an indictable offence; and that he was ordered to be detained in Broadmoor Hospital and to be subject to a restriction order for a period without limit of time.

Dr. Zaman was not present and was not represented.

The Committee was told by Mr. G. J. K. WIDGERY, Solicitor to the General Medical Council, that Dr. Zaman (otherwise known as Dr. Abdullah) was born in India in 1935, qualified in Pakistan in 1958, and came to Britain in 1961, where he was provisionally registered. He had since then held certain hospital appointments. On 24 October 1966 Dr. Zaman had gone to an establishment in the West End of London at which there were young women acting as hostesses. He sat with one of these hostesses for a while and then decided to leave. He went to the door and then, for no apparent reason, pulled out a gun and fired a single shot. The bullet hit one of the hostesses. The girl subsequently recovered.

Four days later a young girl was walking along Upper Woburn Place towards the Euston Road when she felt a hand against her. Turning round, she found that it was a man. Subsequently it emerged that it was Dr. Zaman. He pulled out a gun and fired twice at the girl. The bullets passed through her abdomen, causing her serious injury, and struck two other pedestrians who were in the street. The doctor was arrested later that day and found to have a gun and a number of unused rounds of ammunition which he had purchased shortly before at some shop in London. He had subsequently been convicted at the Central Criminal Court and ordered to be detained in Broadmoor.

Mr. Widgery added that in June 1965 a complaint had been received by the General Medical Council from one of Dr. Zaman's colleagues at the hospital where he was working at the time that he had been assaulted by Dr. Zaman. The Registrar wrote to Dr. Zaman informing him of the complaint, and that it had been noted in the General Medical Council's records and would be taken into account if at any time Dr. Zaman should apply for full or for temporary registration.

After a consideration *in camera* the PRESIDENT announced that by reason of the convictions proved against him the Committee had directed the Registrar to erase from the

Register the name of Qamar Uz Zaman. Dr. Zaman had 28 days within which to lodge an appeal.

Other Cases for Postponed Judgement

In the case of THOMAS WYN ROBERTS, on whom judgement had been postponed in November 1967 on a charge that he had pleaded guilty in March 1966 to 12 charges of obtaining quantities of Methedrine by false pretences, the Committee decided to postpone judgement for a further period of one year.

In the case of WILLIAM JEREMY WYBRANTS GREENE, on whom judgement had been postponed in November 1965 for two years on a charge relating to the abuse of drugs, the Committee, after considering testimony to his conduct in the meantime, recorded a finding that Dr. Greene was not guilty of infamous conduct in a professional respect in relation to the matters alleged against him in the charge.

That concluded the case.

The Committee postponed judgement for a further year in the case of JEFFREY GREY, on whom judgement had been postponed in November 1966 for one year after he had been found guilty of infamous conduct in a professional respect. The inquiry had arisen out of certain false claims to possessing certain medical qualifications which Dr. Grey had made in applying for medical posts. A letter was received from a consultant psychiatrist at a hospital in which Dr. Grey was a patient.

In the case of HENRY JOSEPH CARON, on whom judgement had been postponed in May 1964, May 1965, May 1966, and May 1967, in respect of a charge that in February 1964 he had been convicted of unlawfully procuring dangerous drugs, the Committee determined to postpone their judgement for a further period of six months.

Infamous Conduct

The Committee gave further consideration to charges against HARI CHAND KHANNA, M.B., B.S. 1956, University of Punjab (India), that on 12 May 1965 he was convicted of stealing 11 books valued at £6 15s.; that in March 1966 he had stolen from another doctor 31 N.H.S. prescription forms; that on five occasions between March and May 1966 he had forged documents purporting to be N.H.S. prescriptions signed by another doctor for the supply of drugs to a patient; that on five occasions between the same dates he had obtained or attempted to obtain from a retail chemist various drugs by means of these forged prescriptions; that in respect of this conduct he had appeared at the Stoke-on-Trent Quarter Sessions in May 1966 and pleaded guilty to three offences, and requested eight others of a similar nature to be taken into consideration; and that in relation to these facts he had been guilty of infamous conduct in a professional respect.

The Committee had postponed judgement on these charges for two years in November 1966.

A further charge now before the Committee was that, while employed as locum-tenent registrar in the accident and emergency department of the Nottingham General Hospital, on certain dates between

April and May 1967 Dr. Khanna had stolen various articles belonging to the hospital, and that on certain dates in that period he had stolen from other medical officers and staff at the hospital various items of personal property; that between April and May 1967 he stole from the Derbyshire Royal Infirmary, where he had on two earlier occasions been employed as a medical officer, various quantities of drugs; that in respect of this conduct he had pleaded guilty on 17 May at the Nottingham Magistrates' Court to three charges of larceny and had asked for 23 other offences to be taken into consideration; and that in relation to the facts alleged he had been guilty of infamous conduct in a professional respect.

It was reported that Dr. Khanna had maintained that these further offences were committed under the influence of drugs, and he had stated that he was having treatment for his addiction at the Mapperley Hospital in accordance with the probation order.

A report from a consultant psychiatrist at the Mapperley Hospital stated: "It was my impression at the time (of his admission) that his behaviour was almost certainly the direct result of excessive use of drugs of the amphetamine and barbiturate groups. He admitted to consuming very large quantities of these substances over a period of four years or so, with consequent deterioration both in his general health, his ability to maintain himself in employment, and a total failure to succeed in obtaining the higher qualification in surgery which was his main aim."

After a consideration *in camera*, the PRESIDENT announced the further charge had been proved to the Committee's satisfaction, and it judged Dr. Khanna to be guilty of infamous conduct in a professional respect in relation to these facts. The Committee's concern, said the President, was the greater because of Dr. Khanna's previous record and because within the last fortnight he had pleaded guilty to further thefts and was waiting sentence on that plea.

The Committee decided to postpone judgement until its meeting in February 1968 on its finding that Dr. Khanna had been guilty of infamous conduct in a professional respect.

False Certification and Covering

SURJIT TANDON, M.B., B.S. 1954, University of Punjab (India), appeared before the Committee on charges that in March 1967 she had signed medical certificates in respect of four persons (two men and two women) certifying that they were suffering from injuries or a medical condition and were unable to attend Court, and that she had not seen or examined the persons and had no direct or personal knowledge of their alleged condition as recorded in the certificates. She was further charged that the certificates had to her knowledge been prepared and written, save for her own signature, by Mr. R. R. Facey, who was employed as a secretary in the practice and was not medically qualified, and that the information on the certificates about the alleged condition of the patients had originally been communicated to or acquired by Mr. Facey and not communicated to or acquired by herself. In these circumstances she had knowingly and improperly lent the weight and authority

of her signature, name, and professional opinion to the statements contained in the certificates, "which required and implied the exercise of professional knowledge, skill, and judgement . . ." and in her professional capacity she had caused or permitted the certificates to be issued when they were to her knowledge misleading in that the matters certified were not founded upon her own knowledge and professional judgement of the patients' condition on the relevant date.

A final charge was that to Dr. Tandon's knowledge Mr. Facey on or about 25 or 26 March had interviewed the patients at the surgery premises and examined them, and that she had authorized or permitted Mr. Facey to write the certificates (or had approved them knowing Mr. Facey had written them) on the basis of information acquired by him of the people named in the certificates; and that thereby she had knowingly and improperly encouraged, permitted, or condoned the exercise by an unqualified and unregistered person of the functions of (1) the examination of patients; (2) the assessment of the clinical condition of such patients; and (3) the formation and expression of a medical opinion as to the condition of such patients; "when such functions required the exercise of medical discretion or skill and ought properly to have been exercised by a registered medical practitioner." In relation to the facts alleged Dr. Tandon was charged with being guilty of infamous conduct in a professional respect.

Outline of Case

The Committee was told that all four of the people named in the certificates had been arrested during the small hours of 25 March for offences in respect of which they were subsequently convicted. Later on the morning of 25 March, a Saturday, they were released on bail. On Monday, 27 March, when they had not surrendered to their bail, all except one of the two women were arrested. The officer arresting them found in the possession of one of the men the four certificates which were the subject matter of the charge. Subsequent to the finding of those certificates, the police had been required to investigate accusations that had been made by some or all of the four people of maltreatment of them by the police during the period before they were bailed. It was in the course of those investigations that the police found out more about the injuries certified on the certificates from Dr. Tandon. The nature of the statements made by Dr. Tandon to the police when interviewed by them, and of her statement in reply to a letter from the General Medical Council, were described to the Committee. The statements in some material respects had differed. Dr. Tandon strongly denied in her statement to the General Medical Council the allegation that she had not seen or examined any or all of the four patients. She had seen them at her surgery on the Sunday morning, 26 March 1967, and she had examined them. She had caused the certificates relating to the injuries of the four patients to be made out on the following morning (27 March), and "it was on that morning that I signed those four certificates." Her statement to the police had been made primarily by way of giving answers to questions asked by them.

She had been able to say that Mr. Facey must have seen the patients on 27 March because she understood that he had taken the certificates to them personally and he had told her that the patients would see her on 28 March. "Mr. Facey was not acting on my instructions when he contacted the Court, and it is obvious to me that he had gone much too far to give advice of a legal nature to the patients. . . . Mr. Facey is a West Indian and two of the patients were also West Indians. It could be that he felt he ought to go as far as he could to assist his countrymen."

In evidence Dr. Tandon told the Committee how she had come to examine the four patients mentioned in the certificates on Sunday, 26 March, and confirmed her explanation of the events as given in her statement to the General Medical Council. She maintained that in her statement to the police she had all the time been referring to the Monday. What she told them was: "I have not seen the patients on Monday," not that she had not seen them at all. They must have misunderstood her in this respect. She did not agree that she came to make out the certificates on the Monday simply because of information conveyed to her by Facey, and without having seen the persons concerned at all.

Difficulties of Understanding

Speaking on Dr. Tandon's behalf, Mr. N. LEIGH TAYLOR, of Messrs. Hempsons,

solicitors to the Medical Defence Union, asked whether the Committee could really accept the evidence against her as sufficient in relation to her denials. He submitted that there was a serious risk of her having been misunderstood, and that it would be dangerous to rely on the statements made to the police. They might not, because of difficulties of understanding, have represented a complete record of what she meant.

After a consideration *in camera*, the Committee decided that the facts alleged against Dr. Tandon in the first four charges had been proved to their satisfaction. In the fifth charge it was found proved that Dr. Tandon had known that Mr. Facey on or about 25 or 26 March had interviewed and examined one or other or all of the four people named in the certificates, and it was also found proved that Dr. Tandon had approved the certificates after they had to her knowledge been prepared and written by Mr. Facey.

Plea in Mitigation

Dr. O. C. FORBES, Dr. Tandon's partner, called by Mr. Taylor on her behalf, said that he had been in practice in Birmingham for approximately ten years. He had found Dr. Tandon perfectly satisfactory. She was a person of the highest integrity. "We practise," said Dr. Forbes, "in very difficult circumstances, and what has been on trial

here is not just Dr. Tandon and my particular practice but the difficulties and shortcomings of general practice in a densely populated, migrant area, where sometimes the law and the rules and correct procedure may have to be bent a little in the interests of keeping people alive." These incidents were completely out of character and he believed Dr. Tandon might have been the victim of a conspiracy. He urged that the doctor should not be condemned at the start of her career as a general practitioner merely because she was working in a difficult area and her knowledge of English was less than perfect.

After again deliberating *in camera*, the PRESIDENT announced that the Committee had judged Dr. Tandon to have been guilty of infamous conduct in a professional respect in relation to the facts which were proved against her. It had, however, taken into consideration the testimony, and the assurances given on her behalf, and had determined to postpone judgement on the question of erasure for a period of one year.

Applications for Restoration

The Committee considered applications from CHARLES BRADY, STANLEY MILLAR, and HARRY SIMMONS for the restoration of their names to the *Register* after disciplinary erasure.

All three applications were successful.

Review Body Evidence

Mr. QUINTIN HOGG, Q.C., has been retained in the place of the late Sir JOHN HOBSON, Q.C., to present to the Review Body the evidence on behalf of hospital medical staff.

General Practitioners in Hospital

The Surrey Branch Council of the B.M.A., at a meeting on 8 November, was unanimous in regarding "the further integration of general practitioners into the hospital services as an urgent necessity." The Branch Council stated that it realized that delays in the provision of general-practitioner beds in general hospitals were inevitable, but it thought it was important to find acceptable ways of introducing general practitioners to inpatient work, as has already been achieved in outpatient work.

Expulsion from Membership

The Central Ethical Committee of the B.M.A. recently considered a suggestion that provision should be made in the articles and by-laws

of the Association for the expulsion from membership of members who contravened recommendations of the British Medical Guild.

The Committee reported to the Council on 29 November the solicitor's advice that this was impossible unless the Association became a trade union. When the British Medical Guild had been formed the point had been made that the Association could not compel its members to comply with Association policy. The solicitor had pointed out that that was an essential aspect of the work of a trade union, and was prohibited to a registered company such as the B.M.A. by clauses in its memorandum of articles inserted at the request of the Board of Trade.

Hospital Building

An amendment of the regulations has now raised the financial limit to which regional hospital boards may plan building and engineering schemes without obtaining ministerial approval from £120,000 to £250,000 (exclusive of the cost of fees and equipment). A circular to regional hospital boards (H.M. (67)82) states that the Minister expects boards to continue to use the hospital building procedures (including the application of current cost allowances) in the planning of all schemes financed wholly or partly from

Exchequer funds, even if the cost is less than £250,000.

The circular also states that these changes do not affect the costs at which building schemes have to be included in capital programmes or capital estimates.

Hospitality

A French doctor's daughter, aged 22, living in Paris would like to stay from 21 December to 3 January with a British medical family who have a daughter of similar age.

A Norwegian doctor's daughter aged 20, living in Naresund, would like to stay *au pair* with a British medical family, living in London from as soon as possible for nine months.

A German doctor living in Füssing would like his 18-year-old daughter to stay with a British medical family as a paying guest from 1 April 1968 for six to nine months.

A French doctor living in Tarbes (Hautes-Pyrénées) would be pleased to receive a British doctor's son aged about 15 to stay with his family for 3 to 4 weeks next Easter. The French doctor has a son aged 15 who is interested in Rugby football and swimming.

A German doctor living in Waiblingen would like his 15-year-old daughter to stay with a British medical family for three weeks from 27 July to 17 August 1968. In exchange the doctor would be pleased to receive

a British girl of similar age from 17 August to 7 September.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

H.M. Forces

ROYAL NAVY

Surgeon Commander D. G. Bluett has been placed on the Retired List.

Surgeon Lieutenant-Commander H. E. Black has been placed on the Retired List.

ARMY

Colonel H. V. D'A. Iles, late R.A.M.C., has retired on retired pay.

ROYAL ARMY MEDICAL CORPS

Major J. D. G. Malley, from Reserve of Officers, to be Major.

Captain J. Dowson to be Major.

Short Service Commissions—Major W. J. C. Parker, from Active List, to be Major. Captain E. F. Henderson to be Major.

REGULAR ARMY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Major (Honorary Lieutenant-Colonel) M. M. Medine, M.B.E., having attained the age limit, ceases to belong to the Reserve of Officers, retaining the honorary rank of Lieutenant-Colonel.

Major E. J. Ewell, O.B.E., T.D., has resigned his commission, and has been restored to the rank of Colonel.

Major J. F. Wilson, having attained the age limit, ceases to belong to the Reserve of Officers.

Major J. P. Blandy, from T.A., to be Major. Captain (Acting Major) D. M. Hay, from T. & A.V.R., to be Captain, relinquishing the acting rank of Major.

Short Service Commission—Major T. W. Cross, from Active List, to be Major.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

ROYAL ARMY MEDICAL CORPS

Colonel H. B. Lee, T.D., has been appointed Honorary Colonel, 257 (Eastern) General Hospital (V.) and 221 (Surrey) Field Dressing Station (V.), T. & A.V.R., in a new appointment.

Colonel N. C. Oswald, T.D., has been appointed Honorary Colonel, 217 (Eastern) General Hospital (V.) and 220 (1st Home Counties) Field Dressing Station (V.), T. & A.V.R., in a new appointment. (Substituted for the notification in a *Supplement* to the *London Gazette* dated 4 April 1967.)

Lieutenant-Colonel K. W. N. Palmer, E.R.D., T.D., has been appointed Honorary Colonel, 380 Blood Supply Unit, R.A.M.C. (Volunteers) T. & A.V.R., in a new appointment.

Lieutenant-Colonel H. J. Hambury has been appointed Honorary Colonel, 382 Field Medical Company, R.A.M.C. (Volunteers), T. & A.V.R., in a new appointment.

Major W. A. L. Thompson has been granted the acting rank of Lieutenant-Colonel.

Captain M. Bloch to be Major.

Captain W. V. James has been granted the acting rank of Major.

ROYAL AIR FORCE

Wing Commanders J. G. M. Harrison and M. C. Batchelor have retired.

Squadron Leader E. Anderson has been transferred to the Reserve.

Flight Lieutenant J. A. Baird to be Squadron Leader.

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

Kirk, R. M.: *A Manual of Abdominal Operations*. 1967.

Kraus, F. T.: *Gynecologic Pathology*. 1967.

London, P. S.: *Nursing Emergencies*. 1967.

Macintosh, Sir R., and Mushin, W. W.: *Local Analgesia: Brachial Plexus*, 4th edition. 1967.

Mackichan, N. D.: *Assisting the General Practitioner*. 1967.

Mawson, S. R.: *Diseases of the Ear*, 2nd edition. 1967.

Milner, E.: *Human Neural and Behavioral Development*. 1967.

Murphy, W. T.: *Radiation Therapy*, 2nd edition. 1967.

Novak's *Gynecologic and Obstetric Pathology*, 6th edition. By E. R. Novak and J. D. Woodruff. 1967.

O'Donnell, J. A., and Ball, J. C.: *Narcotic Addiction*. 1966.

Pollock, J. H.: *A Survey of Surgical Shock*. 1966.

Robbins, S. L.: *Pathology*, 3rd edition. 1967.

Silver, H. K., Kempe, C. H., and Bruyn, H. B.: *Handbook of Pediatrics*, 7th edition. 1967.

Simpson, J. F., et al.: *A Synopsis of Otolaryngology*, 2nd edition. 1967.

Slonim, N. B., and Chapin, J. L.: *Respiratory Physiology*. 1967.

Association Notices

Diary of Central Meetings

DECEMBER

- 19 Tues. Liaison Group of Professions on the Monopolies Commission, 2.30 p.m.
- 21 Thurs. Working Party on Amphetamine Preparations, 9.30 a.m.
- 20 Wed. Film Committee, 10 a.m.
- 20 Wed. Staff Side Committee C, Medical Whitley Council (at 41 Belgrave Square, London S.W.1), 10.30 a.m.
- 28 Thurs. Central Ethical Committee, 10 a.m.
- 28 Thurs. Executive Subcommittee (Central Committee for Hospital Medical Services), 10 a.m.
- 28 Thurs. General Purposes Committee, 10.30 a.m.
- 29 Fri. Chairman's Subcommittee (Full-time Medical Teachers and Research Workers Committee), 2 p.m.

JANUARY

- 3 Wed. Private Practice Committee, 2 p.m.
- 4 Thurs. Finance Committee, 2.30 p.m.
- 17 Wed. Annual Meetings Committee, 10.30 a.m.
- 23 Tues. Joint Consultants Committee (at Royal College of Physicians of London), 10 a.m.
- 26 Fri. Venereologists Group Committee, 2 p.m.

FEBRUARY

- 6 Tues. Orthopaedic Group Committee, 2.30 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

BIRMINGHAM DIVISION.—36 Harborne Road, Edgbaston, Tuesday, 19 December, 8 p.m., annual Christmas reception and party.●

BRADFORD DIVISION.—At Outpatient Department, Bradford Royal Infirmary, Tuesday, 19 December. 8.15 p.m., jointly with Bradford Medical-Chirurgical Society. clinical meeting, followed by discussion in Medical Societies' Room.

ROTHERHAM DIVISION.—At Gas Showrooms, Friday, 22 December, 8.30 p.m., champagne party.

Branch and Division Officers Elected

HARROW AND HILLINGDON DIVISION.—Chairman, Dr. D. V. Morgan-Jones. Chairman-elect and Vice-chairman, Dr. J. B. Clark. Honorary Secretary and Treasurer, Dr. P. Knight. Assistant Honorary Secretary, Dr. O. W. Samuel.

ISLE OF MAN BRANCH.—President, Professor T. Ferguson. Honorary Secretary, Dr. L. C. Cowley. Assistant Honorary Secretary and Honorary Treasurer, Dr. J. R. McDonald.

LIVERPOOL DIVISION.—Chairman, Professor F. E. Stock. Vice-chairman, Dr. R. Burns. Honorary Secretary and Treasurer, Dr. W. D. Gray.

MANCHESTER DIVISION.—Chairman, Dr. S. Freeman. Senior Vice-chairman, Dr. A. A. Brown. Junior Vice-chairman, Dr. D. L. Cooke. Honorary Secretary and Treasurer, Dr. T. D. Culbert.

MEDWAY AND GRAVESEND DIVISION.—Chairman, Dr. H. R. Gray. Chairman-elect, Dr. I. G. D. Bell. Vice-chairman, Dr. A. E. Wood. Honorary Secretary, Dr. L. F. McWilliams. Assistant Honorary Secretary, Mr. W. H. C. Hamilton. Honorary Treasurer, Mr. E. J. Greenwood.

MID-HERTS DIVISION.—Chairman, Dr. E. W. Thurston. Chairman-elect and Vice-chairman, Dr. D. C. Beatty. Honorary Secretary, Dr. A. J. B. Luke. Honorary Treasurer, Dr. H. Palmer.

NORTH MIDDLESEX DIVISION.—Chairman, Dr. W. J. G. Meldrum. Chairman-elect, Mr. T. M. Hennebery. Honorary Secretary and Treasurer, Dr. A. M. Freeman.

ROTHERHAM DIVISION.—Chairman, Dr. F. W. M. H. Daly. Chairman-elect, Dr. Mary Hargan. Vice-chairman, Mr. P. D. Livingstone. Honorary Secretary, Dr. R. J. Donaldson. Honorary Treasurer, Dr. R. T. Cooke.

SOUTH WALES AND MONMOUTHSHIRE BRANCH.—President, Dr. J. L. Ryce. President-elect, Dr. Amy Jagger. Honorary Secretary, Dr. S. Gang. Assistant Honorary Secretary, Dr. W. R. King. Honorary Treasurer, Dr. S. Davies.

SOUTH-WEST WALES DIVISION.—Chairman, Mr. S. Morgan. Chairman-elect and Vice-chairman, Mr. R. L. Rees. Honorary Secretary and Treasurer, Dr. J. S. Lewis.

SUFFOLK BRANCH.—President, Dr. J. C. H. Maidment. Vice-presidents, Dr. A. Sherlock, Dr. J. Davis. Honorary Secretary, Dr. R. A. Leader.

THAMES VALLEY DIVISION.—Chairman, Dr. M. G. Webber. Vice-chairman, Dr. P. H. A. Willcox. Honorary Secretary and Treasurer, Dr. D. Paton. Assistant Honorary Secretary, Dr. M. Charrett.

WARRINGTON DIVISION.—Chairman Dr. D. G. Miller. Chairman-elect and Vice-chairman, Mr. W. Wilson. Honorary Secretary and Treasurer, Dr. P. Barber.

WORCHESTERSHIRE AND HEREFORDSHIRE BRANCH.—President, Dr. G. J. Meikle. President-elect, Dr. M. B. McGinn. Honorary Secretary, Dr. A. A. Vickers.

British Medical Journal Supplement

LONDON SATURDAY 23 DECEMBER 1967

CONTENTS

General Medical Services Committee	81	Scottish Committee for Hospital Medical Services	87
Organization Committee	84	B.M.A. Nuffield Library	88
General Medical Services Committee (Scotland)	86	Association Notices	88

General Medical Services Committee

The G.M.S. Committee had some anxiety about the Minister of Health's intentions on hospital private beds. The relevant clauses on the matter in the Health Services and Public Health Bill now before Parliament were the result of a "package deal" agreement between the Minister and the Joint Consultants Committee. A letter from the Minister explained that his purpose was to make the use of beds more flexible, partly so that private patients needing specialist treatment could be accommodated near the facilities they required. The Secretary of the B.M.A. is to ask for clarification of certain points in the clause, and also of clauses to do with the Minister's powers to manufacture "goods." The General Practice Finance Corporation has increased the rate of interest on its loans to 7½%. The Committee agreed that the proposals of a subcommittee of the Welsh Committee of the Association for an experimental scheme for area health boards in Wales should be published and sent to every general practitioner. The Committee's main fear about area health boards was that under them general practitioners would have less influence than they have now. Some speakers thought they would have more.

A meeting of the General Medical Services Committee was held on 7 December, with Dr. J. C. CAMERON in the chair.

and the Committee agreed, that the Chairman of Council and himself should be allowed to take what action was appropriate.

Minister's Remarks

Dr. G. CORMACK referred to some remarks made by the Minister of Health in the course of his Maurice Bloch Lecture at Glasgow University (*B.M.J.*, 16 December, p. 675). He had said that many doctors, perhaps a majority, particularly among the younger doctors, derived great satisfaction from practising their profession in an environment where they could, without hesitating to consider their patient's means, prescribe and carry out whatever treatment they considered was needed. He had continued: "They may well recognize that the Minister's objectives are the same as their own—namely, to provide the best possible service the nation can afford and as quickly as a vast modernization programme permits. But one looks almost in vain to see this attitude reflected in the official voice of the profession or in the public utterances of those who speak for the profession in a representative capacity."

That last remark, said Dr. Cormack, clearly referred to the B.M.A. and its negotiators, and it was tendentious, provocative, and unjustified. The Committee should make the strongest possible representation to the Minister that he should withdraw it.

Other speakers expressed surprise at the nature of the Minister's statement, and suggested that his arguments should be countered.

Dr. W. W. FULTON, who had been present at the lecture, explained that it was one of a series concerning medicine and the community. Most of it had been a historical review and about partnership in medical care, dealing mostly with the administrative side of medicine. Dr. Fulton advised the Committee to do nothing about the remarks, except to maintain vigilance. Dr. I. M. JONES suggested that if a protest was to be made it should be made swiftly, and the Committee should give its chairman power to act. The G.M.S. Committee should point out that its objective was to give the best possible health service to the nation, but that that was not being achieved because of the method of financing the N.H.S.

Dr. D. P. STEVENSON, Secretary, said that if there had been any statement which sought to discredit the profession's representatives it affected others as well as the G.M.S. Committee. He suggested,

Health Services and Public Health Bill

The Committee discussed the Health Services and Public Health Bill (*B.M.J.*, 2 December, p. 562).

Dr. I. M. JONES referred to clauses in the Bill which would enable the Minister to make accommodation in N.H.S. hospitals available for private patients, without the accommodation having to be specially set aside for the purpose. These facilities would be available for "resident patients" who undertook to pay such charges as the Minister might determine. The Minister could determine different charges for different accommodation and for different services and in relation to different circumstances. The provision of private accommodation would not be allowed to prejudice the services available to those who were not private patients.

Dr. Jones said that the Minister was taking powers to change the whole pattern of private bed accommodation in National Health Service hospitals. The effect of the present proposals would be to remove any designated private beds, save possibly in certain specific hospitals. A Minister, said Dr. Jones, did not usually go to the trouble of putting into a Bill powers which he did not intend to use, and this Bill would give him the power to demand that all private patients who wished to occupy private beds in hospitals should go on a hospital waiting list, and even then they would not be guaranteed the type of accommodation which they sought. They might be put into an ordinary ward and charged fees.

This was not only a breach of an undertaking which had been given by Mr. Aneurin Bevan at the start of the Health Service but it ignored the increase in demand for private beds, as shown by the rising membership of various provident schemes. It ignored the expressed desire of the community. Dr. Jones said that the only purpose behind the Minister's proposals was to take a further step on the road to establishing a monopolistic, monolithic machine for organizing medical care which would make it even more difficult for people who wanted to exercise their choice to do so. The Council had agreed to protest on behalf of the Association to the Ministry of Health (*Supplement*, 9 December, p. 71).

Package Deal

Dr. STEVENSON explained that the Council had instructed him to send a letter to the Minister asking to see him on this matter. Dr. Stevenson pointed out that 18 months ago the Minister had asked the Joint Consultants Committee to discuss his proposals for making changes in the provision of private beds in hospitals. He had presented the Committee with a package deal, in which there were at least three important items. Firstly, the Minister intended to carry out a survey of the private bed accommodation throughout the country, and to study it in the light of the comparative bed-occupancy rates in the public and the private sector. When the figures were published they had shown a marked discrepancy between the occupancy rates in the two sectors. In Dr. Stevenson's opinion the figures were distorted because private patients tended to choose when to occupy a bed, and therefore it was not so easy to keep private beds occupied as it was to keep public beds occupied.

The second item in the package deal had been the abolition of the schedule of fees for patients in private beds—a matter of contention for many years. Consultants could now charge what fees they thought appropriate. The third item in the deal had been that, to make more flexible use of pay-beds, it should be possible for patients in private beds to be transferred to public beds. The intention had been to change the existing situation where it was often difficult for patients needing intensive care, or some special facility, to be cared for in a private bed, and there was nothing in the Act which enabled such a patient to be transferred. The Minister had always been permitted to put public patients into private beds, but it was not permissible to transfer a private patient into a public bed because of his medical condition.

The Joint Consultants Committee and the Central Consultants and Specialists Committee, as it was then, had been a party to this package deal (*Supplement*, 21 January, p. 23), and there had been long discussions with the Government on all aspects of it—including the one under discussion, which had been put in largely at the request of the hospital doctors. They had thought that in the long run a flexible use of beds would be to their advantage.

Dr. Stevenson said that there were a number of points which required clarification, and he had written to the Minister asking him to receive a deputation in advance of the general deputation on all aspects of the Bill.

Flexible

Dr. D. L. WILLIAMS said that he favoured private practice, but to defend it on the ground that it gave priority of medical treatment would be a grave mistake. Private practice should be defended because of the relationship between doctor and patient, because of the personal attention of the doctor. He saw no reason for undue worry about the Bill. Though it gave various powers to the present Minister, it was a flexible Bill and it could be used in a different way by a different Minister.

In reply to Dr. A. J. ROWE, who asked whether the Bill was meant to be permissive

or mandatory, Dr. STEVENSON read part of a letter from the Minister in which he explained the intention of the Bill. The existing N.H.S. Acts required beds to be set aside in special accommodation, and particular beds in particular rooms were so designated. "I would prefer," the Minister wrote, "in the interests of flexibility to be able to approve simply the total number of beds in the hospital which at any one time can be used by private patients. Patients requiring specialist treatment could then be accommodated, where this is desirable, near the facilities they needed, in whatever part of the hospital this might be. No doubt hospitals will generally continue to accommodate most of their paying patients in the same way as at present, but the greater flexibility should make it easier to ensure that the fullest possible use is made of all beds."

Dr. CORMACK said that consultants in the Newcastle upon Tyne area were not satisfied with the proposed arrangement. The agreement had been made by the Joint Consultants Committee, which was "not wholly representative." In the teaching hospital in Newcastle the number of pay-beds had been halved. In some hospitals private beds were scattered throughout the hospital for specialist treatment, and there were good grounds for that. A clearly understood procedure for costing pay-beds for each hospital was being abandoned in favour of a national average costing. The Minister could put on any figure he liked. The combination of that dangerous power, linked with the large reduction in the number of pay-beds, could sound the death knell of consultant private practice.

Dr. H. S. HOWIE WOOD was concerned for the future of small cottage hospitals. He knew of one in which there had been eight private beds before the National Health Service. There were now four, and under the new arrangement there would be two. Dr. Stevenson had suggested that pay-beds were a matter which affected consultants rather than general practitioners, but pay-beds in cottage hospitals were an incentive to good general practice. The G.M.S. Committee should do what it could to make sure that they were preserved.

Supply Goods

The CHAIRMAN said that clause 23 of the Bill, which concerned the power of executive councils to supply goods and materials to persons providing certain services, was to regularize the position. Some doubt had been cast on the legality of the Minister's action in arranging for sterile syringes, for example, to be distributed by executive councils. The clause would enable executive councils to supply, with the Minister's consent, to general practitioners, pharmacists, dentists, and opticians any such goods or materials as it seemed to the Minister they needed for providing a service.

Dr. CORMACK said that the clause should be read with clause 30, which stated that the Minister might sell or otherwise dispose of goods "the production or manufacture whereof by him is involved in the provision of hospital and specialist services; and he may produce or manufacture such goods to an extent greater than that necessitated by the provision of such services in order that

they may be supplied to persons other than those to whom they are supplied by way of the provision of such services." That seemed to give the Minister power to manufacture drugs and to distribute them through executive councils, and to require doctors to use them.

Dr. ROWE said that he did not read into it the suggestion that the Minister could manufacture drugs, because elsewhere in the Bill the words drugs and medicines were specifically used where that was intended. However, the CHAIRMAN pointed out that he had been advised that the term "goods" could mean anything.

Dr. STEVENSON said this could be "a serious move on the part of the Government." He said that clause 30 gave the Minister the power to manufacture in excess of hospital requirements. If paragraph 23 referred only to sterile syringes why should it refer to goods and materials being made available to the pharmaceutical services. If the Government went in for the manufacture of pharmaceuticals that could have a serious effect on the drug industry, and that would jeopardize the general practitioners' freedom to prescribe the drug of their choice.

The Committee decided to ask the Minister for clarification of the meaning of these clauses.

Defence Trusts

Dr. J. E. MILLER, Deputy Treasurer of the Defence Trusts, reported that the appeal to local medical committees was going well. However, some had not contributed to the Trusts since 1953. They were Bolton, Cardigan, Durham, Hastings, East Suffolk, Warley, West Bromwich, and West Hartlepool. Orkney, Stirling, and Clackmannan had not contributed since 1955. South Shields had not contributed since 1956; Blackpool, Great Yarmouth, and Wallasey since 1957; Halifax since 1959; Bristol, Lincoln City, and Shetland since 1960; Burnley, Gateshead, and Hull since 1961; Caernarvon since 1962; Dewsbury, Huntingdon and Peterborough, and Liverpool since 1964; and Birmingham, Bury, Carlisle, Dudley, and Lothian and Peebles since 1965. The following had made no contribution in the last year: Aberdeen City, Aberdeen and Kincardine, Banff, Moray and Nairn, Bedford and Luton, Caithness, Denbigh and Flint, Glamorgan, Huddersfield, Middlesbrough, Northumberland, Renfrewshire, Roxburgh, Berwick and Selkirk, and Southampton.

Dr. Miller agreed that some local medical committees thought that, since they had reached their original target by a certain date, they should not pay any more. However, they had been asked for further contributions since that time.

General Practice Finance Corporation

The Committee received a letter from the General Manager of the General Practice Finance Corporation stating that, "with regret," the Corporation's lending rate for fresh loans had been raised to 7½%. The decision had been made only after the bank rate had been raised three times and

because long-term borrowing rates had risen substantially. The increase would be applied forthwith to all fresh loans.

Dr. S. WAND, a member of the Finance Corporation, said that it was much more

concerned with the long-term than the short-term rate. The Corporation had been at pains to keep the rate at 7½% for as long as possible. Every effort would be made to keep the rate as low as possible.

Publicity for General Practice

The Committee considered a memorandum by Dr. W. Hedgcock, Secretary of the Committee, entitled "Favourable Publicity for General Practice." It suggested that certain proposals should be approved for implementation.

The memorandum stated that the majority of editors of medical school magazines would welcome articles about general practice, on vocational training for general practice, and on the organization of general practice. The articles would be distributed as effectively as possible.

The Claire Wand Trustees had recently agreed to award £500 in 1968 for a Claire Wand Fellowship in General Practice. It was to enable a young, recently fully registered doctor of high attainment to undertake a full course of vocational training. Arrangements had been made to advertise the fellowship and to make the appointment. The B.M.A.'s careers department would shortly be advertising regularly in the medical press its offer to give advice on vocational training for general practice and to assist young doctors to find suitable appointments in general practice. It was also suggested that there should be a register of "general practitioners in training." This could be a useful way of making young doctors feel in contact with the B.M.A. through the G.M.S. Committee early in their career.

The memorandum concluded that the biggest deterrent to general-practice recruitment lay in the medical profession itself. It was proposed to submit at intervals appropriate letters from the chairman of the G.M.S. Committee to the medical press and to national newspapers, and to seek further publicity. Their main theme would be to invite all doctors, especially general practitioners, to play their part in encouraging and helping young doctors to train for a career in general practice.

Dr. E. TOWNSEND hoped that these suggestions would be just a first step. Students, when they qualified, tended to be conditioned to hospitals. There was a tendency in universities and medical schools to denigrate general practice, so it should be the G.M.S. Committee's aim to get at the medical student before qualification. Local medical committees and local Divisions of the B.M.A. could help in this.

Career Structure

Dr. B. L. ALEXANDER said that the dean of postgraduate studies in Manchester offered hospital junior staff a plan for a career, and they were given advice on the openings in all the specialties, including general practice. Dr. T. K. COOKE believed that the position would never be altered until a career structure could be offered in general practice. The G.M.S. Committee had always opposed suggestions for a career structure. It had resisted paying a man according to his merits. It had always

come down in favour of not paying one doctor more than another. Such a system would not attract doctors into general practice.

Dr. MILLER spoke of the "jaundiced view" of general practice taken by consultants and hospital staffs, either obliquely or intentionally. All the good work done by articles in students' journals and talking to young men was undone by one single unfavourable action on the part of a consultant who had never been in general practice. A department of general practice should be established in every university town, with the approval of not only the university authorities but also of consultants. At the moment general practice was often joined with social medicine and given a minor part in an already small department. The G.M.S. Committee should take a strong stand now.

Dr. JOAN K. SUTHERLAND disagreed that young men should be tackled in their first year of hospital work. They should not be asked to commit themselves then, but the option should remain open. General practitioners should teach not only in the general practice department but also in the wards. Appointments to the department should lay emphasis on general practice as well as on social medicine.

Dr. C. J. WELLS believed that the education of the future doctor started on the other side of the consulting-room desk, and general practitioners should set an example of what they were trying to do. He feared terms like "social medicine" departments and "community medicine." Dr. A. ELLIOTT reminded the Committee that the report of the Royal Commission on Medical Education would shortly be published. Then the Committee should make its stand. It should say to the Minister, "We expect you to build into the educational system the major specialty of general practice, and we expect you to do it now."

Dr. RIDGE said every family doctor should examine his method of practice and his practice organization. The most powerful incentives were the example set by established general practitioners.

The Committee agreed that the proposals in Dr. Hedgcock's memorandum should be implemented.

Area Health Boards

Dr. G. MURRAY JONES introduced the second report of the Welsh Committee's sub-committee on area health boards. The Council (*Supplement*, 9 December, p. 65) had asked that "the standing committees be asked to forward their further views on the area health boards report to the Welsh Committee not later than three weeks before the date of the January Council meeting." The Council had also decided to set up a working party "to bring the Porritt Report up to date, to study all other relevant reports

on the administrative structure of the National Health Service, and to correlate the views of the standing committees on the subject" before the Minister of Health issued his "Green Paper" on the administrative structure of the N.H.S.

Dr. Jones hoped that the report would receive publicity. Too often the profession had been blamed for destructive criticism of the N.H.S. Here was something which was being offered for its "salvation." He believed that the salvation depended upon decentralization and bringing back a sense of competition. A "Green Paper" was not a policy statement but a paper for information. He hoped that the B.M.A. would keep one step ahead of the Minister of Health.

The Welsh Committee was not saying that area health boards were the solution to all the problems of the National Health Service. It was saying that they should be tried out in Wales. Dr. Murray Jones said the reaction of the local authorities in Wales to the proposals was mixed. Some saw their empires tottering; others thought the proposals sensible.

Local Authority Opinion

Dr. B. D. MORGAN WILLIAMS said that an area health board had been proposed for the Highlands and Islands of Scotland, but he understood that the Inverness Local Medical Committee had thought that the area was too big. It would be difficult for any political party to push this idea through against its own supporters. Local government consisted of supporters of all three parties, and it was likely that the parties would listen to those who took part in local government. It was going to be difficult to convince them that they should lose one of their major functions.

What particularly worried Dr. Williams was the suggested membership of an area health board. It was suggested that there should be included ten representatives of the professions, of whom not less than five would be elected by the medical advisory committee. Even if "not less than five" was seven, how many of those would be general practitioners? The hospital doctors would want one or two, the public health service would want one or two. The general practitioners would be lucky to get more than three out of a total membership of an area health board of 20. That would leave general practice in a less influential position than it was now.

Dr. C. J. SWANSON said that the Birsay Committee (*Supplement*, 8 July, p. 23) had suggested that the best way to administer the medical services of the Highlands and Islands was by an area health board.

Area health boards were a means to an end, the end being the functional integration of the profession. Administrative co-ordination was the first step towards that. It was thought that a population area of about a quarter of a million was right for a board to administer. It would take over all the functions of the Health Service and there would be unity in the profession.

Dr. HOWIE WOOD thought that the experiment of area health boards ought to be tried. An experiment in maximum liaison and co-operation between the three arms of the Service had never been carried out.

Equal Partnership

Dr. D. L. WILLIAMS explained that, according to the Welsh proposals, there would be six or seven area health boards under a Welsh Health Council. It was proposed that there should be equal partnership between the public and the health professions in running the service. Each side of the area health board should be elected and not selected. It was hoped that the local authorities would not be losing power, but in fact in many ways they would be gaining it. At the moment they were completely unrepresented in the administration of the hospitals. The Welsh Health Council would be composed of a Welsh board of health on one side and of the representatives of the area health boards on the other. The idea was that they should settle the problems of the Health Service over the table and be involved in the running of the Service. That was thought to be a way of reconciling central planning with Ministerial responsibility.

Objections have been made about the position of general practitioners. Ideally, Wales would like to eliminate the tripartite administrative system, but it did not think it could go so far as Dr. Swanson would like to in one move. Dr. Williams thought the position of general practitioners would be not only safeguarded but strengthened. Their status as independent contractors would be preserved, and local medical committees would acquire greater powers, because they would act as the subcommittee in general practice of the main medical advisory committee of the area board. General practitioners would be represented on the medical advisory committee of the board. It did not matter how many representatives they would have on the board itself; it was more important to influence the policy decided in the main medical advisory committee of the board, on which general practice would be strongly represented. The interests of general practice lay also in the other branches of the Service.

Dr. Williams said he believed that area health boards would be one of the corner-

stones in the rebuilding of the Health Service. The demand for devolution of control did not spring from Welsh or Scottish nationalism but from a wish to bring control of the Health Service nearer to the people. That was a movement that all could support. The Welsh Committee's report was for discussion.

Dr. SPEAKMAN formally proposed that the report should be published, and sent as soon as possible to every doctor in the country for discussion and debate. He said that the profession must not make the mistake that it made in 1948. This time it must be ahead of the politicians.

Integration

Dr. RIDGE said he wanted to amend Dr. Speakman's motion, so that in addition to sending the report to every doctor the G.M.S. Committee should send out a commentary on it. It was assumed that functional integration would automatically follow administrative integration. In Dr. Ridge's opinion that was a delusion. The working together of individuals from different branches of medicine depended not so much on the administrative set-up as on the people themselves. It was up to the profession to integrate itself. Integration would not follow from integration of the administrative organization.

Dr. Ridge referred to the following statement in the report: "The National Health Service as a whole is necessarily responsible to the public, both in total and in detail, for the public money it spends, and answers at present to Parliament. It is therefore suggested that, while the Minister should continue to be responsible to Parliament for the adequacy of the total sum allotted to the Welsh Health Services, the Welsh Health Council should divide this sum between the area health boards."

The profession, said Dr. Ridge, had just achieved a revolution in that it had got away from a fixed sum in remuneration, yet now

the report was asking to go back to a fixed sum to be divided out. Supposing that there was a sudden increase in population in Wales, or there was an epidemic which called for extra resources, where would the money come from? To go back to a pool system of remuneration would be dangerous.

The second point was one of status. For anyone to suggest that a local medical committee which was a subcommittee of a medical advisory committee, and which influenced the area health board through the medical advisory committee, was in any way comparable to the existing relationship between an active local medical committee and an executive council was to be deluded. General practitioners had secured under executive councils a position of strength, of which there was no parallel anywhere else in the Health Service. General practitioners could occupy key positions in executive councils. Dr. Ridge said that he could see nothing but a reduction in their status under the suggested arrangement.

Dr. D. L. WILLIAMS, in reply, said it was not suggested that local medical committees should be a subcommittee of the medical advisory committee. They would have two functions; firstly, the existing ones, and, secondly, they would act as the subcommittee of the medical advisory committee. It was a dual purpose committee. A lot of what Dr. Ridge had said stemmed from a natural wish not to want to change the *status quo*.

The Committee accepted Dr. Speakman's motion to publish the document and to send it as soon as possible to every general practitioner in the country, for discussion and debate.

It also set up a working party to send out a commentary, as suggested by Dr. Ridge, at a later date, and also to act in accordance with the Council's request to formulate the G.M.S. Committee's views on the administration of the Health Service. The working party was to be asked to prepare a report on the advantages and disadvantages of area health boards, and it was decided that it should consist of members who were for and who were against the scheme.

Organization Committee

A meeting of the Association's Organization Committee was held on 7 December. Dr. J. S. NOBLE was in the chair.

Honorary Secretaries Conferences

The CHAIRMAN presented a report of the Chairman's Subcommittee.

He said that it had considered the future of the conferences of B.M.A. honorary secretaries and it recommended: (1) that an annual United Kingdom conference of honorary secretaries in London was essential, and, in the light of the present need to recruit new members, it was imperative; (2) that the annual conference for newly elected honorary secretaries was also valuable, but, to save money, it should be reduced to one day, immediately preceding the United Kingdom conference; and (3) that, in order to obtain "the optimum value from both conferences," the Organiza-

tion Committee should determine the agenda and arrangements. The Subcommittee believed that conferences of honorary secretaries in regions could also serve a valuable purpose, particularly in future in association with B.M.A. regional councils.

Dr. S. WAND, Treasurer, drew attention to the current financial difficulties of the Association (*Supplement*, 9 December, p. 66), and said that before the Committee agreed that an annual United Kingdom conference of honorary secretaries was essential it should first consider whether there had been any adverse results from not holding the honorary secretaries conference in 1967.

Dr. J. S. ROSS said that a well-organized honorary secretaries' conference was really a "sales drive." It was the time when honorary secretaries should be inspired to recruit new members.

Dr. C. C. LUTTON suggested that there should be a meeting of honorary secretaries

twice a year in every branch area, and an effort made to ensure that at least one representative from each of those meetings attended the central annual conference. He thought that failure to hold an honorary secretaries' conference would have a severe effect on membership in two to three years' time.

Dr. WAND asked whether there was any evidence that the honorary secretaries' conference increased membership, or that the failure to hold a conference last year had been regarded throughout the country as a mistake.

Dr. J. M. DUNLOP supported the continuance of the conference of newly appointed honorary secretaries because it gave them the opportunity to meet B.M.A. staff, which was helpful. Dr. R. P. HENDRY said that he had always thought that the honorary secretaries' conferences were worth attending. The conference was a non-policy-making body, but it was not precluded from dis-

cussing* politics nor from making recommendations to the committees of the Association.

Mutual Need

Dr. A. W. MACARA considered that it was essential to hold the newly appointed honorary secretaries' conference. A newly appointed honorary secretary could not hope, he said, to understand what made the Association tick unless he saw it working at the centre. Dr. Macara did not think any useful economy would result by reducing the length of the conference from two days to one.

Dr. D. BURRELL said that the honorary secretary should feel as needed at Headquarters as Headquarters needed him in the periphery, and without some contact with the central organization keenness in the Division tended to slacken.

The CHAIRMAN suggested that the first recommendation might be taken in two parts. First, he proposed, and the Committee agreed, that an annual U.K. conference of honorary secretaries in London was desirable.

Secondly, he proposed that, in the light of the need to recruit new members, it was imperative to hold a conference in 1968.

Dr. WAND suggested that there was no evidence to show that in the past such conferences had helped recruiting.

The CHAIRMAN reminded Dr. Wand that the Organization Committee had been asked to organize a recruiting drive, and the basis of that drive was that honorary secretaries "should be instructed in an expert manner on recruitment." Of course, said Dr. Noble, there was no evidence to show that a conference had helped recruiting, but he considered that the Council should make the final decision, and that the Organization Committee should base its recommendations on what it believed to be in the best interests of the Association.

Dr. A. N. MATHIAS, Chairman of Representative Body, said that if honorary secretaries were to be recruiting officers then regional conferences would be more valuable than central conferences, because areas where recruitment was particularly needed could be identified.

Dr. R. A. A. R. LAWRENCE moved by way of amendment that the second part of the recommendation should read "and to assist honorary secretaries to deal with proposals relating to organization and recruiting, a conference should be held in 1968."

The amendment, duly seconded, was carried.

The substantive motion was carried by 10 votes to 2 votes.

Dr. DUNLOP moved that the words "also valuable" in recommendation (2) should be deleted and the word "essential" substituted.

The amendment was carried.

The remaining recommendations, as set out, were adopted.

Hastings Wine Club

The CHAIRMAN welcomed Dr. H. G. Dowler, chairman of the Hastings Wine Club, and Dr. L. S. Potter, its secretary, and invited Dr. Dowler to report on the club's activities.

Dr. DOWLER reported that the Hastings Wine Club was a success and its finances were in a healthy state. It gave a service to members which cost the Association nothing. The number of members at present was about 5,500, and the number was increasing. The club's aim was to encourage its members to learn about and to appreciate wines, for which purpose it organized tours of vineyards and arranged wine tastings.

Referring to the trade discount scheme introduced recently by Independent Medical Services Ltd., which included wines and spirits, Dr. Dowler recalled that when he took part in a Council debate on the matter he had expressed the view that it was wrong in principle for a service sponsored by the B.M.A. to set up in direct competition with a service already given by the Association (*Supplement*, 4 November, p. 34). Dr. Dowler also refuted some of the suggestions made in that debate by Dr. I. M. Jones, including the suggestion that the Hastings Wine Club was bound hand and foot to a particular firm.

Dr. J. F. PIGOTT said that the Hastings Wine Club had an educative and social function, and he deprecated the competition from within the Association. There was little reason why Independent Medical Services should compete with the Hastings Wine Club, and he suggested that it should be asked to desist from doing so and to concentrate on its other activities.

Professor D. E. C. MEKE said that the I.M.S. scheme might have set a precedent for all sorts of outside bodies to enter into competition with the Association's activities. He suggested that the Organization Committee should deprecate the action of the Council in facilitating competition from an outside body with the activities of the Association.

The Committee agreed to convey its regret to the Council that the Council had seen fit to sponsor a body other than the Hastings Wine Club "in relation to the supply of wines and spirits to members."

Constitution

The Committee gave further consideration to proposals for the reform of the constitution of the Association, which had been submitted by the East Yorkshire Branch.

Dr. R. L. Luffingham and Dr. W. Ferguson, of the East Yorkshire Branch, attended the meeting and answered a number of questions on specific points raised by members of the Committee. The matter is to be discussed again at the next meeting of the Committee.

Election Addresses

The Committee adopted a recommendation of the Chairman's Subcommittee that the existing procedure governing the support that could be given to candidates in the elections to the Council should be discontinued and replaced by the following procedure: (1) an election address not exceeding 325 words from each candidate could be issued with the voting papers; (2) the names of the sponsors should appear on either the voting paper or the election address; and (3) no other form of

written canvassing, paid for either from private funds or from Association funds, should be permitted.

The Committee also agreed that the procedure adopted for the support and distribution of election addresses in elections to the Council should apply also to elections of representatives of constituencies to the Representative Body and to elections of representatives of constituencies to the Junior Members Forum.

Junior Members Forum

Dr. PIGOTT drew the Committee's attention to a resolution of the Hospital Junior Staffs Group Executive Committee in which it was pointed out that the H.J.S. Group Council was disturbed by the increasing electoral function of the Junior Members Forum.

The Group Council considered that, as the name suggested, the Junior Members Forum was a discussion group where junior members of the B.M.A. in all branches of the profession could meet and exchange ideas. The Group Council did not think the Junior Members Forum should be a policy-making body, and it was concerned that representatives elected by the Forum had at times claimed to speak for hospital junior staff. The Group Council emphasized its belief that any representation of young general practitioners and hospital doctors should come from the Assistants and Young Practitioners Subcommittee and the Hospital Junior Staffs' Group Council respectively.

The CHAIRMAN pointed out that under the revised constitution of the Association the Assistants and Young Practitioners Subcommittee and the Hospital Junior Staffs Group Council were represented on both the Council and the Representative Body. The Junior Members Forum had two representatives on the Representative Body, one of whom must be engaged in other than general practice or the hospital service, and similarly would have two representatives on the Council.

After a short discussion the Organization Committee expressed its sympathy with the views outlined in the resolution, and remitted it to the Chairman's Subcommittee for further consideration, in consultation with the junior-member bodies concerned.

Branches

The Committee adopted recommendations by the Committee on Overseas Affairs that the Borneo Branch of the Association should be dissolved and the possibility of its affiliation with the Sarawak Medical Association be explored, and, similarly, that the Fiji Branch of the Association should be dissolved and the possibility of its affiliation with the Fiji Medical Association be explored.

Membership

The CHAIRMAN reported that the membership figure of the Association was 66,619, compared with 69,747 for the comparable period in 1966. The "home" membership was 49,173, compared with 49,694 for the comparable period in 1966.

General Medical Services Committee (Scotland)

The General Medical Services Committee (Scotland) met on 7 November. Dr. ALISTAIR CLARK was in the chair.

Highlands and Islands

Dr. C. J. SWANSON, chairman of the Highlands and Islands Practitioners' Subcommittee, presented the Subcommittee's comments on the Birsay report (*Supplement*, 8 July, p. 23). He said that, though the Subcommittee endorsed most of the recommendations in the report, it had not supported the recommendation for a Highlands and Islands practice allowance (H.I.P.A.). Instead the Subcommittee preferred the continuance of inducement payments. Much attention had been given to the suggested establishment of a Highlands and Islands Area Health Board.

The Subcommittee had been in favour of that, and had suggested that a small "lay" majority on the board would be advantageous and that the lay members should be appointed by the Secretary of State for Scotland rather than by the local authorities. The Subcommittee had been in no doubt that up-to-date transport and communications were the overriding considerations, and that until these facilities were adequate there could be no resiting of practices.

Dr. S. PEACE said that he and his colleague Dr. D. D. Johnstone were preparing a paper on a salaried service. They had decided that there were two issues which needed clarifying: (1) the definition and function of a general medical practitioner and of his ancillary staff, and (2) the contractual relationship which the doctor in a salaried service would have to accept with the Scottish Home and Health Department. The general practitioners in Orkney were in favour of examining "payment by salary."

Dr. C. S. SANDEMAN did not think it would be feasible to administer the Area Health Board for the Highlands and Islands from either Glasgow or Edinburgh in preference to Inverness.

It was agreed to revise the Subcommittee's comments on the Birsay Report, after which they would be presented to the Scottish Home and Health Department by the Chairman's Subcommittee, together with the Highlands and Islands Practitioners' Subcommittee, on 12 December.

Dispensing Doctors

Dr. SWANSON reported on a meeting held with the Scottish Home and Health Department on 1 November.

There had been an interchange of views, he said, on the principles of dispensing and the differences in practice between Scotland and England. A case had been put forward for a realistic dispensing capitation fee negotiated on the basis of a percentage of what it cost a doctor to "physic" a patient. The fee would vary according to the dispensing statistics of the doctor.

Matters for Further Discussion

The Committee considered a letter from the Dundee Local Medical Committee about reclaiming selective employment tax for part-time employees.

Dr. D. W. K. BUCHANAN said that it should not be necessary to reclaim from two sources. It should suffice to reclaim from the executive council without recourse to the Ministry of Social Security.

It was agreed to take the matter up with the Scottish Home and Health Department.

The General Practice Finance Corporation was criticized again by the Committee for its failure to include loans for equipment. It was decided again to urge on the Scottish Home and Health Department that there should be no need to prove difficulty in borrowing elsewhere, since already the Government possessed reserve powers under the N.H.S. Act, 1966, which could be implemented.

A letter from the Scottish Home and Health Department was before the Committee concerning the scheme for the reimbursement of rent and rates and the "grossing-up" factor to be applied when the practice premises formed part of a doctor's residence. The Committee found it difficult to deal with this matter without fuller financial data, and it was agreed to ask the Department to provide this.

Dr. J. S. GARDINER reported that open access by general practitioners to the radiology department at Falkirk Royal Infirmary had been withdrawn since July without prior consultation with the local doctors. The matter had been taken up with the Western Regional Hospital Board, but to no avail.

The Committee received a circular, which was being issued to executive councils, which described the arrangement for registering adopted children with an N.H.S. doctor.

Dr. JOAN K. SUTHERLAND inquired whether adequate precautions were taken to ensure that the name of the child to be adopted was removed from the medical card before it was forwarded to the executive council.

The Committee received a note on the N.H.S. (Scotland) Hospital Statistics.

Dr. W. M. PATTERSON pointed to the need for publicity about hospital consultations which were not taken up. For instance, the number of outpatients who had not kept appointments at the orthopaedic department of the Edinburgh Royal Infirmary was approximately 30%, he said, and he suggested that a notice might be displayed in doctors' surgeries advising that patients who were unable to attend hospital at the time of their appointments should let the hospital know.

The Committee had been approached by the Scottish Home and Health Department about the appointment of a whole-time locum for general practitioners in Shetland, whose salary would be guaranteed by the Zetland Local Medical Committee.

Dr. PEACE referred to the difficulty in Shetland and in Orkney in procuring locums for holidays and emergencies, and he commended the scheme.

The Committee decided first to get the agreement of the Zetland Local Medical Committee and then to encourage the idea at the Scottish Home and Health Department.

Ambulance Service

The Committee discussed the question of the number of general practitioners who could be nominated to the regional committees of the St. Andrew's Scottish Ambulance Service. Many speakers were not satisfied that two general practitioner members out of a total regional committee membership of 12 was adequate, and it was suggested that four general practitioners would match the number of members nominated by the hospitals—that is, two from the regional hospital board and two from hospital boards of management.

It was agreed that meantime local medical committees should be asked to submit nominations at once to the General Medical Services Committee (Scotland), who would appoint two for each region from such nominations.

Medical Care of Hospital Staff

It was reported that the Scottish Committee for Hospital Medical Services was considering recommending to the Scottish Home and Health Department that the routine medical care and pre-employment examination of hospital staff should be undertaken by general practitioners appointed by hospital boards for this purpose. At present these duties were undertaken in many hospitals by hospital junior medical staff.

Dr. S. J. HADFIELD, Scottish Secretary, explained that the matter would be dealt with in detail in the report of the Joint Committee on the Health of Hospital Staff, under the chairmanship of Sir Ronald Tunbridge.

The Committee agreed to consider the matter again when the report was available.

Single-handed Rural Practitioners

The Committee considered a report that the Rural Practitioners Subcommittee had recently reviewed the existing position of single-handed rural practitioners.

The Subcommittee considered that these doctors were in a disadvantageous position in many ways, but chiefly because of their inability to qualify for the group practice allowance of £200 per doctor. Information had been collected from local medical committees interested in this matter, and it was hoped to make progress with the Home and Health Department on a suggestion that the words "common main surgery" should be removed from the regulations, thus facilitating the formation of groups.

The Committee adopted a resolution of the Subcommittee, which stated that it was not in favour of closing the rural practitioners' fund and incorporating mileage payments in the basic practice allowance, but that it

would accept a proposal to negotiate for "new money" from which mileage payments for maternity medical services should be made.

Reports

The report of a joint medical planning committee on health centres and other "joint-user" premises in Renfrewshire was received.

The Committee decided to remit the report to its Planning Subcommittee for consideration.

Dr. JOAN K. SUTHERLAND pointed out that the Scottish General Dental Services Committee had expressed disquiet about the general development of health centres and had recommended that close co-operation on the matter between the G.M.S. Committee (Scotland) and the Scottish General Dental Services Committee should be maintained.

Another report received by the Committee was the eighteenth report of the Scottish Medical Practices Committee.

The Committee discussed the problem of designated areas, and Dr. W. K. DAVIDSON thought it was time to determine the criteria to be used for classifying an area as "designated." In this connexion it was decided to ask the Planning Subcommittee to consider certain paragraphs of the report.

Dr. SWANSON said that in 1966 only 17 partnership agreements had been granted certificates under Section 36(9) of the N.H.S. Act, 1947, out of a total number of 129 partnerships formed. He stressed the importance of submitting agreements for proposed partnerships to the Scottish Medical Practices Committee.

A memorandum by Dr. C. DALE FALCONER, Assistant Scottish Secretary, entitled "Disaffection Towards General Practice," was received.

The CHAIRMAN said that the document aimed to set out the underlying causes of the current discontent with general practice in the profession which had resulted in fewer doctors entering this branch of medicine.

The Committee decided to consider the document at its next meeting.

Repeat Prescriptions

Ayrshire Local Medical Committee submitted for the Committee's consideration a special card in current use for repeat prescriptions.

The Committee resolved that it was not in favour of the introduction of a card for repeat prescriptions as a general rule, though it was appreciated that general practitioners were at liberty to use these in their practices if they wished to do so.

Scottish Committee for Hospital Medical Services

The Scottish Committee for Hospital Medical Services met in Edinburgh on 4 December. Mr. N. G. C. HENDRY was in the chair.

The CHAIRMAN welcomed Drs. W. Norris, B. Groden, G. M. McAndrew, and K. Sinclair as new members of the Committee.

The Committee agreed with the suggestion of Dr. J. G. M. HAMILTON, Chairman of its Finance Subcommittee, that the title of the Central Consultants and Specialists Committee (Scotland) Fund should be changed to accord with the new title of the Committee. In future the Fund would be known as the Scottish Hospital Medical Services Committee Fund.

Remuneration

A paper was received from the Scottish Home and Health Department setting out suggestions for the pay of general practitioners and others who, though not consultants, were undertaking unsupervised specialist work in certain remote areas. It was reported that the General Medical Services Committee (Scotland) would be examining this document and that there would be a joint meeting with the Home and Health Department to discuss the arrangements.

The CHAIRMAN pointed to the need for some sort of scrutiny of those doctors who were undertaking this work to ensure that their competence and qualifications were suitable. Dr. H. M. URQUHART said that the Committee should not agree to any scrutiny that excluded the thoroughly competent doctor who nevertheless had no higher qualification.

Mr. R. J. A. FRASER considered that the suggestions for special remuneration should be supported, and that the document before the Committee should be used as a basis for discussion.

Hospital Posts

Professor A. FORRESTER submitted a memorandum from the Committee's Anaesthetic Services Subcommittee about senior registrars in the specialty of anaesthetics in Scotland. The memorandum provided figures which showed that in the past two years experience had confirmed the subcommittee's conclusion that the establishment for senior registrars in this specialty was insufficient to provide an adequate number of fully trained and qualified consultants for the expected consultant vacancies. It was submitted that the minimum number of senior registrar posts for the next year should be 24, which was two more than the revised establishment as it now stood.

The Committee agreed to pass the memorandum to the Joint Consultants Committee (Scotland) with a request that it should be submitted to the Scottish Home and Health Department.

The CHAIRMAN remarked that it was encouraging that note was being taken of such documents by the Scottish Home and Health Department.

The Committee was pleased to note that there had been an improvement in the amount of consultation with local doctors before consideration of the establishment of a new medical assistant post. It was reported from each region that the deficiencies in such consultations were being eliminated, and that the Advisory Committee on Consultant Establishments was now being informed of the views of regional committees as well as all other relevant information, when it was considering a request for the establishment of a new post.

The Committee discussed the machinery for the consideration of the report of the Joint Working Party on the Organization of Medical Work in Scotland. Arrangements had already been made for regional discussions. It was decided to obtain copies for hospital junior staff group committees, and

to provide at least one copy in each hospital for the junior staff. Arrangements were made to collate the views of regional committees and to put these before the Committee at its meeting in February.

Dr. HAMILTON said that the main purpose of the report was to suggest lines on which experimentation might follow. Dr. C. D. NEEDHAM did not agree that the tentative nature of the suggestions of the report, if they were there, could be gleaned from reading it.

Joint Consultants Committee

Dr. A. ALLISON spoke of the work of the Joint Consultants Committee (Scotland) since the last meeting. Much of the business was still under discussion with the Scottish Home and Health Department, and reports and papers on various points were awaited. The Committee was still considering its constitution and terms of reference, including the problem of representation of hospital junior staffs on the committee.

Dr. Allison reported that, owing to other commitments, Dr. C. W. Clayson had found it necessary to resign from the Advisory Committee on Consultant Establishments. The Joint Committee's nomination of Mr. J. R. Cameron, P.R.C.S.E., to replace Dr. Clayson had been accepted by the Scottish Home and Health Department.

Dr. Allison informed the committee that Dr. J. G. M. Hamilton had attended, on behalf of the Joint Consultants Committee (Scotland), a conference to consider certain aspects of the Report of the Committee on Senior Nursing Staff Structure (Salmon Committee). Dr. HAMILTON said he would be submitting a report on the conference to the Joint Consultants Committee (Scotland).

Referring to the circular on professional and study leave (S.H.M. 29/1967), Dr. C. J. MACKINLAY said that he was in no doubt that junior staff seemed happier now that something was being done for them in this matter.

The CHAIRMAN said that the Committee would like to know of instances where study leave had been held up by lack of finance. Dr. W. P. U. KENNEDY said that the South-eastern Regional Board seemed willing to pay the expenses of a doctor still in post, but this did not always apply, for example, if someone left a post to take a membership course.

Dr. GRODEN, who represented the Western Region, said that after some initial troubles all was now going well.

Health Service Inquiry

Reference was made to the statement by the Secretary of State for Scotland that he proposed to hold an inquiry into the structure of the Health Service. A paper for discussion from the Scottish Home and Health Department was still awaited.

It was reported to the Committee that the Chairman of the Association's Scottish Council had called a meeting of the chairmen of the principal committees of the Association in Scotland to discuss the method of dealing with the matter. The Chairman of the Scottish Council had said he was anxious that the profession should have an agreed attitude towards integration.

The Scottish Committee for Hospital Medical Services had not formulated a policy on integration, and the Committee agreed to await the discussion paper from the Scottish Home and Health Department before discussing the matter further.

The Committee discussed the Welsh Committee's proposals for a scheme for area health boards in Wales, and it was pointed out that it seemed that half the members of the board would be nominees of local authorities.

The Committee doubted whether this would be acceptable to hospital medical staff. It was agreed that when the document setting out the proposals was published it should be

sent to regional committees for comment, and also to hospital junior staff group committees.

Other Matters

The Committee received a report that the Scottish Home and Health Department was considering what system could be introduced to control capital expenditure by "starting dates," similar to the system which had been agreed in England and Wales. The system in Scotland might necessarily differ, but the idea behind it was to control capital building by regulating the input of new schemes into the programme rather than by requiring the expenditure to conform closely each year to an approved financial estimate.

In response to an invitation to submit views on the future development of the artificial limb services to a working party of the Scottish Home and Health Department, members of the Committee expressed satisfaction with the service provided, and the Committee as a whole thought it had no particular comment to offer. It was suggested, however, that general practitioners might have comments and suggestions to make, and the matter was referred to the G.M.S. Committee (Scotland).

It was reported to the Committee that the Western Regional Hospital Board had, on instructions from the auditors, discontinued an arrangement by which hospital doctors were paid mileage allowance by a lump sum based on an estimate of their mileage.

The Committee agreed that such a system saved both money and trouble, and that an approach should be made to the Scottish Home and Health Department with a suggestion that the system might be re-introduced.

The Committee was informed of the relevant clauses of the Health Service and Public Health Bill which affected the Scottish Hospital Service.

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

- Schneyer, L. H., and Schneyer, C. A. (Editors): *Secretory Mechanisms of Salivary Glands*. 1967.
 Stafford-Clark, D.: *Psychiatry for Students*, 3rd edition. 1967.
 Steptoe, P. C.: *Laparoscopy in Gynaecology*. 1967.
 Talbot, C. H.: *Medicine in Mediaeval England*. 1967.
 Taylor, R. G. W.: *Practical Cytology*. 1967.
 Watson, E. H., and Lowrey, G. H.: *Growth and Development of Children*, 5th edition. 1967.
 Wolstenholme, G., and Porter, R. (Editors): *Drug Responses in Man*. 1967.
 Wyburn, G. M., Warbrick, J. G., and Todd, M. E.: *Concise Anatomy*. 1967.
 Young, J. Z.: *The Memory System of the Brain*. 1966.

Hospitality

A German doctor living in Marl would like his 16-year-old daughter to stay with a British medical family from 28 June to 8 August as a paying guest, and would like her to attend English classes.

A South African doctor living in Johannesburg would like his 13-year-old son to stay with a British medical family during July 1968 on an exchange basis.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

Association Notices

Junior Members Forum

The Junior Members Forum will meet at Birmingham University on Saturday, 6 April, and Sunday, 7 April, 1968, under the Chairmanship of Dr. A. W. Macara, of Bristol. Official representatives to the Forum are drawn from junior members in the hospital service, in general practice, in public health, among university teaching staff, in the armed Forces, in industrial medicine, and in research and administration. In the case of both the hospital service and general practice Great Britain and Northern Ireland are divided into 21 electoral regions.

For the purpose of the Forum the term "junior member" is defined as "young member within 12 years of provisional registration and under the age of 40." Nominations for election of representatives are now being invited from Divisions, hospital junior staffs regional groups, and other bodies within the Association. In addition, individual junior members of the B.M.A. are invited to submit nominations for election. Such nominations should be made and seconded by junior members, with the consent of the nominee, and sent to the Secretary of the British Medical Association, Tavistock Square, London W.C.1, not later than Monday, 22 January.

D. P. STEVENSON,
Secretary.

Diary of Central Meetings

DECEMBER

- 28 Thurs. Central Ethical Committee, 10 a.m.
 28 Thurs. Executive Subcommittee (Central Committee for Hospital Medical Services), 10 a.m.
 28 Thurs. General Purposes Committee, 10.30 a.m.
 29 Fri. Chairman's Subcommittee (Full-time Medical Teachers and Research Workers Committee), 2 p.m.

JANUARY

- 3 Wed. Occupational Health Committee, 10 a.m.
 3 Wed. Private Practice Committee, 2 p.m.
 4 Thurs. Finance Committee, 2.30 p.m.
 17 Wed. Annual Meetings Committee, 10.30 a.m.
 23 Tues. Joint Consultants Committee (at Royal College of Physicians of London), 10 a.m.
 26 Fri. Venereologists Group Committee, 2 p.m.

FEBRUARY

- 6 Tues. Orthopaedic Group Committee, 2.30 p.m.

Branch and Division Meetings to be Held

HARROW AND HILLINGDON DIVISION.—At Edith Martin Memorial Hall, Roxeth Hill, Harrow, Friday, 29 December, 7.30 p.m., teens and twenties Christmas dance.

ST. MARYLEBONE DIVISION.—At 11 Chandos Street, London W., Wednesday, 27 December, 8.30 p.m., general meeting and election of representatives to Annual Representative Meeting.

British Medical Journal Supplement

LONDON SATURDAY 30 DECEMBER 1967

CONTENTS

Central Committee for Hospital Medical Services - - - - -	89	H.M. Forces - - - - -	94
Increases in Prescriptions - - - - -	91	Public Health Medical Officers' Salary Claim - - - - -	94
Services for Epileptics - - - - -	91	Fellowship and Awards for Medical Research - - - - -	94
Committee on Medical Science, Education, and Research - - - - -	92	Diary of Central Meetings - - - - -	94

Central Committee for Hospital Medical Services

The Welsh Committee's second report on area health boards did not get a ready welcome from the Central Committee for Hospital Medical Services. It recommended that the report should not be published without further amendment. Hospital junior medical staff are to have four instead of three seats on the Negotiating Subcommittee and the size of the Subcommittee is to be increased from 15 to 16 members. A memorandum from the Junior Hospital Doctors Association on the representation of junior staff was referred to the Hospital Junior Staffs Group and to the Joint Consultants Committee for comment before the Executive reported its views on it to the Committee. The Committee was dissatisfied about the Minister's action on private hospital beds, and the Joint Consultants Committee is to be asked to send a deputation to the Ministry. Lord Platt, Chairman of the Advisory Committee on Distinction Awards, addressed the Committee in private.

A meeting of the Central Committee for Hospital Medical Services (C.C.H.M.S.) was held on 14 December. Mr. H. H. LANGSTON was in the chair.

The Committee, as a constituent body, gave its formal support to some proposed changes in the composition of the Joint Consultants Committee.

Area Health Boards

The CHAIRMAN reported that the Welsh Committee had produced its second report on area health boards, which it had sought permission of the Council to publish. The Council, at its meeting on 25 October (*Supplement*, 4 November, p. 29), had deferred consideration of the report until it had obtained the comments of the Association's principal standing committees. The report had been referred by the C.C.H.M.S. to Mr. D. Lloyd Griffiths, Mr. H. A. Kidd, and Dr. G. E. Owen Williams to consider.

Mr. H. A. KIDD referred first to the constitution of an area health board, as proposed in the Welsh Committee's report, of 10 public representatives elected by county and county borough councils and 10 representatives of the professions, of whom not fewer than five would be elected by the medical advisory committee. He said there was no objection to that, provided the medical representatives were in active practice.

The second and, in Mr. Kidd's view, more worrying matter concerned private practice. It was doubtful whether there was any real provision for, and indeed little intention of provision being made for, private practice in Wales. "I see this pilot scheme as one which is intended to do away with private practice," he said.

Thirdly, Mr. Kidd thought that if the experimental scheme came into operation in Wales there should be a referendum on it at the end of five years.

Mr. D. LLOYD GRIFFITHS said that, though there was much in the report that was acceptable, it was not a good pilot experiment because it could never be undone once it was started. It would be a great pity if the success or failure of a scheme in Wales was to be a guide to the outcome of similar schemes in many parts of England where circumstances were quite different.

Dr. G. E. OWEN WILLIAMS suggested that the report seemed to have been produced by a group of enthusiasts and added to by

further enthusiasts. In his view the Committee should reserve its position on the question of hospital administration.

Dr. A. SKENE suggested that the Committee should recommend to the Council that some of the 10 public representatives on the area health board should be elected by county and county borough councils, but that there should be machinery, similar to the regional hospital board machinery, which would allow for other representatives to be elected who were not connected with local authorities. It should be recommended also, said Dr. Skene, that in the minimum of five medical members on the board there should be some direct representation of hospital medical staff.

Dr. H. GLYN JONES said it would seem from the report that general practitioners would continue to be "independent contractors." General practitioners had stated that their administrative structure should not be disturbed and that they proposed to keep it completely independent. "They are prepared to mess everybody else about, but their own administrative structure is to stay totally unchanged," he said. If there was to be one administrative structure it should be for the whole Service and no part of it should be excluded.

Mr. KIDD said that in his view it would be a mistake to allow the report to be published with the Committee's blessing. There was nothing in it to protect private practice. Dr. OWEN WILLIAMS referred to the appointment of members of area health boards by local authorities, and said it must be remembered that the proposals were not based on county authorities organized as at present but on the new regions, in each of which there would be one area health board.

The Committee decided by a large majority to recommend to the Council that the second report of the Welsh Committee on area health boards should not be published without further amendment.

Negotiating Subcommittee

The CHAIRMAN drew attention to three resolutions about the representation of hospital junior staff on the new Negotiating Subcommittee. The first was a resolution of the Annual Representative Meeting 1967:

That this Annual Representative Meeting does not approve of the action already taken by the Central Consultants and Specialists Committee

in reducing from four to three the number of junior hospital staff representatives who sit on the negotiating committee for all hospital medical staff, which has 15 seats, and asks the C.C. and S. Committee to reconsider this matter in the light of the recommendations initially made by the Joint Consultants Committee.

The second was a resolution of the Hospital Junior Staffs Group Council:

That the H.J.S. Group Council expresses dissatisfaction with the reduction from four to three of the minimum number of junior staff on the new Negotiating Subcommittee.

The third resolution was one which had been passed by the Council at its meeting on 29 November, on a motion by Dr. H. L. Leaming (*Supplement*, 9 December, p. 71):

That this Council requests that when considering the composition of the negotiating committee the Central Committee for Hospital Medical Services take note of the desirability of ensuring that it contains adequate representation not only of hospital junior staff but also of consultants working exclusively in regional board hospitals.

Dr. E. A. HARVEY-SMITH, Chairman of the Hospital Junior Staffs Group, said that his Group had always wanted a 50% representation of the Negotiating Subcommittee, but unless the total number of members on the Subcommittee was altered it was difficult to see how that could be achieved.

The CHAIRMAN said that rather than alter the total number of members on the Subcommittee it would be easier to add one more junior member at the present stage, because if the Committee considered reducing the consultant representation, which might be necessary if junior representation was to be increased, the matter would have to be referred back to the Joint Consultants Committee.

Dr. SKENE suggested that for the remainder of the session one additional member nominated by the Hospital Junior Staffs Group should be co-opted to the Negotiating Subcommittee. Mr. WALPOLE S. LEWIN thought that the time had now come for the Committee to state clearly that the hospital junior staff should have four seats on the Negotiating Subcommittee.

Mr. KIDD pointed out that of all the members of the Negotiating Subcommittee only three could really be considered to be working in regional hospitals. There were about 8,000 consultants in the country who must spend at least 20 years of their life in their work. There was also a large number of hospital junior staff, said Mr. Kidd, but most of them were not in the hospital service for more than a year. Mr. Kidd said he did not feel happy about always increasing the junior staff representation at the expense of regional consultants.

Dr. HARVEY-SMITH said that he appreciated Mr. Kidd's views, and agreed that regional consultants should be adequately represented. The bulk of the consultants in the country were working in the regions, but their representation on the Negotiating Subcommittee should not be at the expense of the hospital junior staff. Mr. KIDD observed that the hedge-sparrow was not consulted by the cuckoo when it came into its nest.

The Committee finally agreed that the number of seats for hospital junior staff on the Negotiating Subcommittee should be increased from three to four, thus raising the total number of members on the Subcommittee to 16.

Proportional Representation

Dr. H. L. LEAMING referred to the Council's resolution. He said that he thought it essential that the Central Committee for Hospital Medical Services (C.C.H.M.S.) should have the chance of considering its relationship to hospital staff in the regions and to the B.M.A. itself. The C.C.H.M.S. was serviced and financed by the B.M.A., and it was only reasonable that it should pay some attention to the Association's principles and policies. The principle of proportional representation in the Representative Body and the Council had been obtained in the new constitution, and it would mean that hospital medical staff would have more say in B.M.A. matters than ever before. Four-fifths of the consultants in the country worked exclusively in regional board hospitals, and, in Dr. Leaming's view, it was ridiculous that in a negotiating committee numbering 16 four-fifths of the consultants in the country should be represented by only three members.

Dr. OWEN WILLIAMS agreed with the need for some degree of proportional representation on a policy-making committee. The Negotiating Subcommittee had a technical job to do, and in his view a distinction should be made between a policy-making body such as the Central Committee for Hospital Medical Services, and a technical committee such as the Negotiating Subcommittee.

Distinction Awards

At this point the CHAIRMAN welcomed Lord Platt, Chairman of the Advisory Committee on Distinction Awards, who had accepted an invitation to meet the Committee, and to give his observations, *in camera*, on the results of the recent ballot on distinction awards (*Supplement*, 21 October, p. 22). LORD PLATT spoke at some length and answered many questions. At the end he was warmly thanked by the Committee.

Health Services and Public Health Bill

The CHAIRMAN informed the Committee that on the publication of the Health Services and Public Health Bill a meeting of the Medico-legal Subcommittee was convened to consider the clauses in the Bill relating to the hospital service. He invited Dr. S. Cochrane Shanks, the Subcommittee's chairman, to report on its findings.

Dr. COCHRANE SHANKS said that the most important clause in the Bill seemed to be clause 1. It did not alter the Health Minister's existing power to reduce or to increase the number of pay-beds. The Subcommittee had understood that the increased flexibility of "authorization" (as opposed to designating specific beds under the existing Acts) had been regarded by the Joint Consultants Committee as having more advantages than disadvantages, and the Medico-legal Subcommittee had seen no reason to disagree.

Dr. Cochrane Shanks said that it was not clear—and the Health Departments should be asked to clarify the point—whether a paying patient could be admitted under subsection (1) under the care of a whole-time consultant, and, if so, whether any part-time consultant

involved in the treatment of that patient would or would not be entitled to charge a fee.

Mr. ALAN SMALL reported that in the North-west Metropolitan Region pay-beds had been cut by 20% in non-teaching hospitals and by 4.1% in teaching hospitals. There was a staggering difference in the treatment of teaching hospitals and of regional hospitals. If it was impossible to effect a change in the situation he suggested that the teaching hospitals in London might make voluntary cuts so as to enable more pay-beds to remain in the regional hospitals, because there had been deliberate discrimination.

Dr. HARVEY-SMITH supported Mr. Small. It was, he said, a political manoeuvre, and the criterion adopted was based on bed occupancy, which, as everyone concerned knew, was often low because beds were used for N.H.S. patients, and once a bed was occupied by an N.H.S. patient it reduced private occupancy.

Mr. LLOYD GRIFFITHS said it was in his view a matter for regret when a member of the Committee found it necessary to emphasize the difference in treatment accorded to teaching and non-teaching hospitals. Speaking for one provincial centre, he could say that no distinction had been made whatever. The cut had been just as savage in the teaching hospital as in the non-teaching hospital. The savage reduction in private beds in his region had been made on fallacious statistics of beds that were empty because they could not be staffed by nurses.

Dr. LEAMING said that private beds were not provided in order that consultants could earn private fees. The provision of private beds was to enable patients to be treated privately if they so wished. He said that no progress would be made in arguing with the Minister unless evidence could be produced to show that patients who wanted to be treated privately had had to go into general wards.

Dr. J. F. PIGOTT drew attention to a letter from Dr. John Lister and others, which had appeared recently in *The Times*, which had referred to a reduction in the number of private beds from 5,764 to 4,379 as from 1 January 1968. It was a matter of serious concern to the Committee, said Dr. Pigott.

Mr. T. M. HENNEBRY said that the Joint Consultants Committee should continue to press the matter, although it would seem to be too late.

Dr. OWEN WILLIAMS said that he had had access to figures upon which the calculations were based in his region, and there was no gross discrepancy between the docking of beds and bed occupancy in the various categories in the different hospitals.

The Bill had nothing to do with the recent reductions in pay-beds, he said, and it concerned not only the profession and the Ministry but also the public. Dr. Owen Williams said that some thought should be given to the publicity aspect of any case put forward for private beds in hospitals in future.

The Committee agreed to request the Joint Consultants Committee to arrange for a deputation, which should include a representative of the Private Practice Committee, to go to the Ministry of Health on the matter.

Representation of Hospital Junior Staff

The Committee considered a memorandum on the representation of hospital junior staff

which had been submitted to the Council of the B.M.A. by the national executive council of the Junior Hospital Doctors Association, and referred by the Council to the Committee and to the Hospital Junior Staffs Group Council and the Organization Committee.

Dr. PIGOTT, vice-chairman of the Junior Hospital Doctors Association, presenting the memorandum, recalled that it had been prepared at the request of the B.M.A. and it outlined a new structure for the representation of junior staff. It was intended to form a basis for detailed discussions. The J.H.D.A. emphasized that its proposals outlined a democratic system but not an egalitarian one. Representation at the highest level on a basis of one doctor one vote was not asked for.

The memorandum pointed out, said Dr. Pigott, that within the B.M.A. the representation of hospital junior staff had never been satisfactory. The existing structure was paternalistic in concept and in many ways undemocratic in operation. The result was a feeling of impotence and apathy among junior staff at a time when important changes were being planned in the N.H.S.—changes which were likely to have far-reaching effects on the training and career prospects of all junior doctors. It was vital that junior doctors should play a full and equal part in the political life of the profession, and thereby have power to influence their own future.

Dr. SKENE suggested that the memorandum should be considered as a step towards the re-establishment of trust within the profession. Unless there was reasonable unity everyone was lost. Dr. Skene said he would like to think that the energetic and highly intelligent doctors running the J.H.D.A. would be able to find a way with the B.M.A. of coming together and speaking with one voice in the interest of hospital doctors.

Dr. HARVEY-SMITH, who spoke as an individual and not as chairman of the Hospital Junior Staffs Group, said that the memorandum was an honest attempt by a group of hospital doctors who thought that the existing structure was unsatisfactory to suggest improvements in junior staff representation. It was a clear, concise, and precise document which the Committee must welcome. Of course the various points set out in it had been considered in great detail before, and in many respects it sought exactly the same objectives as the Hospital Junior Staffs Group. The main difference in the proposed from the existing organization was that of keeping the junior and senior staff quite separate until their executives met in what was termed in the memorandum the "Hospital Staffs Subcommittee."

Dr. Harvey-Smith said he would not be happy about losing the Hospital Junior Staffs Group Executive's representation on the Central Committee for Hospital Medical Services, which would be the case if the proposed new structure were adopted. If an assurance could be given that the Hospital Junior Staffs Group was represented at all the discussions of the Central Committee for Hospital Medical Services he could see no difficulty in the executive of his Group and that of the J.H.D.A. meeting to form a common executive committee.

Dr. D. GUTTMANN said there were three main points which arose from the proposals set out in the memorandum. The first concerned the position of the Hospital Junior

Staffs Group Council should it become an autonomous committee; the second was the interpolation of an extra committee for the purpose of appointing the negotiating team; and the third the disappearance of the Joint Consultants Committee from the negotiating machinery.

The first two points concerned the greater representation of hospital junior staff, and the Group had been in favour of that for a long time. It was necessary to safeguard the Group's ability to achieve representation in the C.C.H.M.S. and in its various subcommittees.

Suspicion and Mistrust

In general, Dr. Guttman said, there was no doubt that the Junior Hospital Doctors Association and the Hospital Junior Staffs Group had gained support because of the suspicion and distrust between junior and senior staff. In his view that had arisen largely out of ignorance of what took place in committees—not only ignorance of what was said but of the spirit in which it was said. That ignorance had arisen in turn out of apathy. "When I see the number of junior staff in my own hospital and elsewhere who could not care less about the representation of their views or about the future of the N.H.S. and the profession, it frightens me," he continued. It was true that this was partly because 50% of hospital junior staff qualified overseas and had no intention of staying in Britain permanently. But the remaining 50% were concerned in the future of the medical services here.

Dr. Guttman said he was appalled at the difficulty encountered in getting those doctors interested in meetings at central or regional level. It was chiefly a matter of communication, he said, and he did not believe that "B.M.A. News" was enough in that respect. All members of the Central Committee for Hospital Medical Services should make it their job to arouse the interest of junior staff in committee work. "I do not think we can afford to turn a cold shoulder to any person or any body which is prepared to join us, to work with us, and to take an active interest in medico-political matters," concluded Dr. Guttman.

Dr. S. WAND drew attention to a paragraph in the memorandum which read: "It is essential that the H.J.S.G.C. have adequate funds to appoint and maintain a secretariat, to maintain communications, and to reimburse the expenses incurred by thus appointed representatives. Regional organizations must also have access to funds." As Treasurer of the Association, Dr. Wand pointed out that the additional cost of the proposals would be approximately £10,000 a year.

The CHAIRMAN assured the Junior Hospital Doctors Association that the Committee realized that there had been much discontent and distrust among junior staff which it had been slow to recognize. That was a measure of the failure in communications. The memorandum would have to be studied carefully, continued the Chairman, and he suggested it would be discourteous if it was not sent to the Joint Consultants Committee for information. It was also necessary to await the Hospital Junior Staffs Group's comments. When these had been received the

Executive Subcommittee would study the document and provide some comments on it for the consideration of the Central Committee for Hospital Medical Services.

The Chairman thought that the main weakness of the proposals in the memorandum was that junior and senior staff discussions were kept separate until they had gone far up the respective channels. It was essential that the body that ultimately met the Government should be the most powerful, well informed, and authoritative possible, and in designing any new structure that aspect must be carefully considered.

The Committee agreed that the memorandum should be sent to the Joint Consultants Committee and that the Hospital Junior Staffs Group should be asked for its views. After that the Executive Subcommittee would consider all the comments and report to the C.C.H.M.S.

Helicopter Ambulance Service

The Committee gave its full support to a proposal by the Outer Isles Division that the B.M.A. should press for the establishment of a helicopter ambulance service.

Increases in Prescriptions

The Ministry of Health reports an increase in both the number and the cost of prescriptions dispensed by chemists in England and Wales in the second and third quarters 1967 compared with the figures for corresponding periods in the previous year. The number of claims for sickness benefit was substantially higher in both quarters in 1966, and this, the Ministry states, will have affected the prescribing figures.

The number of prescriptions issued during the period April to June 1966 was 61.2 million at a cost of £33.088m.; and during the same period in 1967 67.214 million prescriptions were issued at a cost of £36.7m. In the period July to September 1966 59.1 million prescriptions were issued at a cost of £32.251m., and in the same period in 1967 62.816 million prescriptions were issued at a total cost of £34.473m.

Services for Epilepsy

The B.M.A. has appointed a working party to prepare evidence for submission to the joint subcommittee set up by the Ministry of Health's Standing Committee on Health and its Advisory Committee on Health and Welfare of the Department of Health to review the health and services for epileptics.

The members of the Advisory Committee on Health and its Working Party are Drs. Joan R. E. W. Fisher (London), R. E. W. Fisher (London), W. Lumsden (Colchester), and J. N. Walton (Newbury).

Committee on Medical Science, Education, and Research

The Council is to be urged to set up a board of science and medical education as soon as possible, on the lines proposed in a memorandum by Dr. Ronald Gibson, Chairman of Council, discussed by the Committee. The board would control the medico-scientific and medico-sociological work of the Association, excepting its publications, and would execute its functions through working groups or panels. It would also sponsor inquiries on current scientific and social problems. The board would have its own team of permanent officials.

A meeting of the Association's Committee on Medical Science, Education, and Research was held on 12 December. Mr. A. LAWRENCE ABEL was in the chair.

Labelling of Containers

Dr. N. A. Wynne, director of the poisons information centre at the Royal Victoria Infirmary, Newcastle upon Tyne, attended by invitation to speak to a resolution of the Annual Representative Meeting 1967 which had been moved by the Newcastle upon Tyne Division. The resolution, which had been referred to the Committee by the Council, stated that all commercial preparations available to the public which were poisonous if ingested or inhaled or harmful if applied to the surface of the body should have these facts stated on the label of the container, together with the name or formula of the particular substances concerned.

Dr. WYNNE explained some of the present difficulties. People had been urged to lock away all poisons, but they did not know what substances were poisonous, because it was not stated on the container. To have the manufacturer's name on the label assisted in finding out the contents of the container in cases of poisoning with an unknown substance. Better still to have the formula of the substance named on the label. Sweden had already passed legislation on those lines.

Dr. ARNOLD BROWN thought that the action was too sweeping: much more thought could be given to it.

The Committee was doubtful whether the "commercial preparations" was precise enough—it was intended to relate to anything that could be sold over the counter. Subject to a satisfactory term being decided, the Committee agreed to recommend the Council that the resolution should be the B.M.A. policy.

Science and the B.M.A.

RONALD GIBSON, Chairman of

all spoke to a memorandum setting out proposals for the establishment of a board of education and science of the British Association. He said that the image of the Association seemed to many to fall short of its founders' object of promoting the advancement of science and of maintaining the interests of the medical profession. Its activities, particularly in the last few years, had seemed to be concentrated more on the interests of the profession. Such an imbalance, he said, was not, however, a true reflection of the annual Secretary's report on the Association's medico-sociological activities. In addition, the Association's expenditure on medical research was not commensurate with its activities.

There was room, said Dr. Gibson, for expansion and rationalization of the Association's medico-scientific work. Its Planning Unit had been in operation for a relatively short time, but already it was apparent that doctors whose primary interests were clinical or academic had been impressed by the Association's new initiative. There had been a similar reaction to recent new activities undertaken by the Science Committee. Dr. Gibson believed that if the Association was to expand and redeploy its scientific activities it might attract more members, and, more important, stimulate interest in its existing members. The Association was unique in that its membership included all types of doctors in all types of practice. With this wide range of expertise to draw on the B.M.A. should be able to contribute to the medico-scientific and medico-sociological fields in a way no other medical organization could.

Dr. Gibson's memorandum proposed, as a first step, that all the routine activities already undertaken by the Committee on Medical Science, Education, and Research, together with all the other medico-scientific and medico-sociological work undertaken by the Association, including the commissioning of all investigations and reports, should be reorganized in one department of the Association. The department should be under the control of a small, carefully selected board of eminent men, who would execute its various functions through a more flexible system of working groups or panels. Such a department could sponsor inquiries not only of a medico-scientific but also of a medico-sociological nature—for example, into the social problems of "hard" and "soft" drugs, nutrition, the population explosion, stress diseases, and so on.

The expansion of its Department of Audio-visual Communication would enable the Association to disseminate information on new methods of teaching and of learning by, for instance, television and video tape, programmed learning, and computer-assisted instruction.

Board of Medical Science

The proposal was to concentrate the scientific activities of the Association under the overall direction of a board of medical science and education. The chairman should be a respected member of the profession who was a national figure in medicine. The appointment should be of a limited duration, probably five years. The board should have a membership of probably not more than ten. It would operate through the medium of specially appointed panels. A standing panel would, for example, administer the Nuffield Library and another research awards. Ad hoc panels would be appointed to perform specific tasks. Each panel would be responsible

directly to the board, and normally the board would select the chairman for each panel, would seek representation from the Council or standing committees of the Association (or from other bodies), would invite experts to serve on the panel where applicable, and would nominate one of its own number to serve on a panel when appropriate. The board would have its own team of permanent officials. It was too early at this stage, said Dr. Gibson, to say what relationship the B.M.A.'s Planning Unit should have to the board, but in due course a close liaison must evolve between them.

The initial cost of these proposals ought not to exceed the Association's existing overall scientific budget, since the "exercise" was largely a reorganization of the present activities.

Constitutional Position

The memorandum concluded by explaining the relation of the board to the Council and to the Representative Body. It would be necessary under the B.M.A.'s constitution to ensure that the Council and the Representative Body had a say in the activities of the board, but there would be a need to ensure the independence of the board and of the panels within an overall remit. It would probably emerge that the Representative Body and the Council would have an overall say in the routine administration of the board, but its expert inquiries could either be presented for specific approval or published in a new series of books or pamphlets intended to encourage discussion.

Dr. Gibson explained that this was not a new concept. The Organization Committee had suggested it some years ago as part of a general reorganization of the machinery of the Association. The Organization Committee was concerned with the membership of the Association, and the membership depended on the Association being seen to be of service to doctors in their various disciplines. Nowadays doctors needed continual support, and this the Association would continue to supply through its medico-political activities. Over the years medico-politics had come into the limelight so much that some doctors thought the Association was no longer interested in the promotion of the medical and allied sciences.

The objective of the board would be to ensure that the Association was fulfilling its responsibilities in the medical and allied sciences. There was no question of building a new department at much cost to the Association but of consolidating the existing state of affairs. By creating a board of medical science and education Dr. Gibson hoped that the B.M.A. would both enlarge its membership and prove its right to be considered a forceful entity in the field of medical science.

Discussion on Memorandum

Dr. J. WEDGWOOD said it was time that the Association gave a lead in teaching and research. It had a long way to catch up with other organizations that were doing this work. He hoped the policy would be followed with "great vigour." The facilities of the B.M.A. for research were necessarily limited, and he had thought that the Association tended to dissipate its energies over too wide a field of activity, instead of concentrating on a few. That was a virtue, but it was impractical.

Sir AUBREY LEWIS congratulated the Chairman of Council on producing such a fine statement of the position, and he hoped that the Committee would support the memorandum.

Mr. DAVID BROWN said that he had on a previous occasion asked that the Association should consider co-ordinating its work in undergraduate and postgraduate education, but his proposals had been rejected because of the shortage of money. The board suggested in the memorandum was the answer to what he had in mind, provided the emphasis was on education—particularly with a scientific background. Though the Association could not afford the money for all it might hope to do, such a new project might attract money from other sources. If it had to work on a tiny budget he could not see it developing.

Dr. B. LIVESLEY, speaking as a hospital junior doctor, said that one of the things which had driven young men from the B.M.A. was its engrossment in medico-politics. He hoped that training for specialist and general practice would come within the compass of the new department.

Dr. L. P. GRIME said that the proposed board could co-ordinate the scientific and educational activities of the B.M.A., and Dr. M. M. BULL, in hoping the project would be pursued with enthusiasm, said there should be active liaison with other interested bodies. He asked that preclinical teaching should not be forgotten. The new science of medical sociology was being given greater attention in the universities, and he was pleased to see it included in the outline of the activities of the proposed department.

Professor F. E. STOCK was concerned that the board of education and science should not become in any way separated from the rest of the B.M.A., so that there was one part which seemed to be doing only medico-political work and another the scientific work. The work of the two should be integrated. Professor D. E. C. MEKIE said that thought would have to be given to how the new body should be related to the Association. The danger that the board might be too high-powered should be avoided. It should not consist of specialists in an ivory tower. The board should cater for all types of doctors.

Dr. W. W. FULTON, speaking as a family doctor, said that the B.M.A. should guard against the idea of "them" and "us." The ordinary members should be encouraged not only to take an interest in the work of the board but also to take part in it. Dr. ARNOLD BROWN hoped that the board would be a high-powered body. It should consist of people who were respected and known for their scientific activities. That would cost money, but it would be well spent. The work of the board would, he hoped, result in an increase in B.M.A. membership, and contri-

butions from some of the voluntary societies. There should be one person on the board acquainted with the needs of the public. The board should be independent and it should answer to the Representative Body.

Dr. F. J. C. HERRALD said that the board should seriously consider what it could do best. There were some things it could do better than others, and it would be a mistake to duplicate what another body was doing.

Film Committee

The Committee discussed the position of the Film Committee in relation to the proposed board of education and science.

Sir RONALD TUNBRIDGE said that the Film Committee should not be separate, otherwise it was defeating the object of the board.

In reply to a question by Mr. R. MYLES GIBSON on what the functions of the panels would be, Dr. D. P. STEVENSON, Secretary, said that the board would choose subjects for the panels to consider. For example, the B.M.A. ought to be leading the way with opinions on contentious matters such as whether there ought to be a register of specialists and consultants. There was a new role for the Association in postgraduate centres. There was no end to its activities in medical education. The scheme was also coupled with the plan to regionalize all the activities of the Association.

Members of the Film Committee then joined the meeting. Its chairman, Dr. T. A. QUILLIAM, said that his committee was in sympathy with the new concept of integrating the scientific medical education activities of the B.M.A. The Department of Audio-visual Communications was concerned primarily with doctors, but many of its activities were financed in part by the British Life Offices Association and were directed towards the health education of the general public. He believed that in many ways the functions of the department could best be performed as an independent body.

Dr. VALERIE GRAVES said that, as a producer of educational material, she was always becoming entangled with committees who admired the technology without understanding its limitations. Producers were tired of trying to do things for people who did not know what they could do, and as a result they were suspicious of one more board. The Film Committee was worried about losing the support of the Life Offices Association, who would like to think that the Committee was committed to a definite programme. The Life Offices Association would not like to feel that the Committee's activities were to be merged with another group's activities which were not directly under the control of those to whom the money was originally given.

Fashioned to Fit

Mr. C. ENGEL, director of the Department of Audio-visual Communications, said he saw the role of his department as being to help in the implementation of education at all levels from the undergraduate up to continuing education, including health education, both in teaching and in learning. This meant that the tools had to be fashioned to fit the

end. The organization of the department must have two quite separate bases. One was on activities which were not based on any specific project but were on a continuing basis. The other was the specific projects that could be laid down from above.

After the Film Committee had had a separate discussion it returned. Dr. QUILLIAM said that it was pleased that there should be a board. However, the Film Committee had come to the conclusion that the Department of Audio-visual Communication, advised by the Film Committee as a panel, should be an autonomous organization in that it should have direct access to the board. He appreciated that there should be cross-representation with the panel on education.

Mr. MYLES GIBSON said that he was "disappointed" at the suggestion that audio-visual communication should be separated from medical education. Looking ahead, in the context of continuing medical education, the two could not reasonably be dissociated. He could not see the logic of divorcing them.

Dr. QUILLIAM wondered why the proposed board would be anxious to incorporate the Department of Audio-visual Communication in its activities. The department was an extremely important one, and he would be sorry to see its activities diluted.

The Science Committee adopted the following motions proposed by Professor MEKIE:

- (1) That the recommendations in the memorandum should be approved in principle.
- (2) That the Council should be urged to set up a board of science and medical education as soon as possible.
- (3) That details of the organization of special panels under the general direction of the board should be studied further after the formation of the board.

Postgraduate Medical Centres

The Committee agreed to recommend to the Council that the following recommendations of the Committee's working party on postgraduate medical centres should be adopted.

(1) The scientific and educational aspects of the Association's activities should be fostered by all the means at its disposal.

(2) If the report of the Royal Commission on Medical Education recommended official recognition of the educational functions of postgraduate medical centres it was probable that the centres would be linked with the local university and a local director appointed. Where such arrangements are or are coming into existence, the local B.M.A. honorary or science secretary should be consulted. He should be kept informed of all possible help which could be channelled through him to enable him to work together with the local organizer, dean, or director.

(3) In the working party's view the Association would exercise the greatest influence in centres in those areas where the Association was the only outside body helping in the arrangement of the programme. It is suggested that in these centres the Association should expand its present activities, such as the development of library facilities and audio-visual aids, and play a prominent part in cultural and social activities.

(4) The annual B.M.A. lecture for Divisions should continue to be made available, but an

attempt should be made to integrate the lecture into the programme of postgraduate medical centres.

(5) An attempt might also be made to replace or supplement the lecture by something a little more elaborate, perhaps by inviting the lecturer to take part in a panel discussion or clinicopathological conference.

(6) The Medical Science Committee might recommend to Divisions and Branches speakers or subjects which at the time were showing themselves to be extremely popular and attracting large audiences in other areas.

(7) An experiment might be undertaken into the possibility of arranging weekend meetings locally with one or two speakers from a distance taking part. It is appreciated that this would probably involve the Associa-

tion in greater expense than the cost of a B.M.A. lecture to a Division, but it is suggested that some of the money allocated for B.M.A. lectures might be used for experiment on such weekend meetings in some areas.

H.M. Forces

TERRITORIAL ARMY RESERVE OF OFFICERS: ROYAL ARMY MEDICAL CORPS

Majors G. S. Midgley, M. Macintyre T.D., B. K. Madden, C. D. MacCarthy, J. H. Stranger, L. H. Allan, and W. I. N. Kessel have resigned their commissions, retaining the rank of Major.

Majors G. L. Herbert and G. F. A. Howie have resigned their commissions.
Captains (Honorary Majors) H. R. W. Lunt, T.D. R. B. Martin, C. W. J. Hunt, and J. A. R. Johnson, T.D., have resigned their commissions, retaining the honorary rank of Major.

Public Health Medical Officers' Salary Claim

Agreement on revised salary scales for public health medical officers was reached at a meeting of Whitley Committee C on 20 December. Under the early warning machinery of the Government's prices and incomes legislation the operative date of the award will be 1 July 1967, but both sides of Committee C are to approach the appropriate Ministry to ask for an earlier date. It is hoped that the secretary of the Management Side of Committee C will be able to notify local authorities of the new salary scales early in January, and an M.D.C. circular is being drafted.

Association Notices

Fellowship and Awards for Medical Research

The Council of the British Medical Association invites applications from members for the following fellowship and research awards.

Fellowship

A new whole-time research fellowship to the value of £1,500 is offered to assist research into any subject relating to the causation, prevention, or treatment of disease. It will be tenable for one year, and normally renewable for a second year subject to a satisfactory progress report.

Research Awards

The Council will also consider applications for the Ernest Hart and Walter Dixon Research Awards, each up to the value of £300, and other research awards. The awards are granted to assist specific research work in any subject relating to the causation, prevention, or treatment of disease.

Applications for the fellowship or research awards should be submitted not later than 27 January 1968. The appropriate form and information on the conditions of the awards are obtainable from the Secretary, British Medical Association, Tavistock Square, London W.C.1.

DEREK STEVENSON, *Secretary*.

Diary of Central Meetings

JANUARY

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| 3 | Wed. | Occupational Health Committee, 10 a.m. |
| 3 | Wed. | Private Practice Committee, 2 p.m. |
| 4 | Thurs. | Finance Committee, 2.30 p.m. |
| 5 | Fri. | Executive Subcommittee (Public Health Committee), 10 a.m. |
| 9 | Tues. | Constitution Subcommittee (G.M.S. Committee), 2.30 p.m. |
| 10 | Wed. | Joint Formulary Committee 10.30 a.m. |
| 12 | Fri. | H.J.S. Group Executive Committee, 2.30 p.m. |
| 15 | Mon. | Planning Unit-Primary Medical Care, 6 p.m. |
| 16 | Tues. | Working Party on Health and Welfare of Epileptics, 10.30 a.m. |
| 17 | Wed. | Annual Meetings Committee, 10.30 a.m. |
| 19 | Fri. | Committee on Overseas Affairs, 1.30 p.m. |
| 23 | Tues. | Joint Consultants Committee (at Royal College of Physicians of London), 10 a.m. |
| 23 | Tues. | General Medical Services Committee (Scotland), (at 7 Drumsheugh Gardens, Edinburgh), 10.30 a.m. |
| 26 | Fri. | Venereologists Group Committee, 2 p.m. |

FEBRUARY

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| 1 | Thurs. | Otolaryngologists Group Committee, 2 p.m. |
| 6 | Tues. | Orthopaedic Group Committee, 2.30 p.m. |
| 9 | Fri. | Full-time Medical Teachers and Research Workers Committee, 2 p.m. |
| 14 | Wed. | Joint Formulary Committee, 10.30 a.m. |
| 19 | Mon. | Scottish Committee for Hospital Medical Services (at 7 Drumsheugh Gardens, Edinburgh), 11.15 a.m. |

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

DUMFRIES AND GALLOWAY DIVISION.—Sunday, 7 January, Dr. W. M. Court Brown: "Some Recent Advances in Human Cytogenetics."

HAVERING DIVISION.—At Academic Unit, Oldchurch Hospital, Friday, 5 January, talk by Miss Kathleen M. Frith: "Contraception." Ladies are invited.

LEWISHAM DIVISION.—At Medical Centre, Lewisham Hospital, Friday, 5 January, 8.30 p.m., consultants' wine and cheese party and Division's social evening.

NORTH DEVON DIVISION.—Thursday, 4 January, Mr. G. Blackburn: "Thyroid Surgery."

Branch and Division Officers Elected

BARNESLEY DIVISION.—Chairman, Dr. C. G. Oddy. Honorary Secretary, Dr. D. W. Mayman.

BRIGHTON AND MID-SUSSEX DIVISION.—Chairman, Dr. N. W. A. Harvey. Chairman-elect, Mr. P. V. Wadsworth. Vice-chairman, Mr. S. H. C. Clarke. Honorary Secretary, Dr. F. E. de W. Cayley. Honorary Treasurer, Dr. J. L. Digby Roberts.

CITY OF DUNDEE DIVISION.—Chairman, Dr. J. M. Langlands. Vice-chairman, Dr. D. Green. Honorary Secretary, Dr. W. Yeaman. Honorary Treasurer, Dr. J. Scott Innes.

CONGO BORDER DIVISION.—Chairman, Dr. M. Lowenthal. Honorary Secretary and Treasurer, Dr. C. J. Goosen.

CUMBERLAND DIVISION.—Chairman, Dr. T. Mooney. Vice-chairman, Dr. A. Stevenson. Honorary Secretary and Treasurer, Dr. G. P. Raitt.

DERBYSHIRE BRANCH.—President, Dr. A. P. Tait. President-elect, Dr. E. H. B. Grey. Honorary Secretary, Dr. I. R. D. Proctor. Honorary Treasurer, Dr. R. A. A. R. Lawrence.

FOLKESTONE AND DOVER DIVISION.—Chairman, Mr. D. V. Evans. Vice-chairman, Dr. L. P. Ribet. Honorary Secretary, Dr. I. Foster.

HONG KONG BRANCH.—President, Colonel I. Walsh. Vice-President, Dr. R. G. M. Wedderburn. Honorary Secretary, Dr. Otto Y. T. Au. Honorary Treasurer, Dr. E. Y. C. Lee.

MERSEYSIDE BRANCH.—President, Dr. J. Sugden. Vice-presidents, Dr. H. C. W. Baker, Mr. J. G. Gow. Honorary Secretary and Treasurer, Dr. H. C. W. Baker.

METROPOLITAN COUNTIES BRANCH.—President, Dr. G. M. J. Slot. President-elect, Dr. E. Colin-Russ. Vice-presidents, Dr. O. S. Kohnstamm, Dr. G. Little, Dr. W. B. Pemberton, Dr. J. Wigg. Joint Honorary Secretaries, Dr. A. M. Angel, Dr. E. M. Rosser.

MID-GLAMORGAN DIVISION.—Dr. D. B. Price has been appointed Assistant Honorary Secretary of the Division.

NORTHERN IRELAND BRANCH.—President, Lieutenant-Colonel D. G. C. Whyte. President-elect, Dr. J. S. McKelvey. Vice-president, Dr. M. M. Vida Lemon. Honorary Secretary, Mr. J. W. Wilson. Assistant Honorary Secretary, Dr. J. McA. Taggart.

NORTH-WEST WALES DIVISION.—Chairman, Dr. R. Rees Prytherch. Chairman-elect, Dr. J. B. T. Griffiths. Honorary Secretary and Treasurer, Dr. W. J. Hughes.

ST. HELENS DIVISION.—Chairman, Dr. D. C. Lawton. Honorary Secretary and Treasurer, Dr. J. Sugden. Assistant Honorary Secretary, Dr. E. Wyn Jones.

WEST BROMWICH AND SMETHWICK DIVISION.—Chairman, Dr. B. Conochie. Chairman-elect, Dr. E. M. Allen. Honorary Secretary and Treasurer, Dr. J. E. Evans. Assistant Honorary Secretary, Dr. M. Ramsden.